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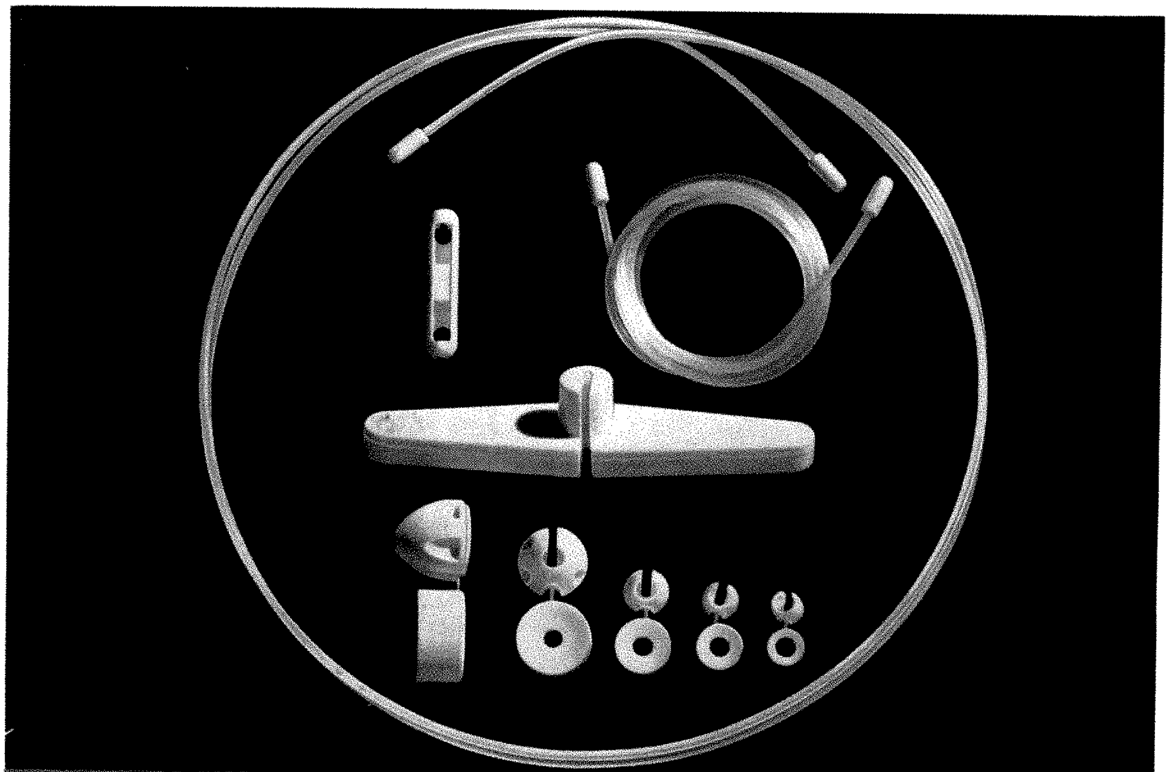

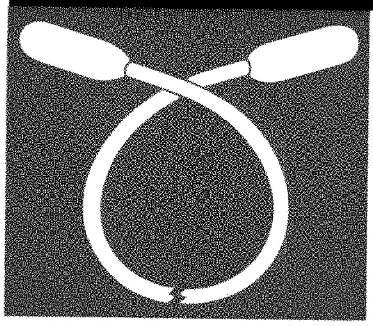

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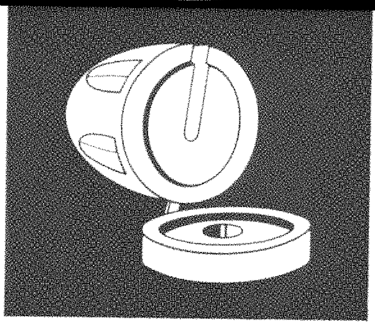

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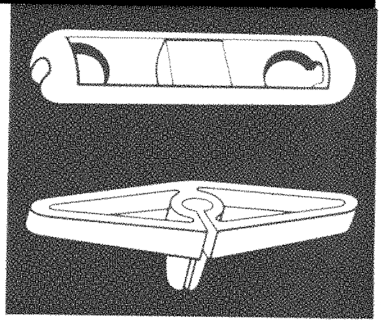

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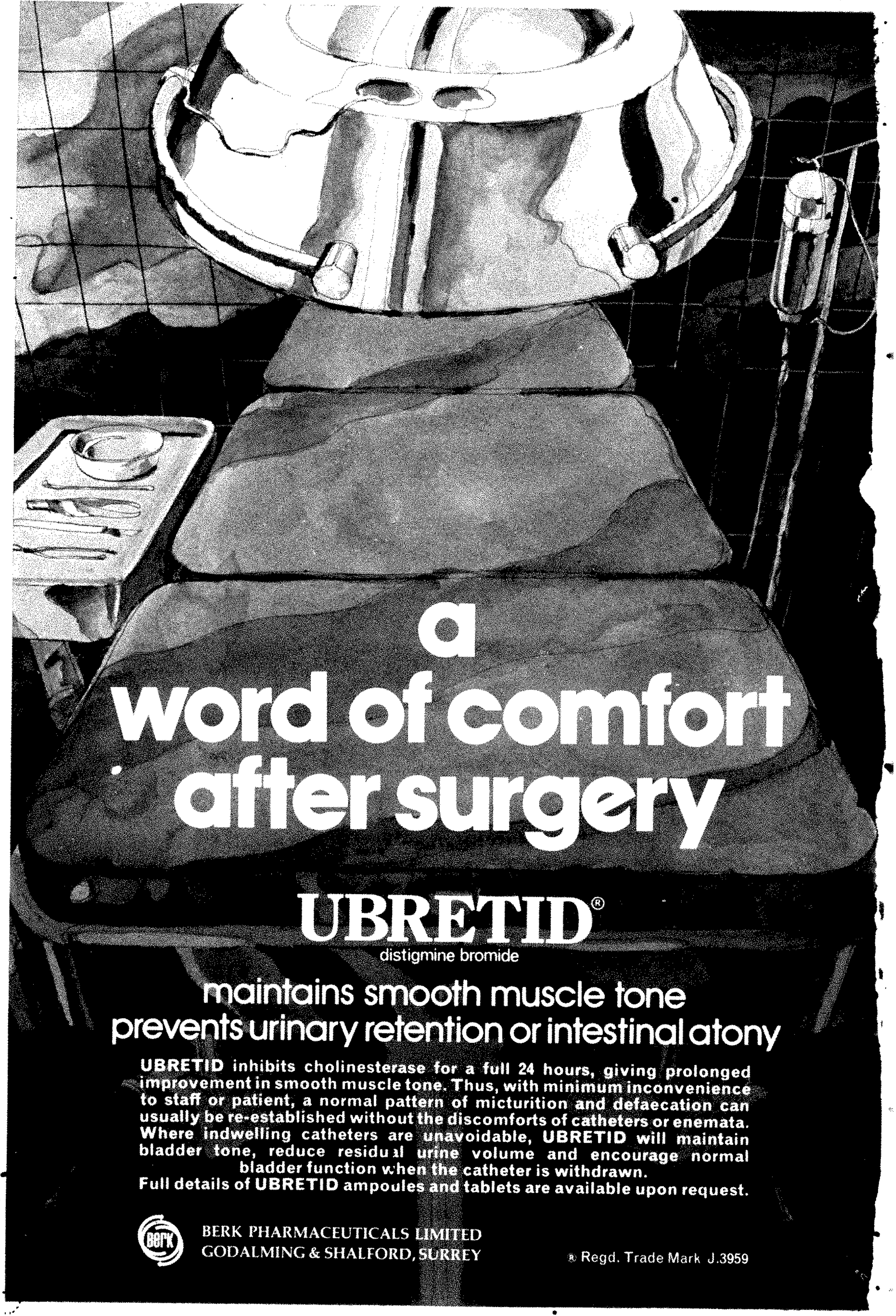

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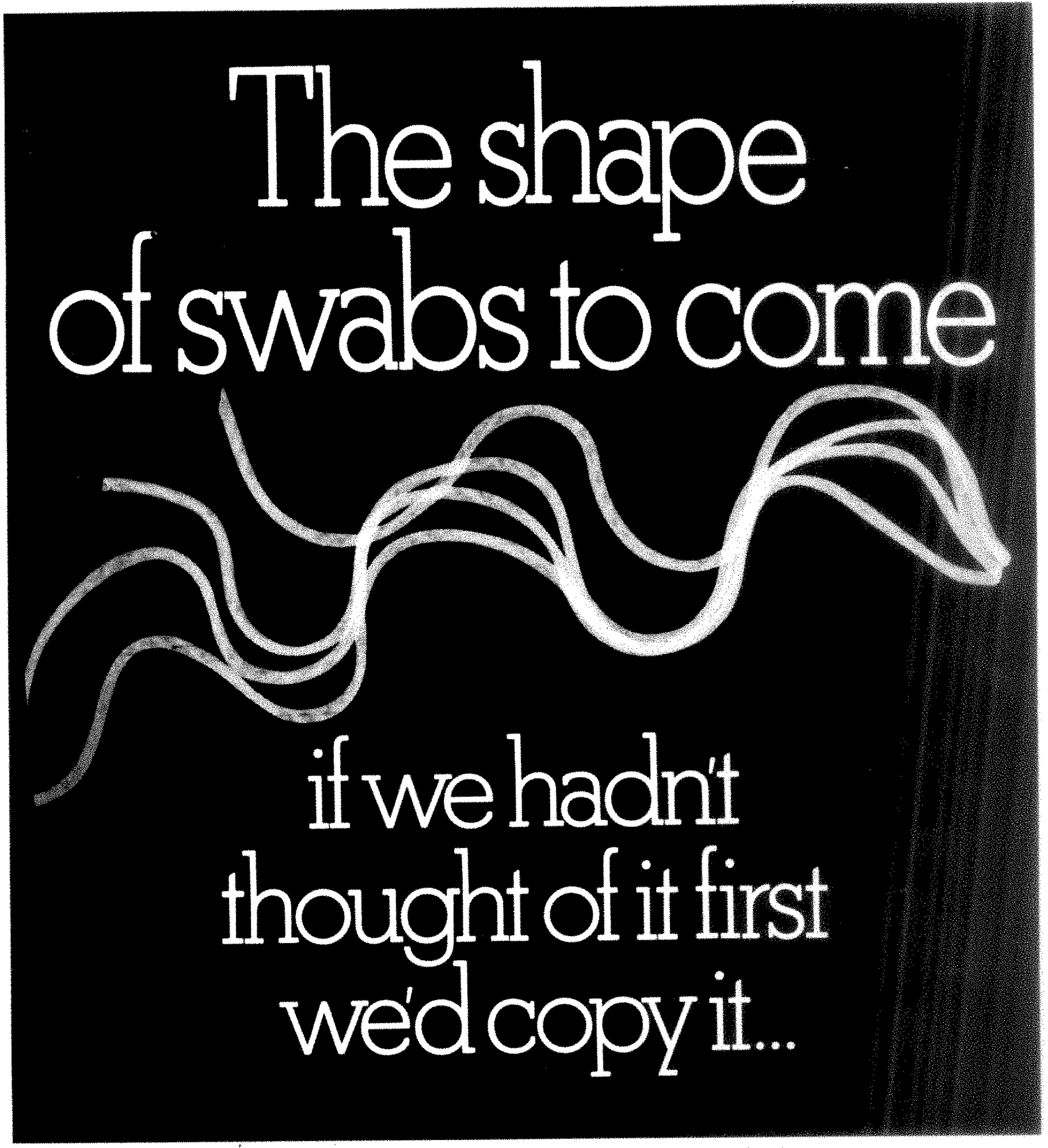

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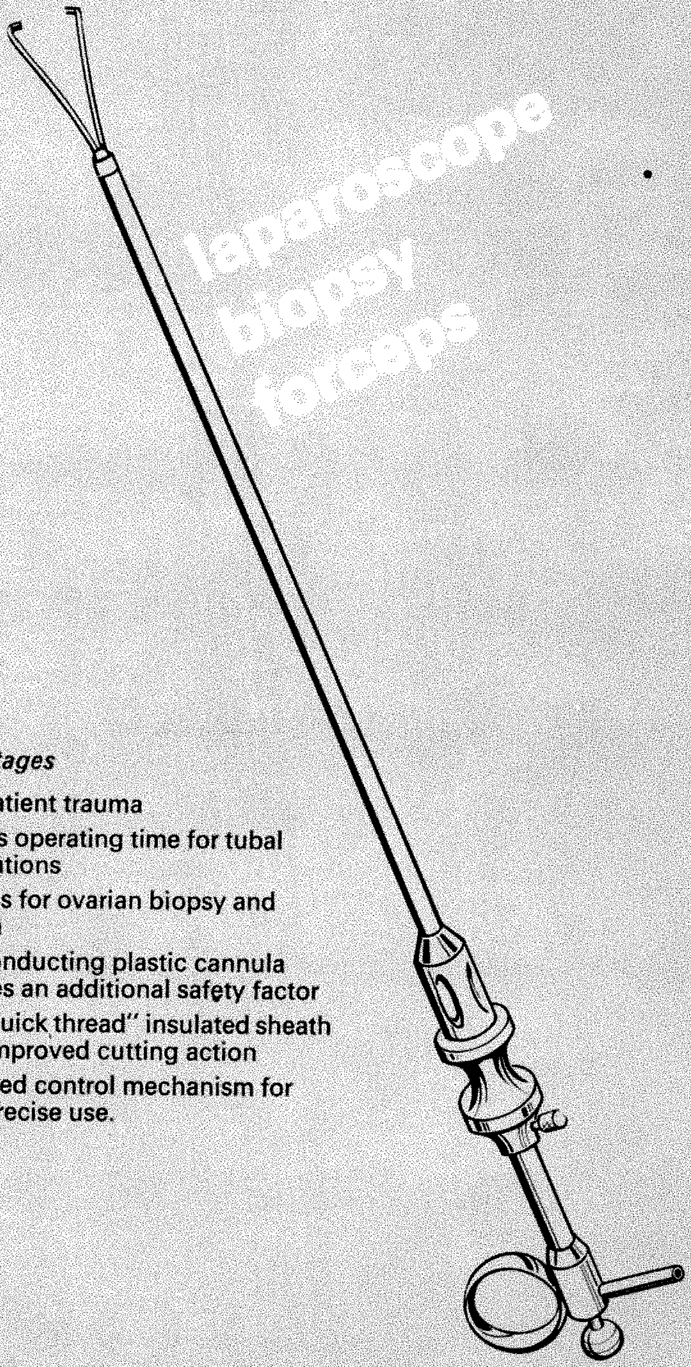

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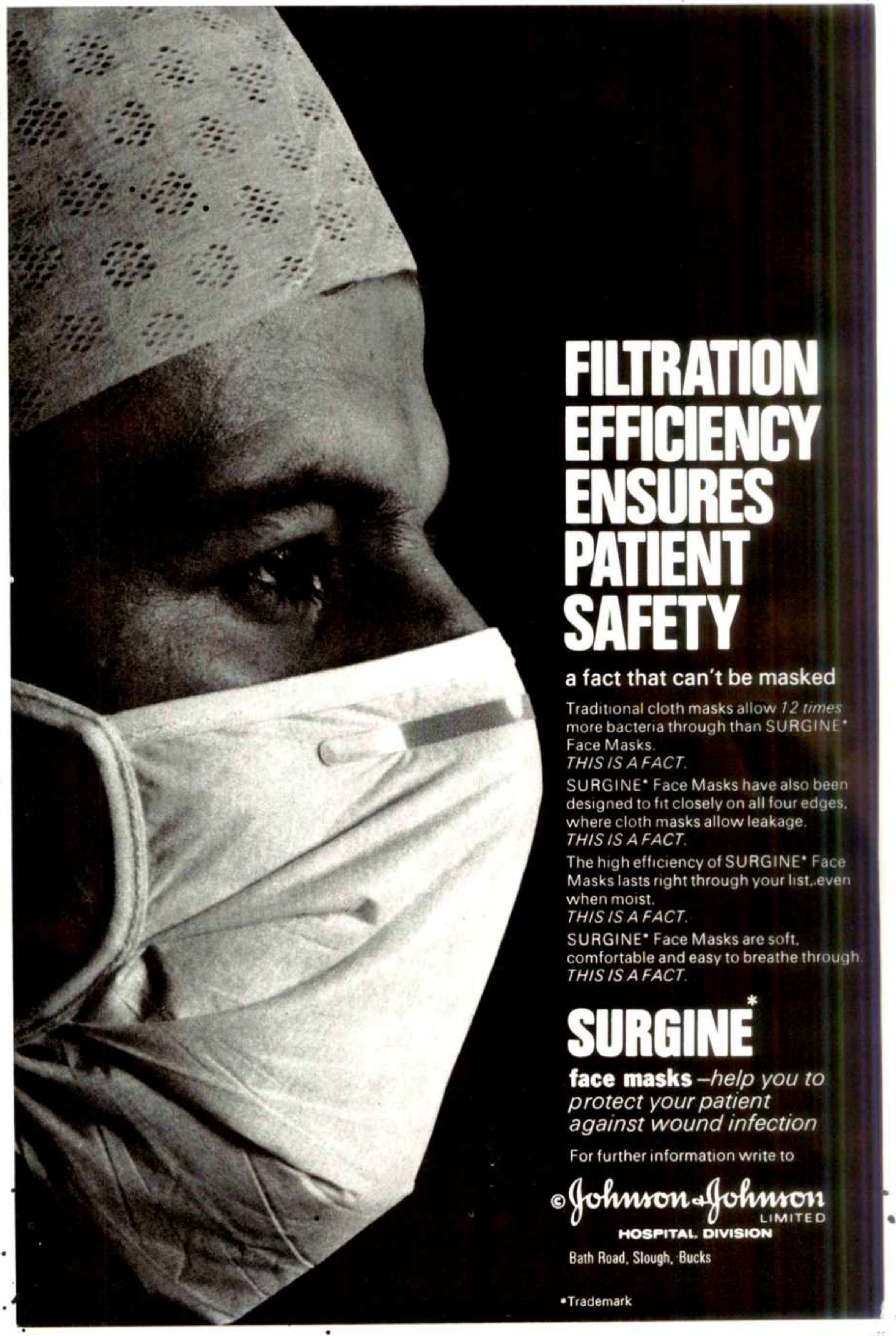

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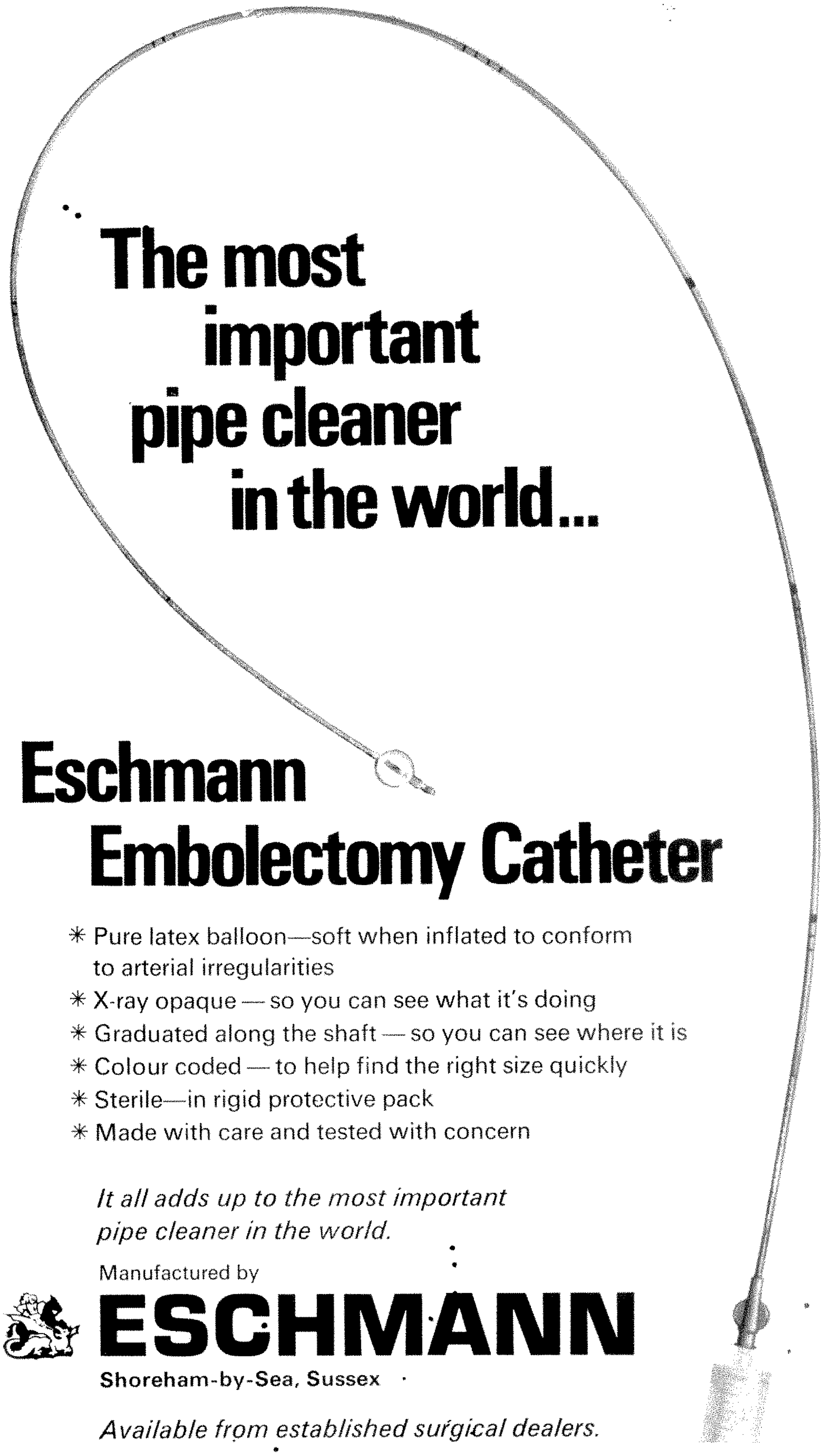

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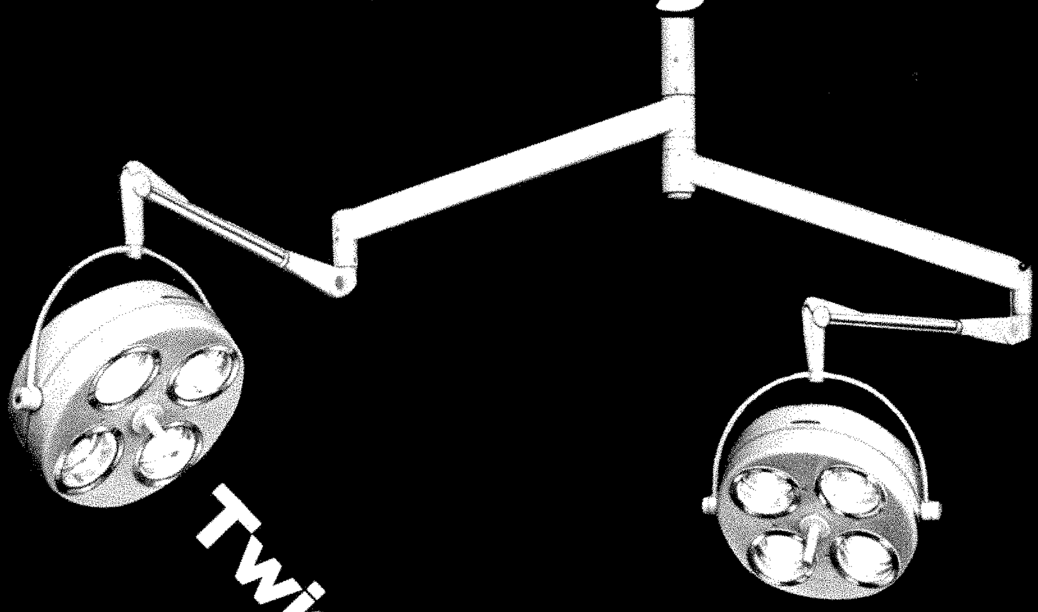

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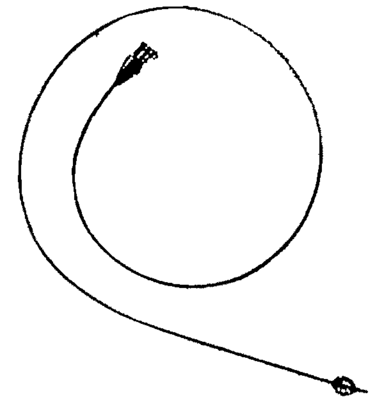

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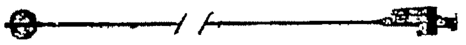

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	92	*Double Lumen Balloon (Whistle Tip)*
	22	*Irrigation*
	41	*Biliary Balloon Probe (Short Tip)*
	42	*Biliary Balloon Probe (Guide Tip)*
	A	*Revision Number*
	080	*Length in Centimeters*
	6F	*French Size of Catheter Body*

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32-080-8F	2.25	4.5	14
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FOGARTY OCCLUSION CATHETER			
62-080-8/14F*	10	30	28
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12C-080-4F	0.75	1.7	
12C-080-5F	1.5	3.0	
12C-080-6F	2.0	4.5	
12C-080-7F	2.5	5.0	
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92-060-6F (Whistle Tip)	1.75	3.0	13
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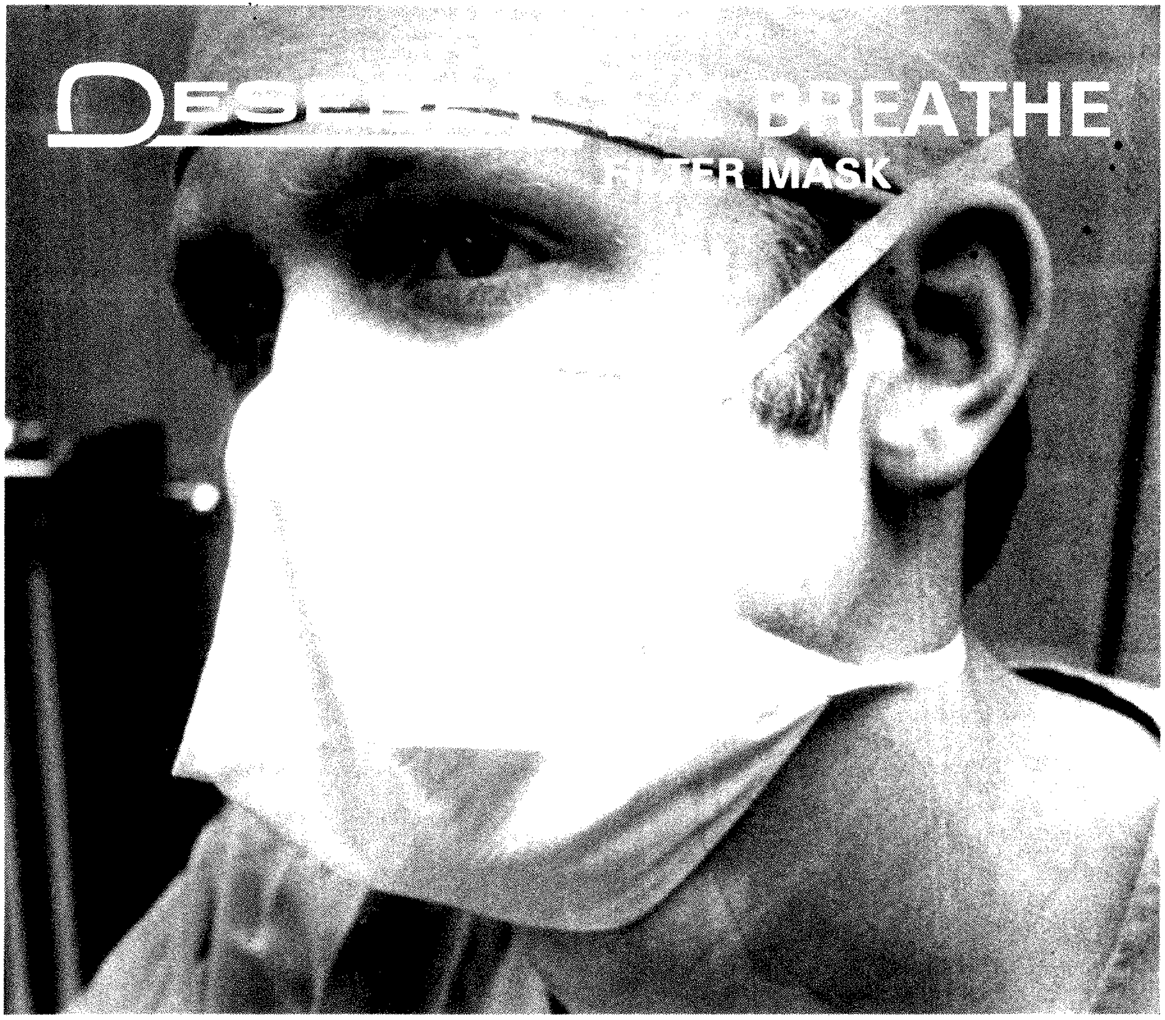

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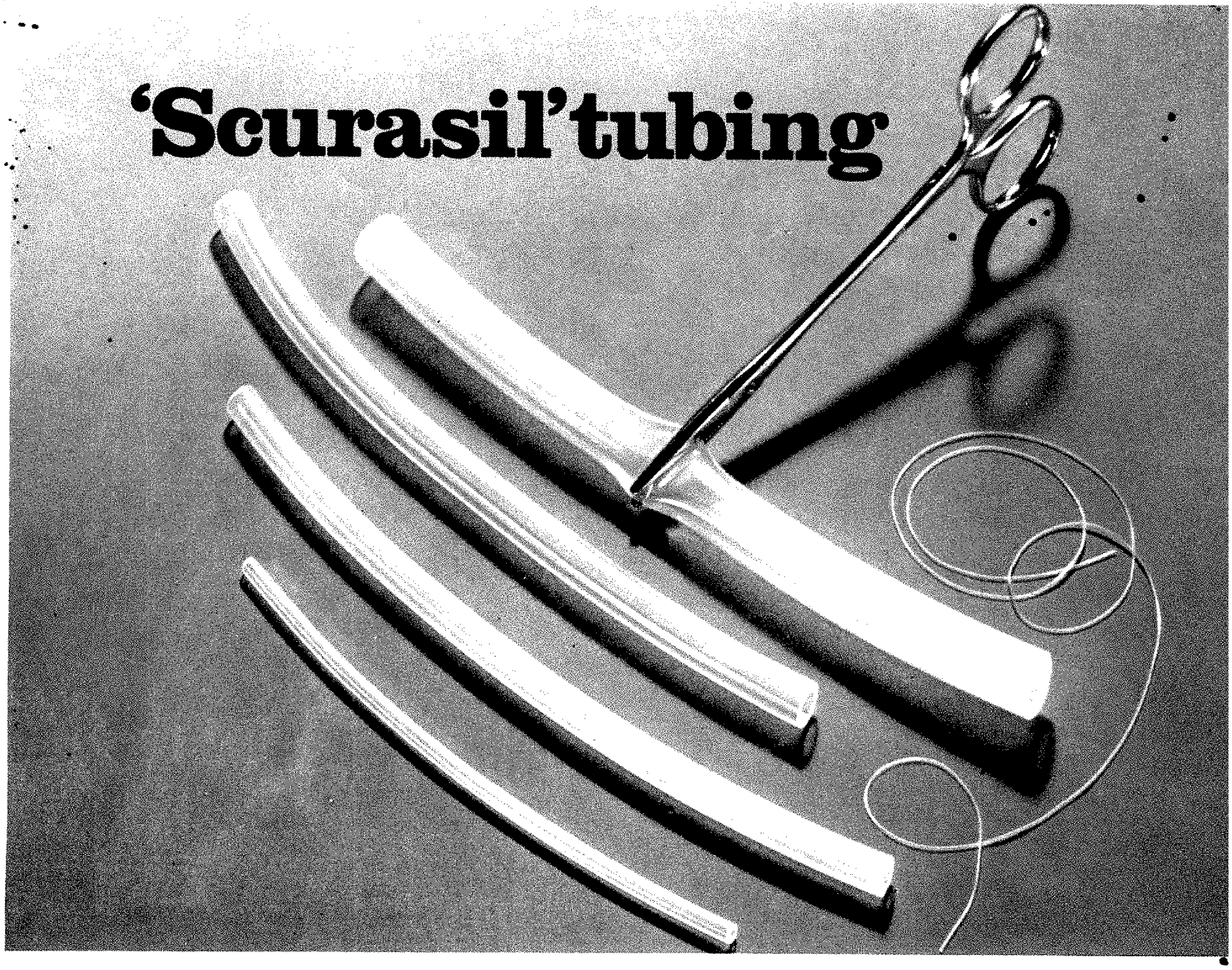

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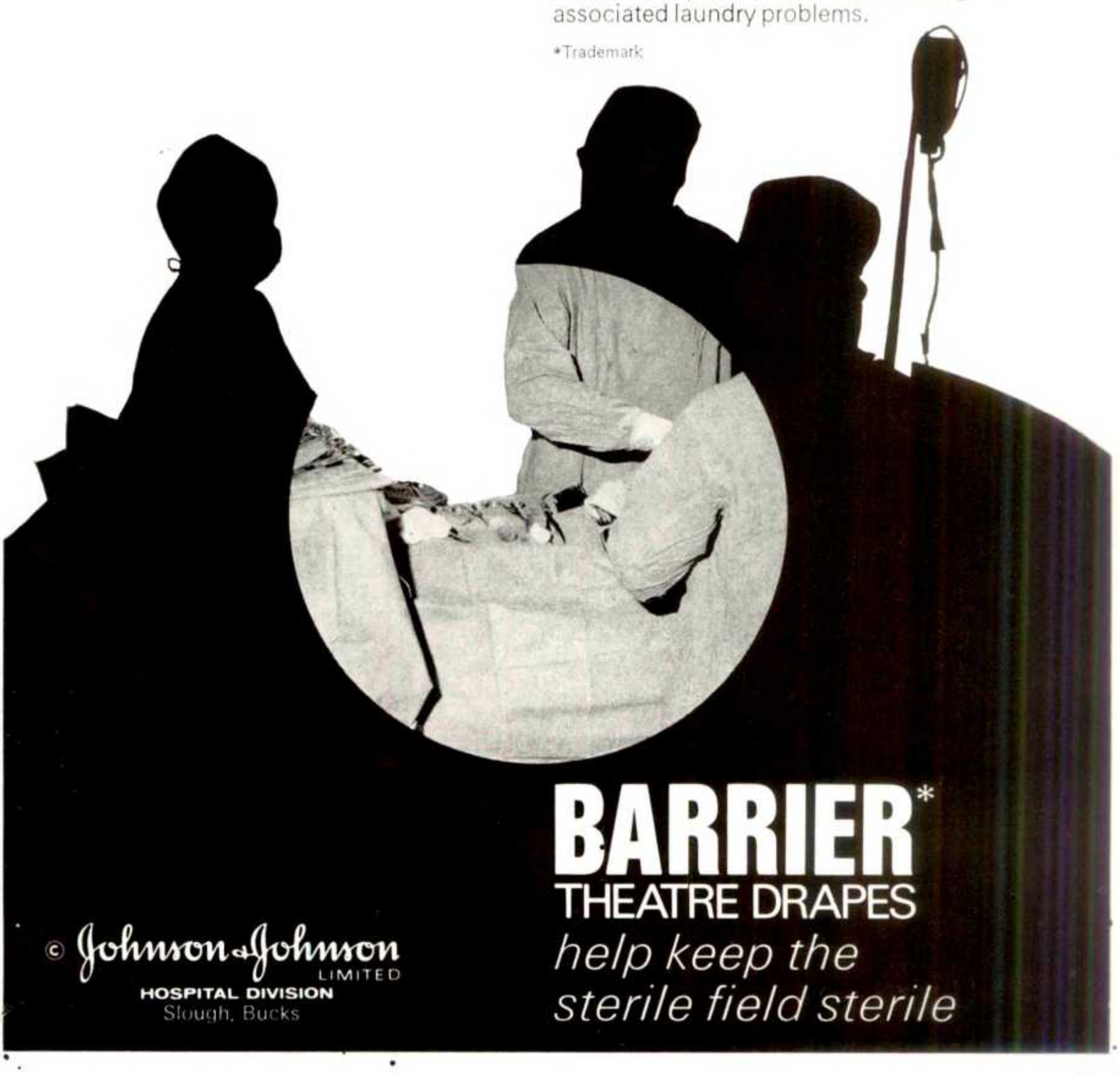

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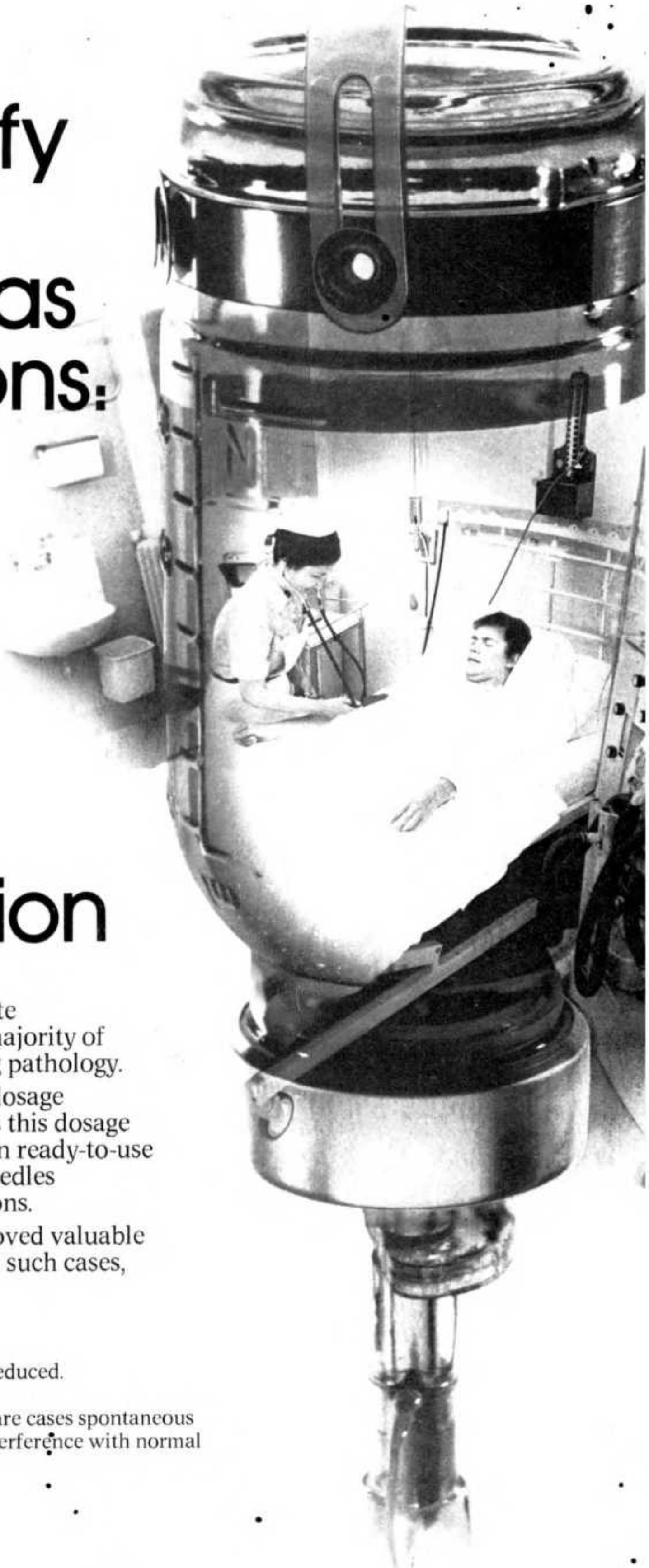

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THE
BRITISH JOURNAL OF SURGERY

Vol. 60 JANUARY, 1973 No. 1

ORIGINAL PAPERS

A REVIEW OF 460 PATIENTS ADMITTED TO THE INTENSIVE-THERAPY UNIT OF A GENERAL HOSPITAL BETWEEN 1965 AND 1969

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SUMMARY

Four hundred and sixty patients with various severe disease processes were admitted to the intensive-therapy unit of a general hospital under the care of the anaesthetic and surgical staff in the 5-year period 1965–9 inclusive. The problems presented by these cases, their prognosis, and the lessons learnt in their management are reported, and the implications for similar units in the future are discussed.

THIS paper is concerned with the surgical patients admitted to a 5-bed intensive-therapy unit in a 450-bed hospital on the northern outskirts of London. The area served by this hospital, which has a total of 100 general surgical beds and 50 orthopaedic beds, is predominantly urban and is traversed by several major roads, including the beginning of the A1 London-to-Scotland trunk road. The total resident population served is of the order of half a million.

HISTORY OF THE INTENSIVE-THERAPY UNIT

The interest of the anaesthetic department of this hospital in respiratory problems has culminated in the design of a series of highly successful 'Barnet' ventilators (Rochford, Welch, and Winks, 1958). In 1960 a recovery ward was opened as an extension to a twin-theatre unit. This annexe to the operating theatres was intended to provide care for up to 8 hours after surgery. General advances in the understanding of the principles underlying the respiratory physiology of surgical patients during and after operation has resulted in the requirement of a specialized unit open for 24 hours a day in which personnel and equipment can be centred to provide a high standard of care for seriously ill patients. *Fig.* 1 shows the architect's plan of the unit which was built in communication with the operating theatres and recovery ward (Rochford, 1965); this was opened at the beginning of 1965. It is the intention of this paper to review the 460 patients who were primarily under the care of the surgeons and who were treated in the unit during the period from January, 1965, to December, 1969. It must be stressed that the unit is not restricted to surgical case care. *Fig.* 2 shows the relation of surgical admissions to the unit's overall intake.

A recently published comprehensive review from the University of Pittsburgh (Safar and Grenvick, 1971) considers the parallel development and organization of intensive care and therapy in North America over the past decade. The main author has been at the centre of development studies which have covered the emergent period of such units.

THE FUNCTION OF AN INTENSIVE-THERAPY UNIT

Lawson (1967) has categorized the types of surgical patient who benefit from intensive therapy. These are:—

1. Elective admissions for:—
   a. Major vascular surgery.
   b. Replacement surgery.
   c. Endocrine surgery.
2. Elective admissions of poor-risk cases.
3. Emergency admissions.

In the paper by Lawson (1967) dealing with an intensive-therapy unit in a major teaching hospital the close proximity of a major accident centre resulted in the absence of trauma cases in the series. In our series of nearly 500 admissions Lawson's first and third categories will be retained, but it has been our experience that the poor-risk cases in a general hospital are virtually all emergency rather than elective admissions. These cases require operative procedures of varying degrees of seriousness, the degree of difficulty of the operation being raised by ancillary problems of age and concomitant medical conditions. Our fourth group is concerned with cases of multiple trauma. The figures in *Table I* show the following proportion of cases: trauma, 29·8 per cent; postoperative, 13·04 per cent; poor-risk, 43·5 per cent; major surgery, 13·7 per cent.

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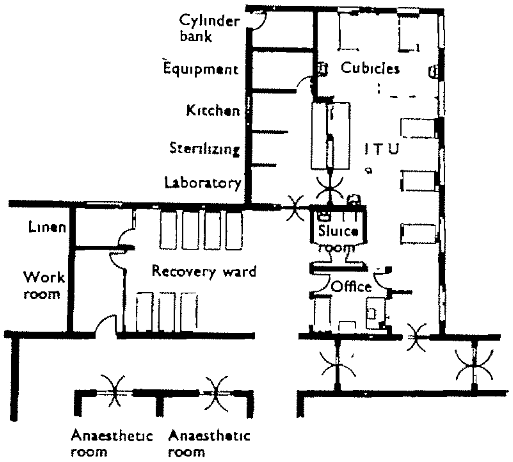

FIG. 1.—Architect's plan of the intensive-therapy unit and recovery ward.

The 5-bed unit takes patients referred for treatment from all specialities in the hospital and the administration of the admissions to the department is under the control of the duty anaesthetic registrar.

NURSING STAFF

The unit has 3 full-time sisters and there are normally 4 staff nurses who have been through the 6-month course organized by the unit to train nurses in intensive care. At any one time there will be upwards of 6 staff nurses on the course. The high standard of training has been reflected in the publication of a volume concerned with nursing procedures in such a unit (Gardner and Sheldon, 1967). The whole pattern of intensive therapy emerging from experience in various centres throughout the country is that trained nursing staff will carry out more and more of the emergency steps required in resuscitative procedures. There is no reason why after an adequate period of training emergency intubation and the initiation of respirator ventilation should not be within the capabilities of an intensive-therapy unit sister.

The unit staff are progressive in their regular reassessment of the patients in the unit to determine whether the needs of the patient require his treatment in the intensive-therapy complex. We have been most anxious to avoid falling into the trap of nursing all seriously ill patients in a specialized unit, thereby depriving student nurses in training on the general wards of the experience of nursing such patients under the supervision of the surgical ward sisters. It is our contention that the intensive-therapy unit empty of patients does not indicate that the unit is not taking on enough work but that, in fact, since some of the work carried on in the intensive-therapy unit is more akin to that of an operating theatre than of a normal ward there should be times when the unit can stand down.

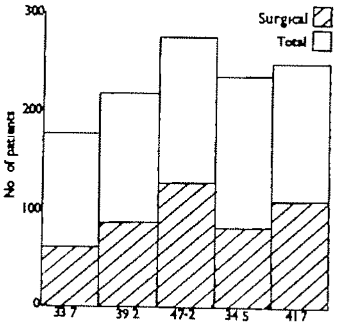

FIG. 2.—Total number of patients in the intensive-therapy unit in each of the 5 years under review. The figures at the bottom of the graph refer to the percentage of surgical patients for each year.

RATIONALE OF ADMISSION TO THE INTENSIVE-THERAPY UNIT

Examination of the general pattern of surgical patient care shows that four basic phases can be discerned in the medical staff responsibility. These are: (1) referral and examination, (2) diagnosis, (3) definitive treatment (operative or conservative), and (4) recovery. As the severity of any given illness increases so more of these stages have to be carried out on an in-patient basis. In the case of patients with serious conditions where the specific illness frequently has shock as a major component two further stages must be interposed into this scheme. These are (2*a*) resuscitation, and (3*a*) post-treatment monitoring of vital functions.

In the case of the most seriously ill, e.g., patients with major trauma or vascular catastrophes, it is often necessary to carry out emergency treatment or support respiration and cardiac function before any diagnostic evaluation can take place.

Units which look after patients who manifest major patho/physiological states require reserves of manpower, materials, and space that are not available on the general wards because of cost/utilization requirements. The concentration of personnel and equipment on a 24-hour availability basis with sufficient space around the patient to give access to the resuscitation team is of prime importance in such units. Vourch (1967) describes similar conclusions from a large French unit. Safar and Grenvick (1971) recognize these factors of importance in the evolution of American intensive-therapy units.

Route of Admission to Intensive-therapy Units.—Patients in the different groups, as already outlined, show obvious variations in their hospital treatment before reaching the intensive-therapy unit.

1. Immediate admission to the intensive-therapy unit:—

a. Major trauma cases who on assessment in the casualty department show severe dysfunction of several systems are transferred immediately to the intensive-therapy unit for management.

b. Patients manifesting shock because of gastro-intestinal tract bleeding or peritonitis and those with septicaemia are similarly managed, and it has been our experience that the proximity of the operating theatre means that the problems of moving an ill patient around the hospital are minimized when it is apparent that the time for operation is correct.

Table I.—Admissions to the Intensive-therapy Unit over the 5 Years 1965–9

Reason for Admission	No of Patients admitted					Total No. of Patients	Percentage of 460 Patients
	1965	1966	1967	1968	1969		
Trauma	20	30	29	28	30	137	29·8
Readmit	0	0	0	0	1	1	
Deaths	9	8	6	8	6	37	
Postoperative	8	9	14	12	17	60	13·04
Readmit	0	0	1	1	0	2	
Deaths	1	2	2	6	1	12	
Poor risk	20	36	67	35	42	200	43·5
Readmit	0	1	6	3	1	11	
Deaths	13	18	21	12	16	80	
Major surgery	12	11	17	7	16	63	13·7
Readmit	1	2	1	3	0	7	
Deaths	1	2	3	1	2	9	
Total surgical admissions	60	86	127	82	105	460 patients	
Readmit	1	3	8	7	2	481 admissions	
Deaths	24	30	32	27	25	138 deaths	
Total No. of patients (medical and surgical)	178	219	275	238	253	1162	
Percentage of surgical patients	33·7	39 2	46 2	34·4	41·7		

Total admissions, average per month, 19 36, surgical admissions, average per month, 8 66. Overall mortality, 28·7 per cent of patients 29·8 per cent of admissions.

c. Certain specialized cases, essentially requiring respiratory care, are transferred to the unit from other centres. These include patients with tetanus, respiratory insufficiency, fat emboli, and neonatal problems. Patients with tetanus have been separately considered (Rochford, 1969).

2. Patients undergoing major surgery of various types and those in whom problems develop during the course of operation are admitted to the unit from the operating theatre, having spent the preoperative period in a general ward.

3. An intermediate class of patient exists, many of whom are also categorized as 'poor-risk'. These patients are transferred to the unit from the general wards, either medical or surgical, prior to operation to enable evaluation of their cardiac and respiratory states. They return to the unit after operation for monitoring and continuation of resuscitative therapy and are later discharged back to their ward of origin.

4. Late admissions. Chest conditions such as atelectasis and embolization are the most common postoperative complications, followed by cardiac problems such as infarction and dysrhythmias. Delayed ileus, wound dehiscence, and fistulae are the major conditions in the abdomen which merit admission to the unit at this stage.

The intensive-therapy unit has obvious connotations of crisis both to the patient and relatives in so far as they recognize the high degree of individual care that the incumbent is receiving. Hewitt (1970) has reviewed the subjective responses of patients who have been treated in such units and found that although about half the patients were worried by various facets of their time in the intensive-therapy unit, insight of their state of illness was not mentioned as being a particular cause of concern. We have in all cases tried to play down the 'crisis aspect' to the patient, particularly since, with a 5 per cent re-admission rate, one is anxious to avoid a precipitate drop in morale when a patient realizes he or she has to be returned to the unit. The mean time spent in the unit was less for the patients who survived than for those who died, and this can be taken as evidence of the fact that the patients whose recovery was progressing satisfactorily were returned to the general ward, whereas those whose condition was unsatisfactory were kept for further treatment. A corollary of this is that resources of nursing and medical staff can be fully directed to those with the greatest need.

Recordings.—A specially designed, large, single-sheet chart is available for each patient on a day-to-day basis; changeover takes place at 12 noon, by which time it has been our experience that the morning's laboratory results are to hand for assessment, prior to ordering the treatment for the following 24 hours. The patient's ward notes are kept at hand in the unit, but it is stressed that all the information relating to the patient's course in the intensive-therapy unit should be on the special charts. These can be filed after the patient has been discharged from the unit and are subsequently available for perusal.

STATISTICAL CONSIDERATIONS OF UNIT UTILIZATION

The two major factors expected to affect the use of intensive-care beds are the arrival patterns of patients and their length of stay in the unit. *Fig.* 3 A shows the Poisson distribution of the variation in the number of patients arriving each day from various sources at the intensive-therapy unit. *Fig.* 3 B shows the exponential graph of the type of length-of-stay distribution found for all cases. From these findings we can construct a simple theoretical model to predict the bed occupancy of the unit. The model is as follows:—

1. Patients who arrive when the unit is full do not form a queue but are treated elsewhere. This is likely to be an oversimplification of what happens in practice. For instance, an extra bed may be put up or other patients may be discharged to make room.

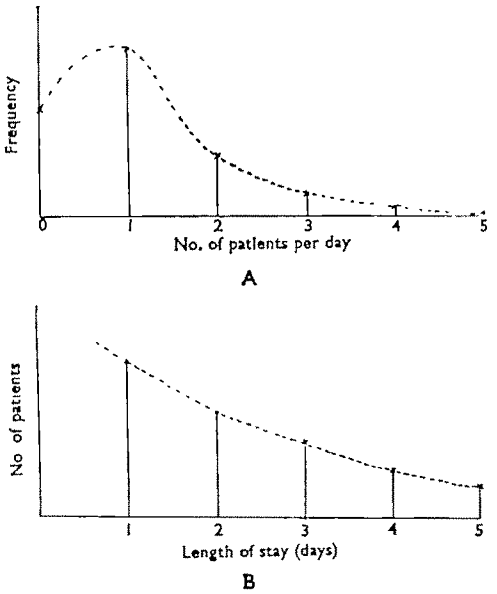

FIG. 3.—A, Frequency distribution of the number of admissions per day to an intensive-therapy unit. B, Length-of-stay distribution in an intensive-therapy unit.

2. The operational policies are constant.

3. The arrival of patients is completely random with a mean arrival rate of *a*.

4. The length of stay of patients is exponentially distributed with a mean *b*.

Then, the occupancy (*p*) of *n* beds in an *m*-bed intensive-therapy unit is:—

$$Pn-\frac{sn}{R\times n!},$$

where $m>n$, $s = ab$, and

$$R = \sum_{n=1}^{m}\frac{sn}{n!}.$$

This model can be further refined to take account of any admission or discharge policies associated with the number of patients in the unit, e.g., the admission policy may be to restrict admissions to particular types of patient if the unit is nearly full. To do this we calculate the arrival rates and discharge rates of patients for each bed state, i.e., when there is 1 patient in the unit, when there are 2 patients in the unit, and so on. So instead of means *a* and *b* we have, for example, for a 3-bed unit:—

a_0, Arrival rate when unit unoccupied,
a_1, Arrival rate when 1 bed is occupied,
a_2, Arrival rate when 2 beds are occupied,

and

c_1, Discharge rate when 1 bed is occupied,
c_1, Discharge rate when 2 beds are occupied,
c_2, Discharge rate when 3 beds are occupied.

Then, as a refined model, the occupancy of *n* beds (in an *m*-bed unit) is given by:—

$$Pn = \frac{1}{p}\frac{a_0 a_1 \dots a_n{}^{-1}}{c_1 c_2 \dots c_m},$$

where

$$p = 1+\frac{a_0}{c_1}+\frac{a_0 a_1}{c_1 c_2}+\dots\frac{a_0 \dots a}{c_1 \dots}$$

and $P_0 = 1/p$.

The results show that as the model for an intensive-therapy unit we can us with confidence the effects of any chang or discharge policies. *Table II* shows b time for our own unit for a typical peri

Table II.—BED-OCCUPANCY TIME FOR T THERAPY UNIT FROM OCTOBER, 1967, TO D

No. of Beds in Use	*Percentage of Time*
0	12·5
1	34·3
2	24·6
3	19·7
4	6·0
5	1·7
6	1·3

These figures refer to all admissions.

ANALYSIS OF OVERALL FI

Fig. 2 and *Table I* show the gener surgical admissions to be between 80 year over the 5 years 1965–9, but with in 1967. It was decided to different winter and summer admissions to the u purpose 'winter' is the 6 months fro March inclusive and 'summer' is fr September inclusive (*Table III*). The m stay of patients undergoing care in t therapy unit during winter and summ shown in *Fig*. 7.

Readmissions.—Twenty-one pati be readmitted to the unit during the 5-year period. Of these, 18 patients major-surgery and poor-risk groups. readmission in order of frequency were breakdown, 8; chest complications, dehiscence, 2; re-exploration of the c duct, 1; gastrectomy after gastrotomy, thorax after oesophagogastrectomy, 1; 1; post-pancreatectomy, 1.

Mortality.—*Table I* shows the mo for the groups under consideration. mortality was 28·7 per cent, with the showing a most encouraging drop in co the first year for which the unit was in particular it will be seen from *Fig*. 4 that the mortality in trauma cases has 54·5 to 20·0 per cent and in the poor- figures have dropped from 73·3 to 2 (winter figures).

ANALYSIS OF INDIVIDUAL

1. POOR-RISK CASES

The total number of patients admitt course of the 5 years who were consid under this heading was 200. There w among these patients and *Table V* sho disease-process groups with figures fo and mortality in each subgroup. T discussed later.

The predominance of gastro-intestinal tract disorders in this group is immediately obvious.

The total mortality for the poor-risk group was 80 patients (40 per cent). Considered in isolation this might seem a high figure, but against this must be set the improvement which has been manifest over the 5 years of the study, and also the fact that 80 per cent of the patients were more than 50 years of age and 47 per cent were over 60 years old. *Fig.* 5 shows the age distribution of the patients and the associated mortality. The largest number of patients occurred in the 70–80-year age-group. The average age of the poor-risk patients during the 5 years under review was 62·8 years.

There were approximately 2 men to every woman in the poor-risk series, and this is shown graphically in *Fig.* 6. This, to some extent, is the result of chronic pulmonary disease occurring more frequently in males. *Table VI* compares the number of incidents of chronic cardiopulmonary disease and acute chest infections recorded in the two sexes in the 200 poor-risk patients.

Length of Stay in Hospital prior to Admission to the Intensive-therapy Unit.—The disease categories seen cover a range of conditions whose time scale in terms of speed of progression varies enormously. Thus, the patient with an aortic dissection is seriously ill within minutes of the onset of the disease process and will be admitted to hospital and the intensive-therapy unit for resuscitation and an attempt at surgical corrective treatment. At the other end of the scale, patients with chronic peptic ulcer disease aggravated by chronic bronchitis, or arising because of steroid therapy in a patient with an ulcer diathesis, may well be in hospital for a considerable period of time on a medical régime before the referring physician asks for a surgical consultation.

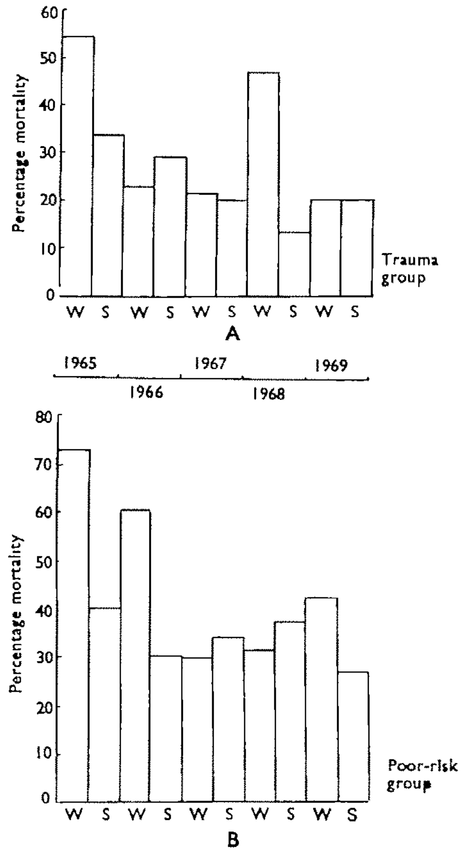

FIG. 4.—Patient mortality expressed as a percentage of the admissions in the trauma group (A) and in the poor-risk group (B).

Table III.—PERCENTAGE OF TOTAL SURGICAL ADMISSIONS PER ANNUM IN EACH GROUP SUBDIVIDED INTO WINTER (W) AND SUMMER (S) 6-MONTH PERIODS

REASON FOR ADMISSION	1965		1966		1967		1968		1969	
	W	S	W	S	W	S	W	S	W	S
Trauma	18·25	15·0	14·8	19·0	6·9	15·3	15·3	18·3	41·2	14·2
Postoperative	10·0	3·0	5·8	4·5	7·7	5·4	9·4	4·7	9·57	6·5
Poor risk	25·0	8·0	26·6	14·8	33·3	20·6	19·5	23·1	25·0	14·0
Major surgery	15·0	5·0	6·95	5·8	7·7	5·4	1·22	7·3	6·65	8·4

Table IV.—PERCENTAGE MORTALITY IN THE TRAUMA AND POOR-RISK GROUPS FOR EACH 6-MONTH PERIOD

REASON FOR ADMISSION	1965		1966		1967		1968		1969	
	W	S	W	S	W	S	W	S	W	S
Trauma	54·5	33·3	23·0	29·2	22·0	20·0	46·2	13·3	20·0	20·0
Poor risk	73·3	40·0	60·0	30·8	30·2	33·2	31·3	36·8	42·9	26·4

Alternatively, such a 'chronic' ulcer patient may suffer a disastrous bleed or perforation which makes urgent surgical treatment imperative.

Another group of patients can be identified, namely those in hospital receiving medical treatment for a non-surgical condition and who develop an associated complication which requires surgical correction or who present with a surgical disease as a separate condition while they are in hospital. *Fig.* 8 shows the distribution of the patients according to the number of days that they were in hospital prior to admission to the intensive-therapy unit. The majority is admitted to the unit within 24 hours of attending the hospital, but there can be seen to be a separate population which is referred late to the surgeon. The commonest problems in this category were 11 cases where patients on a medical régime for peptic ulcer required surgery and 14 cases who developed obstruction while already in hospital. Investigation of the deaths in this subgroup revealed a mortality of 16 per cent.

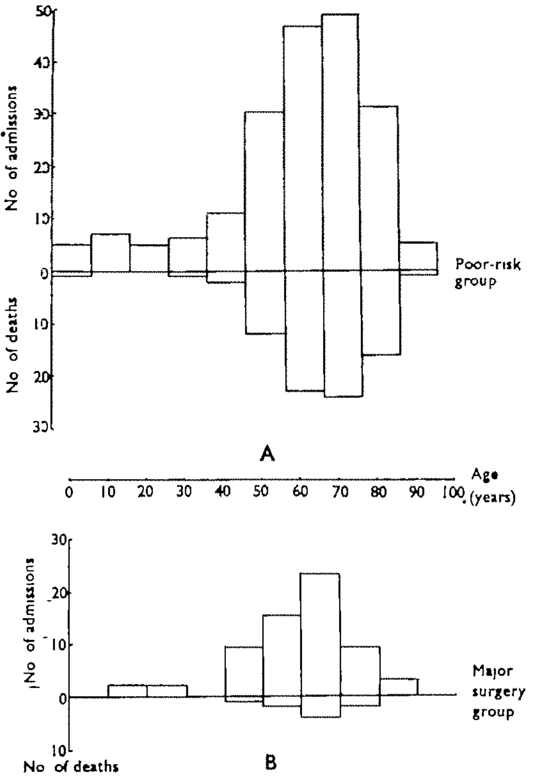

FIG. 5.—Age distribution and mortality for patients in the poor-risk group (A) and in the major surgery group (B).

Table V.—MAJOR DISEASE PROCESSES COMPARED WITH THE NUMBER OF ADMISSIONS, READMISSIONS, AND DEATHS IN THE POOR-RISK GROUP

DISEASE PROCESS	NO. OF ADMISSIONS	NO. OF READMISSIONS	NO. OF DEATHS
Peptic ulcer	46	5	19
Obstruction	48	3	28
Peritonitis	32	0	9
Prostatic enlargement	15	0	1
Vascular disease	24	2	15
Hepatobiliary disease	6	1	2
Orthopaedic cases	9	1	4
Wound dehiscence	3	1	1
Obstetric/gynaecological cases	4	0	0
Primary respiratory disease	5	0	1
Others	2	0	0

Fig. 9 compares the age range and mortality in the patients with ulcer disease, obstruction, and peritonitis, which together made up 63 per cent of the total patients in this group.

Patients with Peptic Ulcer Disease.—The 46 patients in this group included 37 males, of whom 15 died, and 9 females, of whom 4 died. There were three main reasons for the admission of these patients to the unit.

1. Age. *Fig.* 9 A shows that a large percentage of the patients in the category were over 65 years. Peptic ulcer is a chronic disease which normally manifests itself in early middle age. The low national mortality figures for the various vagotomy and drainage procedures have resulted in general practitioners and physicians referring a large number of their patients with recurrent ulcer disease for surgery to forestall serious problems and also to avoid committing the patients to a life of severe dietary restriction. In a large series McLeod and Carter (1971) showed that the maximum age incidence was in the 50–59 age-group for male patients and in the 40–49 age-group for female patients. Thus the age distribution showed an almost normal curve with loading obviously on the younger side. These authors

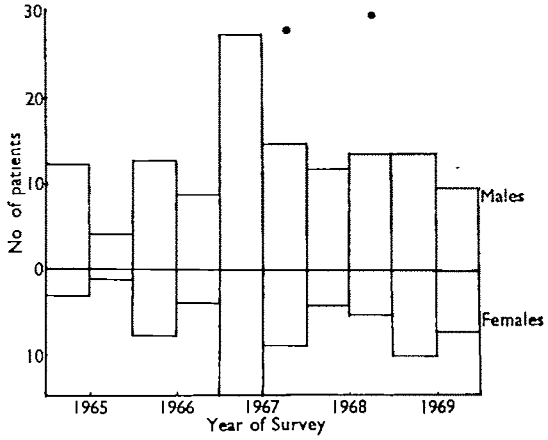

FIG. 6.—Male : female ratio in the poor-risk group.

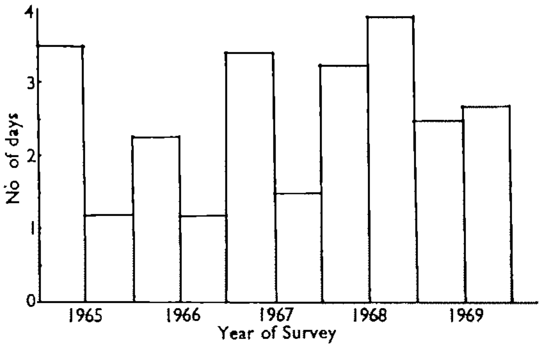

FIG. 7.—Average length of stay of all surgical patients in the intensive-therapy unit for successive winter and summer periods, 1965–9.

Table VI.—DISTRIBUTION OF CARDIOPULMONARY DISEASE AND CHEST INFECTIONS IN MALES AND FEMALES

DISEASE	NO OF PATIENTS	
	Males	Females
Chronic bronchitis	22	2
Asthma	3	1
Acute chest disease	19	11
Congestive cardiac failure	16	5

suggested that about 70 per cent of the cases in their series represented chronic ulcers. It is therefore to be expected that in patients presenting at a later age the ulcers will tend to be extremely indurated and often fixed to neighbouring intra-abdominal structures. Perforation to major vessels is common and resection difficult.

Table VII.—OPERATIONS PERFORMED IN 46 CASES OF PEPTIC ULCER

OPERATION	NO. OF PATIENTS	NO OF DEATHS
Perforation oversewn	13	5
Partial gastrectomy	20	8
Vagotomy and gastro-enterostomy	2	0
Pyloroplasty	1	1
Gastro-enterostomy	2	1
Partial gastrectomy and bowel resection	1	0
Resection of stomal ulcer	1	1
Drainage of subphrenic abscess	1	0
Removal of leiomyoma	1	1
Gastrotomy and direct suture of bleeding ulcer	1	0
Gastrotomy and under-running of erosions	1	0
No operation	2	1

Table VIII.—CAUSES OF INTESTINAL OBSTRUCTION

Cause of Obstruction	*No of Cases*
Hernias (external)	15
Neoplasm	11
Adhesions and bands	6
Non-mechanical ileus	4
Colitis	2
Carcinoid	1
Prolapsed rectum	1
Gall-stone ileus	1
Appendicitis	2
Bowel vascular disease	1
Undiagnosed	4

Table IX.—CARDIORESPIRATORY DISEASES OCCURRING IN PATIENTS WITH INTESTINAL OBSTRUCTION

Cardiorespiratory Disease	*No of Cases*
Patients with chronic bronchitis and emphysema	17
Acute chest infection	11
Congestive cardiac failure	9
Myocardial infection	2
Rheumatic heart disease	2
Asthma	1
Hypertension	1

2. The patient may present with one of two major complications of the primary lesion, namely haemorrhage or peritonitis. In our series of 46 cases, 23 patients presented with haemorrhage and 20 patients with peritonitis, while 14 out of the total number had severe shock from either of these causes.

3. The presence of other related or non-related medical conditions may weigh the balance in deciding to temporize on a medical régime in a patient with an ulcer which in a more fit patient would be worthy of surgery. In this series the following associated problems were seen. Seventeen patients had respiratory-tract disorders ranging from chronic bronchitis to previous pulmonary resection. There were 8 patients with cardiac disorders and 5 on steroid therapy. *Table VII* lists the operations that were performed on these 46 patients and the right-hand column shows the mortality for each procedure.

The primary causes of death in these patients were evaluated as being due to chest infection in 6 cases and cardiovascular disease in 6. There were also 6 deaths referable to intra-abdominal infection. (For comparison of the mortality figures *see* Schiller, Truelove, and Gwyn Williams, 1970).

Patients with Intestinal Obstruction.—There were 51 admissions in this series comprising 48 patients. Their ages ranged from 6 weeks to 94 years, the average being 69·1 years. *Fig.* 9 B shows that 40 of the 48 patients under consideration were over the age of 60 years at the time of operation. The male to female ratio was 28 : 20 and the 27 deaths that occurred were distributed equally between the sexes in the ratio of 17 males to 10 females. The causes of obstruction which was diagnosed or confirmed at laparotomy were as shown in *Table VIII*.

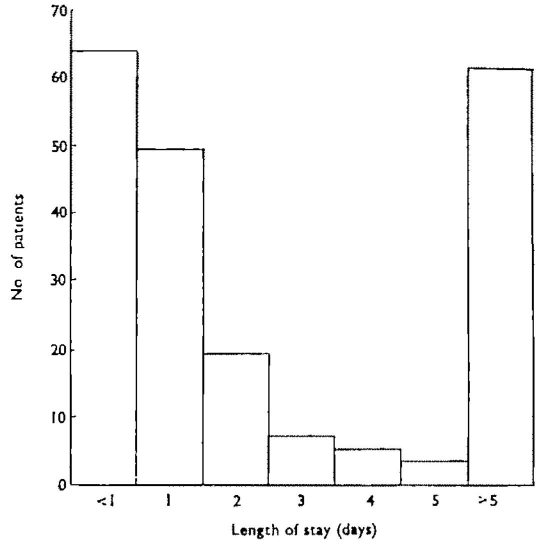

FIG. 8.—Number of days that poor-risk patients were in the hospital prior to admission to the intensive-therapy unit.

Table X.—CAUSES OF PERITONITIS

Cause of Peritonitis	*No. of Cases*
Late perforated appendix	10
Colon perforation	6
Pancreatitis	5
Bowel infarction from mesenteric vascular disease	5
Adhesions and bowel necrosis	2
Anastomotic leak	1
Reduplication cyst perforation	1
Jejunal necrosis, cause unknown	1
No peritonitis at operation	1

The high instance of diseases of the cardiorespiratory systems occurring in these patients cannot be over-emphasized. The relevant figures are shown in *Table IX*. Many of the conditions in this group coexisted. Other complicating factors were shock, anaemia, and metabolic imbalance secondary to fluid loss.

The major causes of death were cardiopulmonary failure (12 cases) and peritonitis (10 cases). The progress of malignant disease accounted for 4 deaths, bleeding from oesophageal varices 1, and renal failure 1.

Patients with Peritonitis.—*Fig.* 9 C shows the age range of the patients, and it is noticeable that a greater proportion of young people occurred in this group compared with the peptic ulcer and obstruction cases. Twenty males and 12 females were admitted to the intensive-therapy unit with peritonitis; of these, 4 males and 5 females died.

Operation was carried out in all except 2 of the patients, in whom acute pancreatitis was diagnosed from the history and confirmed by laboratory and clinical findings and thus immediate operation was deemed not necessary.

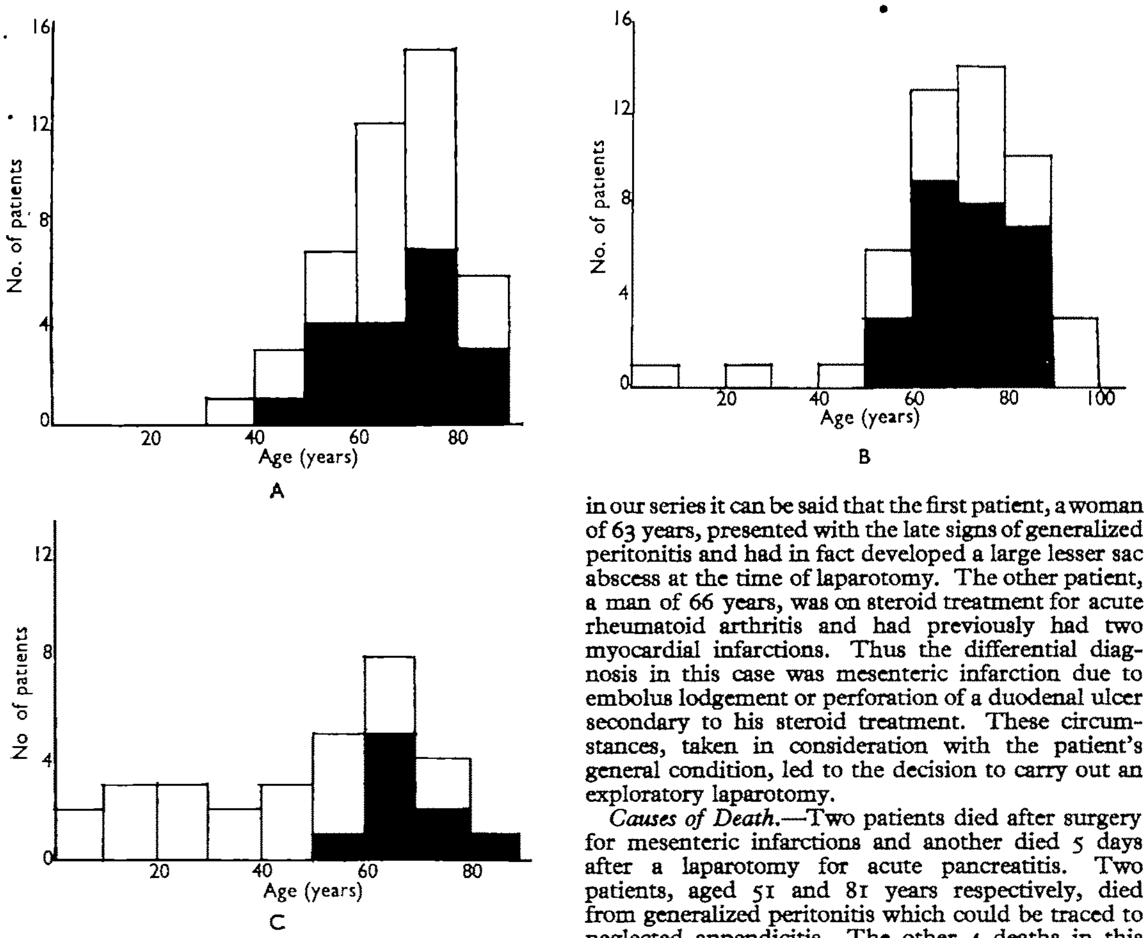

FIG 9.—Mortality and age-range in patients with (A) ulcer disease, (B) obstruction; (C) peritonitis. ■, No. of deaths.

The causes of peritonitis as established at operation (except in the 2 cases not submitted to operation) were as shown in *Table X*.

One case, a child of 6 years in whom no peritonitis was found at operation, was diagnosed as a high retrocaecal appendix with marked dehydration, air hunger, guarding, and rebound. Re-evaluation after a negative laparotomy revealed a right basal pneumonia.

The common general complications were mainly pulmonary in nature. Local complications included 10 abscesses and 2 wound dehiscences.

Patients with Pancreatitis.—Five patients with pancreatitis are included in the peritonitis group, and 2 of these underwent laparotomy shortly after their admission. Although general surgeons are increasingly aware of this condition and the advantages of instituting a conservative régime of therapy, it is nevertheless a common experience that a high proportion of these patients undergo laparotomy (Diaco, Miller, and Copeland, 1969). In 'defence' of the fact that early operation was performed on 2 patients in our series it can be said that the first patient, a woman of 63 years, presented with the late signs of generalized peritonitis and had in fact developed a large lesser sac abscess at the time of laparotomy. The other patient, a man of 66 years, was on steroid treatment for acute rheumatoid arthritis and had previously had two myocardial infarctions. Thus the differential diagnosis in this case was mesenteric infarction due to embolus lodgement or perforation of a duodenal ulcer secondary to his steroid treatment. These circumstances, taken in consideration with the patient's general condition, led to the decision to carry out an exploratory laparotomy.

Causes of Death.—Two patients died after surgery for mesenteric infarctions and another died 5 days after a laparotomy for acute pancreatitis. Two patients, aged 51 and 81 years respectively, died from generalized peritonitis which could be traced to neglected appendicitis. The other 4 deaths in this group were due to generalized peritonitis caused by perforation of a colon neoplasm, perforation of a diverticulum mass, and perforation of a colon in a patient with distal proctocolitis, and haemorrhage into hepatic secondaries respectively. *Fig*. 9 C shows that only 1 of the 9 deaths occurred in patients less than 60 years of age.

Prostatic Hypertrophy.—Over the 5-year period approximately 600 prostatectomies were performed in the hospital and the ones that merited intensive-therapy care under the poor-risk heading totalled 15. The age range of these patients was 57–92 years with a mean of 75·2 years. Complications could be divided into two groups.

General problems were mainly cardiopulmonary in origin (13 cases), while local difficulties usually related to bleeding from the enlarged gland (4 cases) and the hypotensive effects of the bleeding on the elderly patients' circulation. It is interesting to record that of these 15 poor-risk patients, only 1 succumbed and he was found at post-mortem examination to have an occult carcinoma of the bronchus.

Comparison of these patients with those in comparable series of poor operative risk patients who underwent cryoprostatectomy shows that the mortality in our series was less than that in patients who were submitted to cryoprobe instrumentation (Gill and Fraser, 1970).

Other cases of prostatic hypertrophy who were admitted to the unit are considered in the postoperative series (*vide infra*).

Vascular Disease.—In no group of emergency admissions is the surgeon faced with greater problems than those in this category. The generalized nature of the arteriosclerotic degeneration of the arterial tree with its risks to cerebral, coronary, and renal parenchyma not infrequently manifests itself by dissection, leakage, or blockage of major trunks with the attendant, rapidly advancing problems of severe pain and poor distal perfusion. *Fig.* 10 shows the age and mortality distribution of the patients in this group and *Table XI* gives a breakdown of the lesions.

Table XI.—REASON FOR EMERGENCY ADMISSION AND NUMBER OF DEATHS IN PATIENTS WITH VASCULAR DISEASE

Lesion	*No. of Cases*	*No of Deaths*
Aortic disease		
Leak	12	9
Dissection	2	
Emboli		
Iliac	1	3
Femoral	4	
Endarterectomy	3	1
Amputation	1	0

Oesophageal Varices.—Two patients died after direct surgery on the bleeding vessels at the oesophagogastric junction.

The high mortality-rate of 62 per cent in this small group of vascular emergencies, i.e., 15 out of 24 patients died, compares unfavourably with a mortality of 14 per cent (3 out of 22 patients) in the elective major vascular disease cases considered under the major surgery heading (*vide infra*). From these limited figures, therefore, there would appear to be a fourfold risk attendant upon emergency procedures.

Biliary-tract Disease.—Six patients were admitted to the unit at the time of biliary-tract surgery because of attendant complications. Two patients had previously sustained myocardial infarction and 1 patient was on mono-amine oxidase inhibitors for depression. A woman of 52 years was admitted to the unit from the preoperative ward having sustained a subarachnoid haemorrhage while awaiting cholecystectomy. Operation was not performed and she died of the cerebrovascular accident. The other admissions in this group were a male of 53 years, who sustained a large pulmonary embolus after cholecystectomy, and a patient with carcinoma of the pancreas who died after a cholecystojejunostomy had been performed.

Orthopaedic Diseases.—Nine cases were admitted after elective orthopaedic surgery; 6 of these were women who had required surgery for a fractured neck of the femur. The age range of these patients was 70–95 years, with a mean of 83 years. Complicating factors included acute and chronic chest infections, congestive cardiac failure, diabetes, and postoperative hypotension. One of the 6 patients had to be readmitted because of her diabetes going out of control in the postoperative period, but she was eventually fit enough to return to the general ward. The other admissions in this group were a man of 68 years with an acutely prolapsed vertebral disk who died of coexistent cardiac failure, and a man of 31 years who had a skin-graft following an infected spinal fusion scar. The final case was a youth of 19 with a fractured shaft of the femur who had a major fat embolus and was admitted with extreme hypoxia. This case has been reported elsewhere (Ross, 1970).

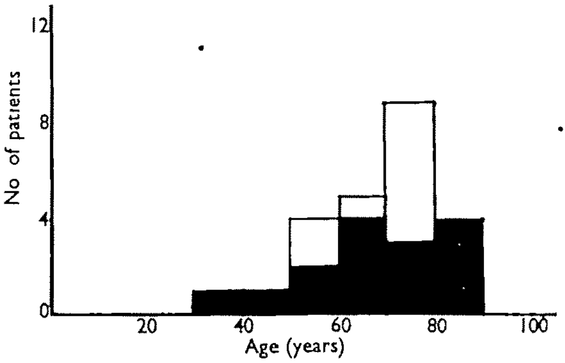

FIG. 10.—Mortality and age-range in patients with emergency vascular disease.

General Considerations of Other Minor Groups.—

1. *Wound Dehiscence.*—Three patients were admitted because of wound dehiscence. Two of the patients had acute or chronic chest conditions and 1 was a diabetic. One of these patients had to be readmitted with a further dehiscence 10 days after his second suture. This event should always be considered in a very serious light. The patient survived both these setbacks and was eventually discharged home. In a large series of cases of wound dehiscence the mortality associated with the incident is given as 11 per cent (Wolf, 1950) and 20 per cent (Mann, Spinazzola, Lindemith, LeVine, and Kuczerepa, 1962).

2. *Obstetric and Gynaecological Cases.*—Our colleagues in this speciality only found it necessary to admit 4 patients to the unit during the 5 years under review. These cases were:—

1. Therapeutic abortion for uraemia (blood-urea 380 mg. per cent).
2. Shock consequent upon secondary uterine haemorrhage.
3. Severe pre-eclamptic toxaemia at 34 weeks' gestation.
4. A patient who had undergone hysterectomy and suffered a severe exacerbation of asthma while in the recovery unit.

Comment.—From the description of the variety of cases which make up the acute admissions considered under the heading of poor-risk cases it can be seen that the challenge to the unit is ever present. Of the 200 patients reviewed, only 19 (9·5 per cent) had malignant disease. Thus, despite their age and multiple system failure either because of, or coexistent with, their primary disease, the majority of poor-risk patients who are taken care of in the intensive-therapy unit can look forward to an eventual return to a normal way of life.

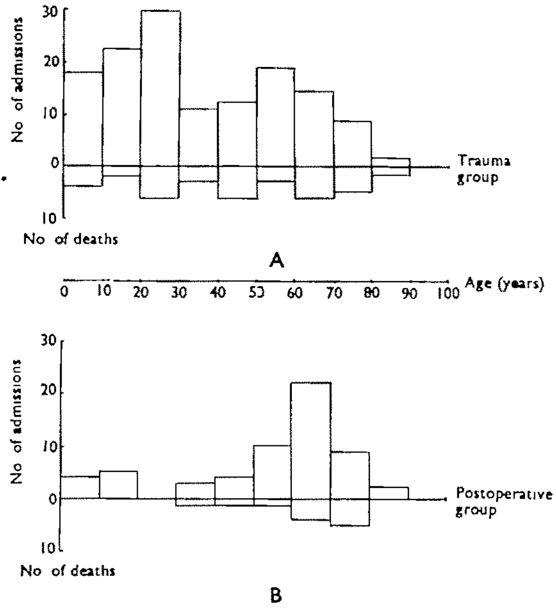

FIG 11.—Mortality and age-range in patients in (A) the trauma group and (B) the postoperative group

We have learnt the benefits of transferring patients early to the unit if their general condition is poor prior to intended or essential surgery. The presence of equipment and personnel and the position of the unit at the hub of the hospital allow rapid and frequent checking of the patient by the duty surgical registrar during a period of resuscitation before timed surgery. The practitioner on duty in a busy hospital should never be worried by the occasional case which after full assessment in the unit is clearly not in need of intensive therapy. Rather he should aim never to miss bringing to the unit those whose disease potentialities are such that they may suddenly be in dire need of many of the services which are only available in the intensive-therapy unit/operating theatre complex.

ANALYSIS OF INDIVIDUAL GROUPS

2. PROBLEMS OCCURRING DURING THE COURSE OF OPERATION

Table I shows that 13·04 per cent of all the patients admitted to the unit came in the category of operative problems. There were 12 deaths among the 60 patients and *Fig.* 11 shows these mortalities in relation to the age distribution. The major cause of death in these patients was myocardial disease (6 patients).

Discussion of General Figures.—The patients in this group all suffered some unexpected incident in the period during which they were in the theatre suite. As a result they were admitted for observation and treatment. In the 26 patients under the age of 60 years there were 3 deaths. Among 22 patients in their sixth decade there were 4 deaths, but in the 11 patients over the age of 70 there were 5 deaths, which indicates that the older patient faces the risk of degenerative cardiac disease giving rise to complications during surgery and, with their physiological resilience lessened because of increased age, recovery after the unexpected incident is less certain. Of the 8 young people (i.e., less than 20 years) admitted in this category, 4 were referred from ear, nose, and throat surgeons. Considering the extremely large volume of routine ear, nose, and throat surgery in this age-group this is an acceptably low operative complication rate. However, the problems that occur, namely haemorrhage, respiratory obstruction, and clot inhalation, are serious (Roberts, 1965). It is common experience that haemorrhage after tonsillectomy, either of a primary or secondary nature, is notoriously difficult to quantify. It is only when the melaena is observed in the days following operation that the surgeon is made aware of the concealed component of the haemorrhage in the child who he has been observing.

Table XII.—REASON FOR ADMISSION TO THE INTENSIVE-THERAPY UNIT IN PATIENTS UNDERGOING HEAD AND NECK SURGERY

TYPE OF SURGERY	REASON FOR ADMISSION TO THE INTENSIVE-THERAPY UNIT	NO. OF CASES
Ear, nose, and throat	Haemorrhage	3
	Inhalation of clot	1
	Congenital heart disease	1
	Epiglottis biopsy	1
Thyroidectomy	Haemorrhage	2
	Respiratory distress (1 tracheostomy)	3
	Observation following total thyroidectomy	2

Table XIII.—RESPIRATORY PROBLEMS DURING OPERATION CAUSING ADMISSION TO THE INTENSIVE-THERAPY UNIT

Respiratory Problem	*No. of Incidents*
Slow reversal after curarization	7
Probable/certain inhalation of gastric contents	4
Stridor	3
Postoperative cyanosis	3
Hypotension	2
Bronchospasm	1
Congestive cardiac failure and pneumonia	1
Bilateral pneumothorax	1

Two deaths in the younger age-group occurred. One, a 30-year-old woman, died 4 days after an appendicectomy during the course of which she suffered a cardiac arrest because of a fault in the anaesthetic machine. The other, a 44-year-old diabetic grand multipara (para 12) with a known deep-vein thrombosis, died of a pulmonary embolus on the tenth day after a Caesarean section. She had been on Warfarin for 6 days at the time of her death.

Specific Analysis of Patients.—Five major groups of patients could be discerned and these are grouped as follows:—

1. *Head and Neck Surgery.*—The details of this group are shown in *Table XII*. There were no deaths in this group.

2. *Respiratory Problems.*—There were 15 patients in this category, of whom 1 had to be readmitted.

They were undergoing a wide range of surgical procedures and in most cases were admitted to the unit at the request of the anaesthetist who was taking the case for the reasons given in *Table XIII*.

The only death in this group was that of a 78-year-old woman whose respiration was never adequate after an oesophagogastrectomy.

3. *Cardiovascular System Problems*.—There were 26 patients in this group. Of these, 14 were undergoing various general and orthopaedic procedures and 12 were undergoing prostatectomy. It has been our policy to use epidural anaesthesia whenever it is technically feasible for this operation. With well-trained anaesthetic staff who are alert to the problems which may arise in these cases the morbidity is negligible and the mortality acceptable.

In the 12 prostatectomy cases under review, 5 showed cardiovascular malfunctions and there were 7 cases of postoperative bleeding. There were 2 deaths; both patients had cardiac arrest during surgery and died shortly afterwards. Post-mortem examination revealed that both patients had suffered large myocardial infarctions.

In the remainder of patients in this group there were 7 episodes of cardiac arrest and 6 patients showed prolonged hypotension, 1 of these suffering gross arrhythmias. Five of the patients who suffered cardiac arrest on the operating table died; 2 immediately and 3 after a period of gradual deterioration in the unit following operation.

4. *Problems relating to the Central Nervous System*.—One patient died in status epilepticus because of advanced cerebral secondaries from carcinoma of the breast. Two patients were shown to have hypothermia (32·3° C.) after operation. One of these cases had unfortunately been on chlorpromazine for a long time prior to surgery, and it is thought that the effect of this drug on her heat-regulating mechanism contributed to her hypothermia and eventual death from bronchopneumonia.

5. *Bacteriaemic Shock*.—Two patients were admitted to the unit with hypotension and rigors after urethral instrumentation. Both recovered satisfactorily and they were discharged back to the ward on the following day after antibiotic therapy.

Comments.—The close liaison established in the recovery ward/intensive-therapy unit complex by virtue of admission control by the anaesthetic department and the fact that the intensive-therapy unit nurses spend a considerable proportion of their time in the operating theatre with the anaesthetist have resulted in good teamwork and easy transfer of patients who have had anaesthetic problems from one part of the complex to another. It is important that the same people should continue to watch over and manage a patient during the critical hours following an unforeseen incident. The relatively high concentration of medical staff in the operating-theatre complex during routine lists means that advice is immediately available for the nurses should the condition of one of these patients deteriorate.

ANALYSIS OF INDIVIDUAL CASES

3. MAJOR ELECTIVE SURGERY

Sixty-three patients out of the total series were admitted to the intensive-therapy unit after major elective surgery. In most cases they were admitted for routine monitoring during the immediate postoperative phase to ensure adequacy of respiration and stabilization of the haemodynamic state. In the case of patients who had undergone vascular procedures maintenance of a satisfactory peripheral flow as evidenced by skin colour and temperature, palpation of distal pulses, and good urinary output is most important. Seven patients (11 per cent) had to be readmitted during their postoperative course; virtually all of these admissions were occasioned by the development of sputum retention, atelectasis, and pulmonary consolidation following major upper gastro-intestinal procedures. In an excellent monograph published in 1957 Anscombe showed the relationship between various abdominal incisions and ventilatory capacity of patients expressed as a percentage of their preoperative capacity. It is to be expected that in a group of patients undergoing procedures which require upper abdominal incisions there should be marked interference with respiratory excursion and capacity and unwillingness to utilize the respiratory reserves available because of pain.

The close co-operation between the physiotherapy staff and the intensive-therapy unit is of great value. The physiotherapists can become more involved with the management of the patients than is common in the general wards, and with the greater frequency of their visits to the unit all the patients receive more physiotherapy treatment than would be possible in the general wards. The nursing staff also have time to watch, and subsequently emulate the physiotherapy staff, and are able to give remedial treatment at hours when the physiotherapists are not normally available. This is particularly important during the night immediately following operation.

The age distribution and mortality are shown in *Fig*. 5 B. There were 9 deaths in the series, 6 of these being due to chest infections and 2 the result of colon infarction after major aortic grafting. One patient with advanced metastatic tumour from a breast primary died 2 days after adrenalectomy.

Specific Analysis of Patients.—

1. *Vascular Disorders*.—Twenty patients underwent major elective vascular surgery; 11 operations involved aortic replacement for an aneurysm and 9 were aortodistal grafts. Two patients died; both patients appeared to be unable to maintain the circulation to their mid-descending and sigmoid colon without the inferior mesenteric contribution. One other patient died of chest infection after aortic replacement; tracheostomy was performed when it became apparent that his postoperative respiratory requirements could not be maintained without prolonged artificial ventilation, but despite this his condition rapidly deteriorated.

It is important to compare and contrast the mortality in this series of patients with those patients in whom it was necessary to perform emergency vascular surgery, who have been considered in the poor-risk category (*see Fig*. 10).

2. *Upper Gastro-intestinal Tract Surgery*.—The operations performed are shown in *Table XIV*.

A mortality of 4 out of 21 patients is acceptable where such major operations are concerned, and the morbidity in terms of postoperative complications was extremely low. Thus, 5 patients had radiological and clinical evidence of chest infection, 1 patient suffered a pneumothorax, and 1 patient had an anastomotic leak after an oesophagogastrectomy. This latter patient subsequently died of bronchopneumonia.

Table XIV.—OPERATIONS PERFORMED IN PATIENTS UNDERGOING GASTRO-INTESTINAL TRACT SURGERY

Operation	*No. of Cases*	*No of Deaths*
Oesophagectomy	7	1
Oesophagogastrectomy	2	—
Total gastrectomy	5	1
Whipple operation	6	2
Thoraco-laparotomy	1	—

3. *Lower Gastro-intestinal Tract Surgery*.—Fourteen patients were accepted into the unit after major surgery of the lower gastro-intestinal tract. There were 9 cases of carcinoma of the rectum necessitating abdominoperineal resection. Panproctocolectomy was performed in 4 cases with ulcerative colitis. The remaining case underwent laparotomy and small-bowel resection for Crohn's disease.

Two patients in this group died; 1 of bronchopneumonia following panproctocolectomy for ulcerative colitis at the age of 58 years. This patient had a tracheostomy in an attempt to control his severe respiratory infection but he eventually succumbed. A man of 70 years died of uraemia and pneumonia 6 days after an abdominoperineal resection. Morbidity and complications were otherwise minimal, and the average period of stay in the unit of the surviving cases was 1 day.

4. *Major Endocrine Surgery*.—Six patients (all women) in this category were admitted. All underwent bilateral adrenalectomy. Five patients had metastatic breast neoplasms and 1 had Cushing's disease. The 5 patients with primary breast lesions also underwent oophorectomy at the same time. Mortality was limited to 1 woman of 44 who was accepted for operation with full realization of her desperate condition. She had massive pulmonary metastases and haemoptysis and severe pain from hypertrophic pulmonary osteo-arthropathy. Operation was attempted in an effort to effect some regression in the size of the pulmonary deposits which were causing extreme discomfort. The attempt failed and she died 4 days after operation.

5. *Major Ear, Nose, and Throat Surgery*.—The intensive-therapy unit was asked to provide facilities for monitoring a youth of 19 after the closure of a tracheal fistula which was the end-result of a tracheostomy performed while he was deeply unconscious following a major road-traffic accident. There was also a male of 60 years who was observed following a resection of an arytenoid neoplasm. Both these patients were returned to the ear, nose, and throat unit without incident.

Comments.—It will be apparent from the remarks made concerning low morbidity and short period of stay in the unit that many of the patients who underwent major surgery had an uneventful postoperative course. It may therefore be argued that these patients could well have been returned to the general ward for routine postoperative supervision. It is, however, our view that one of the essentials of surveillance after major surgery is that the patient should be in the full view of the nursing staff. This statement has two facets:—

1. The nurse in charge of such patients should not have to leave them except for the briefest intervals. The continuity of observation by a trained nurse is most valuable, both to the patient in ensuring his continued progress and to the nurse in allowing her to take full responsibility over a period of time when the patient's condition may show marked variations.

2. It is virtually impossible in a general ward to provide an arrangement whereby the seriously ill patient can be constantly observed under satisfactory illumination without causing a marked disturbance to other sleeping patients.

We feel that scrupulous attention to detail during the immediate postoperative period can result in a haemodynamically stable and mentally alert patient being returned to the general wards within 24 hours. In a hospital such as the one in which this survey has been carried out where night staff on the postoperative wards are frequently looking after 8 or 10 patients returning from operation per day the retention of the most major cases in the recovery ward/intensive-therapy unit complex ensures that the other postoperative patients are adequately and equally supervised.

ANALYSIS OF INDIVIDUAL CASES

4. TRAUMA

Fig. 2 shows the absolute numbers and relative percentages of patients admitted in this category. As has been explained at the outset of this paper, the hospital's catchment area includes several fast urban motorways approaching London from the north, and many of the patients admitted in this category received their injuries as a result of high-velocity accidents on these roads.

Table XV.—POSITION OF INJURY IN 137 CASES OF MAJOR TRAUMA

Position of Injury	*No. of Cases*
Face/head	82
Chest	28
Multiple rib	30
Abdomen	31
Spine/pelvis	27
Major arm/leg	65
Total	263

Injury index = 1·927.

The epidemiology of road accidents has recently been reviewed (Bull, 1970). The quantification of the degree of severity of one accident compared with another is extremely difficult and involves the assessment of many independent variables. *Table XV* shows that, on average, each casualty admitted to the intensive-therapy unit for care had sustained two distinct major injuries either of which alone would constitute severe trauma. This figure is comparable with an injury index of 2·266, cited by Brooks, Nahum, and Siegel (1970).

The age distribution (*Figs.* 11 A, 12) shows the high incidence of injury in the first three decades suffered by the adventurous and impetuous male. There is a second peak in the fifth decade which probably corresponds to accidents occurring to pedestrians, and readers are referred to Bull's (1970) graph. *Table XVI* shows the marked male/female difference both in overall number of trauma cases and in the associated mortality.

The mortality figure for this group is high, the overall death-rate being 37 out of 137 patients. *Fig.* 13 shows that by far the largest number of deaths occurred within 24 hours of admission, i.e., 23 out of the 37 deaths.

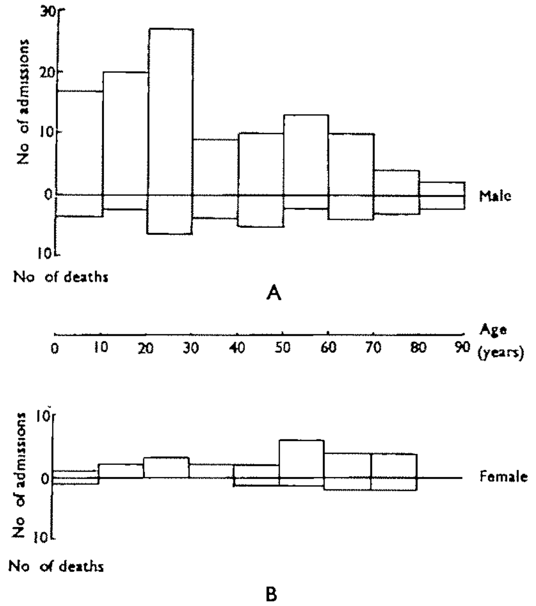

FIG. 12.—Age distribution for male (A) and female (B) trauma admissions, with the associated mortality.

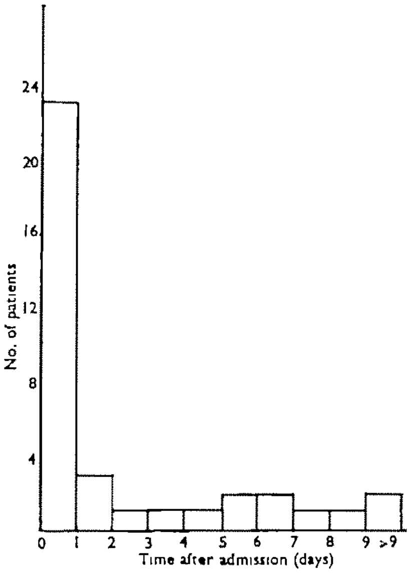

FIG. 13.—Day of death of 37 major trauma patients admitted to the unit.

Table XVI.—AGE AND SEX COMPARED WITH MORTALITY IN THE TRAUMA GROUP

SEX	AGE (years)								
	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80+
No. of males No. of deaths	17 3	20 2	27 6	9 3	10 5	13 2	10 4	4 3	2 2
No. of females No. of deaths	1 1	2 —	3 —	2 —	2 1	6 1	4 2	4 2	— —

Totals: males: 113, deaths 30; females: 24, deaths 7.

Analysis of Mortality Figures.—In many cases the cause of death given at the post-mortem examination was 'multiple injuries'. However, analysis of the clinical course of the patients taken in conjunction with the post-mortem diagnosis has enabled a reasonable assessment to be made of the major cause of death. *Table XVII* reviews the 37 deaths in this series.

Specific Analysis of Patients.—

Head Injuries.—Lewin (1966) quotes a figure of 60 per cent of road-traffic accident deaths being associated with head injuries. The present series shows that a head injury was a major factor in the death of 23 of the 37 patients who succumbed (62·7 per cent). In the overall group of patients with major trauma 80 out of 137 patients (58·4 per cent) had head injuries. Major head injury, i.e., skull fracture, with or without extra- or subdural haematoma and localizing signs, occurred in 48 cases. There were 26 patients with concussion of a moderate to minor degree, 4 mandibular fractures, and 2 patients with severe facial lacerations.

Chest Injuries.—There were 10 cases in which there was evidence of trauma to the heart or mediastinum, 11 patients who manifested pulmonary injury, 6 patients with flail chests, and 31 patients with multiple rib fractures. The average number of rib fractures was 6, the range being 2–18.

The amount of blood-loss into the soft tissues of the chest wall when many ribs are fractured is rarely appreciated. Abrams (1961) has stated that a litre of blood can be present between the chest-wall muscles before there is any external sign of swelling. Taken in conjunction with the fact that rib fractures may cause pleural rupture and an associated haemothorax, it can be seen that there is ample reason for the post-traumatic fall in haemoglobin level which is common in patients who have suffered chest-wall injuries. If the bruising to the chest has been severe there may be associated interstitial pulmonary haematoma, and Abrams (1961) has described the summation of (1) oligaemia, (2) pulmonary damage, and (3) decreased respiratory excursion as giving rise to a serious interference with normal pulmonary function. If the patient has pre-existing lung disease or poor respiratory excursion due to age or obesity only a minor chest-wall injury may be necessary to create a serious situation.

Table XVII.—CAUSE OF DEATH IN 37 CASES OF MAJOR TRAUMA

Cause of Death	*No. of Cases*
Head injuries:	
Head injury alone	14
Head injury and chest lesion	5
Head injury and orthopaedic lesion	2
Head injury and abdominal lesion	2
Total	23
Chest conditions:	
Fat embolus	1
Bronchopneumonia	1
Rib fracture and torn diaphragm	1
Heart rupture	1
Major rib fractures with instability	2
Total	6
Orthopaedic injuries:	
Major pelvic fractures	2
Extensive leg fractures	1
Bilateral traumatic amputation of legs	1
Total	4
Abdominal vascular injuries:	
Ruptured inferior vena cava	2
Ruptured aorta	1
Major hepatic lacerations	1
Total	4

Tracheostomy: Fifteen tracheostomies were performed during the 5-year period. Of these, 7 were performed for primary chest conditions, of which 2 patients eventually died. Seven tracheostomies were performed on patients with prolonged unconsciousness following head injury and 3 of these succumbed. One patient required a tracheostomy for a neck stab wound.

Table XVIII.—FRACTURES IN 67 CASES OF MAJOR TRAUMA

Position of Fracture	*No of Cases*
Femur	35
Tibia and fibula	25
Pelvis	21
Arm	13
Lumbar spine	7
Thoracic spine	1
Cervical spine	1
Total	103

Abdominal Injuries.—There were 13 cases of rupture or lacerations of solid viscera; spleen 5, kidney 6, and liver 2. In 5 patients major venous tears occurred. Jejunal rupture was seen once, and there were 3 cases of abdominal lacerations and stabbing. Two patients who had rupture of the inferior vena cava failed to survive. Post-mortem examination of these patients revealed lacerations of the vena cava at the point of insertion of the hepatic vein just below the diaphragm.

Musculo-skeletal Injuries.—It has already been noted that the quantification of the degree of trauma is extremely difficult where so many variables exist. In *Table XVIII* the number of fractures sustained by different bony structures is itemized, but this can in itself give little indication of the degree of associated soft-tissue trauma.

There was a total of 103 incidents of fracture in 67 patients. Seventeen of the 67 patients had only peripheral injury, i.e., there was no associated head, chest, or abdominal trauma. Of these patients, 5 died. Ten patients out of the 50 who had a peripheral, i.e., musculoskeletal, and a central system injury died. Of the factors listed in *Table XVIII*, only the arm-bone fractures cannot be considered as constituting major orthopaedic trauma. Despite this, the total of 103 incidents of fracture in 67 patients indicates that systemic injury and falling circulating blood-volume combined to give a potentially dangerous shock state in all the patients under consideration in this category.

Comments.—Many of the patients admitted after trauma had sustained injuries to the upper body which were nearly mortal, and *Fig.* 13 should be considered in the light of this fact. The majority of these patients had severe head injuries and were deeply unconscious from the outset. Their associated lesions usually required transfusion and support, but with vital centres in the midbrain not functioning the pattern of falling temperature, unstable blood-pressure, and the necessity for an increasing amount of respiratory support was commonly seen. This pattern culminated in the absence of spontaneous respiration and eventual circulatory arrest.

Those patients whose injuries are most severe but not mortal form a group which provides one of the greatest challenges in current surgery. In addition to the urgent need for circulatory support there is the essential forward planning to counteract possible renal shutdown, and, as unforeseen variations in the patient's clinical course appear, it is necessary to give thought to major complications such as fat embolization, traumatic aortic aneurysm, late manifestations of head injury, and unrevealed spinal fractures in an effort to explain symptoms and signs which may arise.

DISCUSSION

The challenge of work in an intensive-therapy unit in a general hospital is seen to arise from several factors. On the one hand, there is a group of young people arriving as a result of trauma incidents who are acutely ill and who require urgent care if they are to survive. Another major group of patients consists of the elderly with diseases of the gastro-intestinal tract who often present late with their symptoms. The overall incidence of malignant disease in all the patients in this series is of the order of 15 per cent; thus there can be a reasonable expectation of return to normality in a high proportion of our patients if treatment is successful. There is, however, often little time to spare in instituting diagnosis, resuscitation, and definitive treatment. It is therefore important for the medical staff to establish the priorities, particularly with regard to biochemical analysis and radiology which will enable them to confirm their diagnosis and so institute effective treatment.

The high mortality in certain poor-risk cases has already been alluded to. Thus, in the obstruction series 28 out of 48 patients succumbed; 19 out of 46 peptic ulcer patients died; in the emergency vascular series there were 15 deaths out of 24 patients. In most cases the patients with peptic ulcer and the vascular diseases had been known sufferers from their complaint, although with varying degrees of seriousness, for some time. Surgical treatment for these conditions may well be extensive and in some cases is precluded by age or other associated disease factors. However, it must be the impression that more positive evaluation of patient symptomatology at the level of primary medical care might result in more of these patients being admitted for elective surgery (with the demonstrated lower mortality) than has hitherto been the case.

The greatest problem is often one of interdepartmental management in so far as there may be the requirement to arrange neurosurgical investigation or dialysis support at another hospital within 24 hours of a major accident. There is a natural reluctance to move a patient who has just achieved haemodynamic stability and thus the difficulty will not be solved until there are more centralized major accident centres with all such specialities represented so that interhospital transfer can be avoided. We may see in the future such centres equipped with fast transport of an advanced nature for the collection of patients from outlying units, but at present the benefit of specific required care, e.g., haemodialysis, has to be balanced against the difficulties of transporting the severely injured patient to the specialized centre and the effect of such moves on the patient's general condition.

The concomitant progression of cardiac and pulmonary disease with age in patients living in a primarily urban area in Britain is another factor which would seem to point patients to earlier surgical treatment. In the peptic ulcer series 13 of the 19 deaths were attributed to cardiopulmonary causes, and in the obstruction series 12 of the 28 deaths were similarly itemized. It is difficult to speculate as to the numbers of these patients who would have survived operation with prior and more leisurely cardiopulmonary investigation and treatment, but comparison of the mortality in emergency vascular cases with the death-rate in the elective series described under Major Surgical Procedures is illuminating and probably points the way to the type of mortality figures expected.

Over the course of a 5-year period the results achieved by the unit have primarily been due to the more rapid evaluation of the clinical state of the patient and interpretation of the physiological and biochemical deficits associated therewith. This has in turn enabled corrections to be applied to achieve haemodynamic stability. It is in this general way that more rapid recovery can be achieved and morbidity and mortality figures consequently fall.

CONCLUSIONS

1. The importance of a stand-by medical and nursing organization ready within minutes to receive a seriously ill patient from home, accident site, or another ward in the hospital has been demonstrated. This system benefits the patient and is the most effective way of utilizing equipment which would otherwise have to be duplicated throughout a general hospital.

2. Clear access to the patient for several medical and ancillary personnel simultaneously is essential if urgent procedures are to be carried out on the seriously ill patient in the minimum time. This facet of care can best be managed in an intensive-therapy unit.

3. Proximity of the intensive-therapy unit and the operating theatre is a great advantage both in terms of primary surgery and any subsequent procedure which may be deemed necessary because of complications which arise (e.g., sputum retention) or when a staged surgical operative régime has been planned.

4. The instruction of new medical resident staff and nursing personnel can best be carried out on an informal and continuous basis in a small unit where patients are being observed and equipment is constantly in use.

5. A well-run unit rapidly develops a high morale which carries it through times when the results in terms of patient salvage are poor. The teamwork which is essential in providing a comprehensive 24-hour staffing requires continuous exchange of ideas and teaching at all levels in the unit, and frequent reviews of the methods by which results are achieved are essential.

6. The identification of the physiopathological changes seen in shock and the pharmacological management of these variations from normal represent a major field of surgical research. The careful observations of trained nursing staff in an intensive-therapy unit thus act as a firm base on which clinical evaluation and research can be founded.

Acknowledgements.—I wish to thank the consultant surgeons at Barnet General Hospital for their help and encouragement during my 2-year tenure of the post of Resident Surgical Officer. Mr. Alan Small, Mr. V. J. Downie, Mr. D. A. Bailey, and Mr. B. D. Stutter were most kind in allowing me to study their patients. Dr. Eric Gardner gave much encouragement at the inception of this project and I am indebted to Miss Angela Gardner for the statistical model.

The senior intensive-therapy unit sisters, Miss Rosemary Pope and Miss Mary Healey, are cordially thanked for their help in the unit at all times and for their willingness to assist in checking details from the intensive-therapy unit records.

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THE CALCIUM PALMITATE GALL-STONE

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SUMMARY

Crystallographic studies have recently shown that calcium palmitate is the fourth most abundant crystalline constituent of gall-stones. In a study of the gall-stones from 31 consecutive patients undergoing operation at University College Hospital, London, in 1970, 2 patients were found whose stones contained calcium palmitate as the sole crystalline constituent, and a stone from a third patient had this compound as the major component. Three other patients had small beads of calcium palmitate in stones consisting predominantly of cholesterol. Some points of interest concerning these stone-formers are reported.

IN a recent statistical study of the characteristics of a collection of 331 gall-stones from 8 countries (Sutor and Wooley, 1971) the crystalline composition of the stones was determined by the X-ray powder method. Calcium palmitate was present in 36 per cent of the stones and accounted for 6 per cent of all the crystalline material in the series. Five stones consisted entirely of this compound. In 18 others it was present as a major component and in 16 as a minor one.

Prior to the work of Sutor in 1970 calcium palmitate had not been reported as a constituent of gall-stones from any country except Japan. Palmitic acid together with oleic and linoleic acids comprise 80 per cent of the fatty acids present in human bile, but 90 per cent of these acids are conjugated to lecithin (Blomstrand and Ekdahl, 1960) and therefore are unlikely to precipitate.

Little if any information is available concerning the conditions giving rise to calcium palmitate gall-stones, and we therefore present here preliminary data on a few such stone-formers found in a survey of the composition of bile and gall-stones from patients undergoing surgery for gall-stone disease at University College Hospital, London, in 1970.

MATERIALS AND METHODS

Thirty-one consecutive unselected patients formed the group in which the calcium palmitate stone-formers occurred. The gall-stones obtained at operation were washed, blotted dry, weighed, placed in formalin solution in distilled water for 24 hours, then washed, and air dried. The stones were analysed by the X-ray powder method, as described by Sutor and Wooley (1969), using a Nonius Guinier-type camera and filtered copper radiation. To determine the approximate amounts of crystalline material present the X-ray diffraction patterns obtained were matched against standard ones for known constituents of gall-stones. Bile was obtained at operation both from the gall-bladder and from the common bile-duct, taking care as far as possible to avoid contamination of the common bile-duct bile by the gall-bladder bile. The bile samples were analysed chemically. Total cholate concentration was determined by the method of Irvin, Johnson, and Kopala (1944), phospholipid concentration by a modification of the method of Fiske and Subbarrow (1925), and cholesterol concentration by a method derived from that of Babson, Shapiro, and Phillips (1962) and Leffler and McDougald (1963). Total bile-salt was estimated by assuming a relatively constant total cholate to bile-salt ratio in human bile of 1 : 2·7 (Sjövall, 1960).

Table I.—DATA FOR THE PATIENTS IN THE PRESENT SERIES

PATIENT	AGE AND SEX	PARITY	GALL-BLADDER FUNCTION	TIME SINCE ONSET OF SYMPTOMS (mth.)
1	73 F.	1	Normal	12
2	79 F.	0	Non-functioning	6
3	74 M.	—	Non-functioning	$\frac{1}{2}$
4	64 F.	0	Normal	4
5	67 F.	0	Non-functioning	5
6	47 F.	7	Non-functioning	6

Patients 1–3, gall-stones of 95–100 per cent calcium palmitate.
Patients 4–6, gall-stones of 1–3 per cent calcium palmitate.

RESULTS

Two of the patients had stones in which the only crystalline material present was calcium palmitate (Patients 1 and 2 in *Tables I–III*). Another patient (No. 3) had a stone in which calcium palmitate was the major component, the minor one being vaterite (a form of calcium carbonate). Three patients (Nos. 4–6) had small beads of calcium palmitate (Sutor, 1970) in stones otherwise consisting of cholesterol, except for 1 stone which probably contained a small amount of calcite (another form of calcium carbonate). The calcium palmitate beads accounted for only 1–3 per cent of the crystalline material of these stones.

The age, sex, and parity of the patients, the time since the onset of their symptoms, and their gall-bladder functions are given in *Table I*. Data for the gall-stones are presented in *Table II*. The results of the bile analyses, expressed in mmol per litre, are shown in *Table III*. These values were converted to percentages of the total molar concentration of the three constituents, phospholipid, cholesterol, and bile-salt, and plotted on a phase diagram in *Fig.* 1 (Hofmann and Small, 1967). This diagram shows in the lower left-hand corner the micellar area where cholesterol is soluble, and biles outside this region are supersaturated with respect to cholesterol and have the potential to crystallize.

Table II.—DATA FOR THE GALL-STONES FOUND IN PATIENTS IN THE PRESENT SERIES

PATIENT	NO. OF STONES	WEIGHT OF STONES (g)	SITE OF STONES
1	1	1·3	Common bile-duct
2	1	7·2	Common bile-duct
3	1	3·3	Gall-bladder
4	103	6·6	Gall-bladder
5	3	55·0	Gall-bladder
6	7	7·5	Gall-bladder

Table III.—COMPOSITION OF BILE (mmol/litre) FROM PATIENTS IN THE PRESENT SERIES

PATIENT	GALL-BLADDER BILE			COMMON BILE-DUCT BILE		
	Phospholipid	Cholesterol	Total Bile-salt	Phospholipid	Cholesterol	Total Bile-salt
1	7·36	1·84	26·01	2·09	1·34	9·57
2	8·01	1·89	33·47	7·99	1·86	31·66
3	13·81	4·57	40·93	8·50	3·15	22·18
4	12·05	6·98	42·70	—	—	—
5	No bile in gall-bladder			—	6·46	19·29
6	7·23	5·97	13·40	7·05	3·59	11·04

—, Insufficient bile to make measurement.

DISCUSSION

The patients having stones consisting almost entirely of calcium palmitate tend to be older than the other types of stone-formers, but the numbers are too small for the differences to be significant. These patients produced only single stones, which in 2 instances were found in the common bile-duct. At operation in these 2 cases the surgeon noted particularly that the gall-bladder appeared remarkably normal macroscopically, being free from overt signs of inflammatory change. Histologically, however, there was plentiful evidence of chronic inflammation. There were only 2 other common bile-duct stones in the series; these were in patients with cholesterol stones, both of whom had previously undergone cholecystectomy for cholelithiasis. It is rare to find stones in the common duct without stones in the gall-bladder, and the possibility that palmitate stones nucleate and grow in the bile-duct should be considered.

The composition of both the common bile-duct bile and gall-bladder bile from the patients with calcium palmitate stones is within the micellar zone of cholesterol solubility in bile. However, bile from patients having only a small trace of calcium palmitate in the form of beads in their stones had a composition outside this micellar region (*Fig.* 1). In the gall-bladder bile from a calcium palmitate stone-former there is less cholesterol than in the corresponding common bile-duct bile (*Fig.* 1). By contrast, in gall-bladder bile from cholesterol stone-formers the mean concentration of cholesterol is greater than that for common bile-duct bile (Sutor, Cowie, and Clark, 1973).

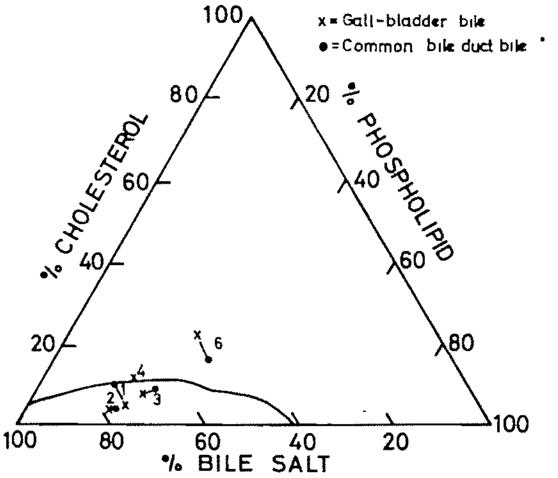

FIG. 1.—Phase diagram for bile from patients with calcium palmitate in their gall-stones. Patients 1–3, gall-stones of 95–100 per cent calcium palmitate. Patients 4–6, gall-stones of 1–3 per cent calcium palmitate.

From these data a picture emerges of the type of patient who has been found to develop calcium palmitate stones. Bearing in mind that so far too few of such patients have been found for statistically significant evaluations to be made, it is interesting to speculate whether future findings will be similar to those reported in this preliminary study. In particular we will be suspicious that the elderly patient, of low parity in the case of a female, who at operation is found to have a single, soft, pultaceous stone in the common bile-duct (especially if the gall-bladder is macroscopically normal) and whose gall-bladder bile and common bile-duct bile show no abnormality with respect to cholesterol solubility, may have a calcium palmitate stone.

In the study of the composition of gall-stones from different countries, Sutor and Wooley (1971) found several stones consisting entirely or predominantly of calcium palmitate. Unfortunately, detailed clinical information was not available, only the age and sex of the patients being known. There were 5 stones consisting entirely of calcium palmitate and of these, 2 came from males aged 74 and 78 and 2 from females aged 52 and 37. The age and sex of the fifth patient were unknown. Six other stones containing a major amount of calcium palmitate and one other (minor) constituent came from 5 males aged 63, 63, 63, 68, and 74 respectively, and 1 female aged 28. These data substantiate that calcium palmitate stones are more common amongst elderly patients.

Acknowledgements.—We thank the surgeons at University College Hospital for allowing material from their patients to be studied and Miss J. Fowler and Miss G. S. Dines for making the bile analyses. We are grateful to the Medical Research Council and the Nuffield Foundation for financial assistance.

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ABDOMINAL ACTINOMYCOSIS

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SUMMARY

A case of sigmoid actinomycosis is described and the cases of abdominal actinomycosis presenting at the Manchester Royal Infirmary over the past 20 years are reviewed. The whole problem of abdominal actinomycosis is discussed, with special reference to the sites of infection and mode of treatment. The relevant literature is reviewed.

THE first clinical description of actinomycosis has been attributed to Von Langenbeck (1845). In 1877 Bollinger demonstrated that a fungus was the infective agent in producing the hard masses that occurred in the jaw bones of cattle. The following year Harz (1878) suggested the name *Actinomyces bovis* for this fungus. At the same time Israel (1878) was studying material obtained from a patient with suppuration in the neck. He noted granules which contained the same mycelia as those described by Bollinger (1877) in cattle. Israel, who remained active in the study of actinomycosis, considered that it is an endogenous anaerobic infection and despite suggestions that it is an exogenous aerobic infection by such workers as Bostroem (1890) this theory has been upheld ever since. About 20 per cent of cases of actinomycosis have the primary site of infection in the abdomen (Cope, 1938), the majority originating in the region of the caecum. Other less common sites are the stomach, duodenum, genito-urinary tract, and colon. The sigmoid colon is a very rare site of infection, and this is why we decided to report the present case.

REVIEW OF CASES

During the past 20 years 7 cases of abdominal actinomycosis have been treated at Manchester Royal Infirmary. The total number of cases of actinomycosis treated at the same hospital during this period was 13. This represents an unusually high proportion with the primary site of infection in the abdomen, which is probably explained by the fact that the cervical cases would most probably have been referred to a dental hospital. Of the 7 cases, 5 originated in the appendix, 1 in the sigmoid colon, and 1 in either the gall-bladder or the duodenum. In all these cases the diagnosis was confirmed by growth of the actinomyces on culture or by the discovery of the typical colonies in histological sections. Suspected cases not confirmed by either histology or bacteriology have not been included.

CASE REPORTS

Case 1.—A 29-year-old housewife was admitted to Manchester Royal Infirmary in September, 1970, complaining of pain in her left iliac fossa which had persisted for 4 months. She had lost about 3 kg. in weight but there was no change in bowel habit. Her only other complaint was of mild frequency of micturition. On examination she was very pale with a temperature of 38° C. Palpation of her abdomen revealed a firm tender mass, 10 cm. in diameter, in her left iliac fossa. The mass was fixed to the left side of her pelvis and rectal examination revealed a tender swelling in the pouch of Douglas on the left side. The haemoglobin was 10·3 g. per cent and the white-cell count was 12,000 c.mm. with a normal differential. A midstream specimen of urine showed no pus cells.

A laparotomy was performed on 14 Sept. through a left lower paramedian incision. A fixed mass was found in the left iliac fossa adherent to the side-wall of the pelvis and involving the sigmoid colon. The left Fallopian tube and ovary were not involved, but the transverse colon and omentum were tethered to the upper margin of the mass. The mass itself was composed of dense fibrous tissue and contained multiple abscesses. The nature of the pathology was not clear from the macroscopic appearance. The abscesses were drained and specimens of the pus were sent for culture. Portions of the walls of the abscesses were sent for histological examination by frozen and paraffin sections. The frozen sections were reported as showing non-specific acute inflammation. The wound was closed and the area drained through a separate stab incision. No 'sulphur granules' were seen at this time. Bacteriological studies showed Gram-positive cocci which failed to grow on culture. The biopsies revealed acute abscesses with surrounding granulation tissue and mature fibrous tissue. No specific granulomata were seen.

Postoperatively the patient was given 2 pints of blood and started on penicillin, 1 MU. 6-hourly, and streptomycin, 0·5 g. twice daily intramuscularly. As bacterial cultures were sterile antibiotics were discontinued after

5 days, by which time her temperature was normal. The wound healed well and she was allowed home 10 days later on no specific treatment. She was seen for follow-up on 6 Nov., when she still complained of a dull ache in her left iliac fossa. Her haemoglobin and white-cell count were normal at this stage and a barium-enema examination, although showing no specific abnormality, revealed some rigidity and atypical irregularity in the sigmoid colon. The radiologist suggested that she might have Crohn's disease. She attended again on 11 Dec., when she complained of a recurrence of the swelling in her left iliac fossa with a discharge from the site of her previous drain. She was started on ampicillin, 250 mg. four times a day orally, and was seen a week later when her condition was unchanged. One month later the mass was larger and she was admitted to hospital for the second time. She was again pyrexial with a temperature of 37·8° C., but her white-cell count was only 10,300 c.mm. Her haemoglobin had dropped to 12·1 g. per cent. Her erythrocyte sedimentation rate was 95 mm. in the first hour. A colonoscopy was carried out and no abnormality was seen to the limit of the examination. The instrument could not, however, be passed beyond the distal sigmoid colon owing to the rigidity of this part of the bowel.

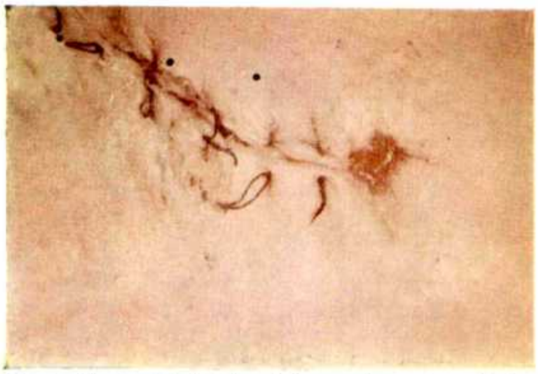

FIG. 1.—*Case* 1. The incision of the second operation with the sinus and granulations.

A second operation was performed on 28 Jan., 1971, when the sinus at the previous drain site was excised and an abscess involving the full thickness of the abdominal wall was opened. Yellow granules were noted in the pus and a clinical diagnosis of actinomycosis was made. The abscess was drained and after multiple biopsies had been taken the wound was closed around a corrugated drain (*Fig.* 1). The clinical diagnosis was confirmed both on culture and histological examination (*Figs.* 2, 3). The organism was found to be sensitive to penicillin, tetracycline, and erythromycin. She was therefore started on long-term penicillin therapy, 1 MU. 6-hourly intramuscularly for the first week, 1 MU. 12-hourly intramuscularly for 1 week, followed by 1 MU. daily intramuscularly as an out-patient for 1 month. This was supplemented by oral penicillin 'V', 250 mg. four times a day for 2 months. Her erythrocyte sedimentation rate, which was 111 mm. per hour at the time of the second operation, returned to normal limits after 2 weeks of treatment and after 2 months of treatment all traces of the mass had disappeared and the sinus had not recurred. Her liver-function tests at the height of the infection had shown a reversal of the albumin/globulin ratio (albumin, 2·8 g. per cent; globulin, 5·1 g. per cent), suggesting involvement of the liver by the fungal infection. At the end of the course of treatment her liver-function tests had returned to normal.

Case 2.—A female, aged 21 years, presented with a 2-month history of pain in her right groin preceded by 3 months' general malaise. Three weeks before admission she had developed a swelling in her right iliac fossa which had started to discharge after a week. On examination she was found to have a mass, 8 cm. in diameter, in her right groin which was discharging yellow pus. No granules were found in the pus which on first culture failed to reveal *Actinomyces*. Her haemoglobin was 7 g. per cent and her white-cell count was 15,000 c.mm. with 89 per cent of polymorphs. At operation the abscess was drained and culture of the pus revealed actinomycosis. She was given a 2-month course of soluble penicillin, 2 MU. daily, following which the sinus healed.

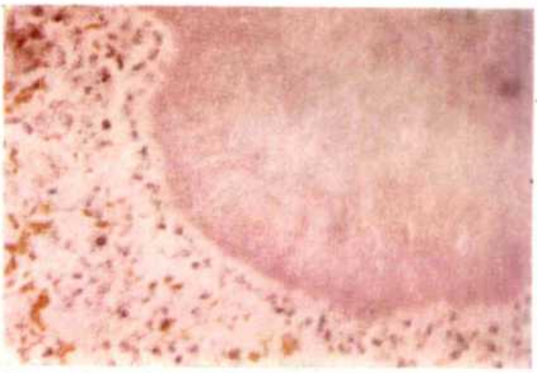

FIG. 2.—*Case* 1. Section of the sulphur granule, demonstrating how the name 'ray fungus' arose.

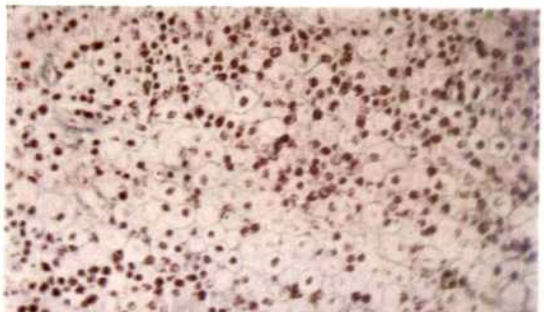

FIG. 3.—*Case* 1. Section showing the typical foamy macrophages seen around the lesions.

Case 3.—A female, aged 27 years, gave a long history of recurrent attacks of small-bowel obstruction for which she had had three operations prior to her presentation in May, 1951. Examination of her abdomen at this time revealed abdominal distension with a palpable mass in her right iliac fossa. At laparotomy there was a mass in the caecum. Biopsies were taken and an ileotransverse anastomosis was performed. The biopsies revealed no specific abnormality and a provisional diagnosis of either Crohn's disease, or carcinoma, or tuberculosis was made. In November of the same year she returned with a discharging sinus in her right iliac fossa and at this time 'sulphur granules' were seen in the pus. A diagnosis of actinomycosis was made. She was therefore started on soluble penicillin, 1 MU. daily intramuscularly. Unfortunately, she died shortly afterwards.

Case 4.—A female, aged 30 years, presented with a 6-week history of general malaise and pain in the right iliac fossa. On examination there was a palpable mass in her right iliac fossa. At laparotomy the appendix was found to enter a mass which contained a moderate amount of pus. The abscess was simply drained and she was started on 1 MU. of penicillin twice daily intramuscularly which was continued for 2 months. Culture of the pus confirmed the diagnosis of actinomycosis. The sinus cleared up permanently after 3 months.

Case 5.—A male, aged 41 years, presented in 1953 with history of pain in his right hypochondrium and dyspnoea. His temperature was 38·5°C. and a diagnosis of acute cholecystitis was made. Subsequently, however, the gall-bladder was found to function normally on radiography. Whilst in hospital he developed a fluctuant swelling in his right flank which was thought to be a perinephric abscess. This was drained and culture of the pus grew a non-haemolytic streptococcus. He was put on streptomycin intramuscularly. In 1957 he developed a recurrence of the pain in his right hypochondrium and was put on the waiting list for cholecystectomy. Before this could be done he was admitted as an emergency with an area of cellulitis over his right costal margin. He was put on penicillin therapy and the area was aspirated on three occasions with negative culture. Following this, the area was explored and the abscess drained. Culture on this occasion grew only a non-haemolytic streptococcus. In 1959 the abscess recurred. It was explored more thoroughly and was found to track subdiaphragmatically. Culture of the pus on this occasion revealed *Actinomyces*. He was put on repeated courses of penicillin intramuscularly. After three further flare-ups of the infection the condition subsided.

Case 6.—A male, aged 17 years, had an appendix abscess drained in November, 1953, at which time it was impossible to remove the appendix. In January, 1954, an operation was performed to remove the appendix which was adherent to the bladder. The appendix was successfully removed but the wound discharged yellow pus post-operatively. The discharge persisted until May, 1954, when another abscess developed in his left lumbar region. This was drained and revealed thick yellow pus which grew *Escherichia coli*, non-haemolytic streptococcus, and *Staphylococcus aureus*. Without antibiotic therapy the discharge from his appendix wound and the lumbar abscess subsided. In July, 1954, he developed an abscess in his sacral region. This abscess was aspirated and revealed *Actinomyces*. He was started on penicillin, 1 MU. intramuscularly twice daily. After 1 month of treatment the sinus finally healed.

Case 7.—A male, aged 13 years, gave a 2-week history of diarrhoea following which he had developed an abscess in his right groin. A diagnosis of inguinal lymphadenitis was made and he was started on penicillin 600,000 U. daily. The abscess failed to subside and 1 month later was drained, revealing *Actinomyces*. Streptomycin was added to the penicillin therapy and the abscess cleared up. Three years later he was admitted with acute appendicitis. At operation the appendix was found to be adherent to the scar of the previous drainage wound in the groin. Following the removal of the appendix he made a good recovery.

DISCUSSION

Pathogenesis of Abdominal Actinomycosis.—The organism responsible for abdominal actinomycosis is an anaerobic, Gram-positive, branching filamentous fungus which is related in many respects to bacteria. *Actinomyces israeli* is a common saprophyte in the mouth and gastro-intestinal tract, the endogenous nature of the infection being virtually beyond doubt. Slack (1942), who examined 100 pairs of tonsils from routine tonsillectomies, found colonies of anaerobic actinomycetes in 14 per cent of cases. The organism enters the abdominal cavity from the alimentary tract in the majority of cases and infection from the genital tract, diaphragm, or blood-stream is extremely rare (Cope, 1938). The actinomycetes cannot penetrate healthy mucosa and damage to the mucosa by trauma, disease, or surgery is an essential prerequisite to infection. Having penetrated the bowel, the organism proliferates, leading to the production of a mass of dense, almost woody, fibrous tissue. Areas of this mass usually undergo softening with the production of abscesses, which may rupture through the abdominal wall producing sinuses, penetrate into adjacent viscera causing fistulae, or rupture through the diaphragm leading to pulmonary actinomycosis. Lymphatic spread in actinomycosis does not occur, presumably because of the large size of the filaments; lymphadenitis is due to the secondary infection which is very common. Blood spread, however, is quite common and hepatic involvement via the portal vein leads to the typical 'honeycomb' liver.

Actinomycotic pus consists of a dense infiltration of mainly polymorphs, in the centre of which are colonies of actinomycetes forming the 'sulphur granule'. This sulphur granule or mycelium tends to be surrounded by club-shaped excrescences which radiate outwards, giving rise to the alternative name of 'ray fungus'. These clubs are not formed in artificial culture and are produced by deposition of host lipid on to the mycelium (Walter and Israel, 1963).

Abdominal Localization.—Apart from the neck, the abdomen is the commonest site for actinomycosis, accounting for one-fifth of the cases (Cope, 1938). The ileocaecal region is the usual site as a result of a perforated appendix, but no site is immune.

Stomach and Duodenum.—Perigastric actinomycosis occurs only when the gastric mucosa is diseased or after gastric surgery. The actinomycetes cannot survive in a healthy stomach (Cope, 1938). Nathan (1929) reviewed gastric actinomycosis and described a fatal case which was found to have a large callous ulcer penetrating into the liver and pancreas. He attributed the rarity of the infection in this site not to gastric acidity but to vigorous motility preventing the fungus from settling. Cope (1938) believed that perforation of the mucosa was essential. Perigastric actinomycosis occurs in two circumstances: either associated with a perforated ulcer or following gastric surgery. A common feature in all the cases described is a latent period before the onset. Till (1946) described a case presenting 4 months after a perforated gastric ulcer. More recently Pheils, Reid, and Ross (1964) and Ashton and Slaney (1963) have described cases following gastric surgery. The infection in Ashton and Slaney's case complicated a leaking duodenal stump. Again a long latent period was noted. A rare complication of gastric actinomycosis was reported by Wilson (1961), who described pyloric stenosis following infection in the antrum. The stenosis responded dramatically to parenteral penicillin and sulphadiazine.

Gall-bladder and Pancreas.—Invasion of the pancreas and biliary tree by the fungus is extremely rare. The pancreas most probably becomes infected by direct spread from the stomach or duodenum owing to penetration by a peptic ulcer. Fontan, Serrano-Rios, Navarro, Oliva, and Ramirez (1969) described a fatal case in a 62-year-old man who had multiple actinomycotic abscesses in the pancreas and liver. The present *Case* 5 probably represents a case of actinomycotic cholecystitis and we have found only

2 other established cases in the literature (Mayo-Robson, 1905; Rewerts, 1964). The mode of infection of the gall-bladder by the fungus is less well understood. Mayo-Robson (1905) felt that infection did not occur via the skin, blood-stream, or lymphatics or by direct spread from the gut as no other lesion was present in his case. He believed that the infection reached the gall-bladder by retrograde spread up the bile-duct from the duodenum. Cope (1938) pointed out that once the organism has penetrated the bowel the mucosa heals and may show no sign of the initial infection, so that this is the most likely route of infection in actinomycotic cholecystitis.

Jejunum and Ileum.—The extreme rarity of actinomycosis in these regions has been explained by the rapid passage of the small-bowel contents. A more important reason may be the infrequency of penetrating lesions of the mucosa. A feature of the infection is the relatively normal appearance of the bowel at operation, the bulk of the inflammation occurring in the mesentery. Rigler (1964) described a case occurring in the ileum following perforation by a fish bone, and stressed the importance of complete excision where possible.

Ileocaecal Region.—This was the commonest site in the present series, as was also found in other reports (Cope, 1938). The source of infection in virtually all the cases is the appendix, 'periappendicular actinomycosis' being a more accurate name. The most interesting feature is the differing modes of presentation, which explain why this well-recognized condition is so often misdiagnosed. Cope (1938) classified pericaecal actinomycosis into two clinical types: (1) those which start with an attack of acute, usually perforated appendicitis; (2) those which start insidiously and first reveal themselves by the presence of a lump. He considered the former to be the commonest mode of presentation and certainly most of the cases described in the literature have come to light following an acute appendicitis (Wilson, 1961; Duncan, 1965). It is interesting that none of the cases in our series was of this type. Four presented as a mass in the right iliac fossa and 1 as recurrent attacks of small-bowel obstruction. After the disease has become established in this region, unless it is treated, it progresses in a classic way irrespective of its mode of presentation, with the formation of a hard craggy mass with associated sinuses or fistulae.

Colon.—Apart from the caecal region colonic actinomycosis occurs most frequently in the transverse and sigmoid regions. Because of the rarity of the disease in these sites the diagnosis is usually made late, a presumptive diagnosis of carcinoma, diverticular mass, or Crohn's disease usually being made. Palmisano and Russin (1969) and Salmo, Rudolf, and Makki (1969) both described cases occurring in the transverse colon. In the latter case a preoperative diagnosis of carcinoma of the stomach was made; it was only after resection of the affected colon that the diagnosis came to light. Actinomycosis of the sigmoid colon is even rarer, but previous cases have been described by Cope (1938) and Piper, Stoner, Mitra, and Talerman (1969). The rarity in this region is difficult to understand as perforation of the bowel secondary to diverticular disease and carcinoma occurs most commonly in the sigmoid colon. An even more difficult fact to explain is the rarity of the infection following perforation of diverticula anywhere in the colon. We were unable to find any cases of actinomycosis following perforated diverticulitis. Although no cases of vesicocolic fistula have been recorded complicating actinomycosis, Piper and others (1969) described a case of ileovesical fistula which they attribute to actinomycosis arising in the sigmoid colon.

Anorectal Region.—Actinomycosis may arise primarily in the rectum and anal canal or may involve the perirectal tissues secondarily by downward spread from the iliac fossa. As would be expected, the infection tends to flourish in the loose tissues of the ischiorectal fossa, with a tendency to spread posteriorly rather than anteriorly (Morson, 1961). Perirectal actinomycosis may, therefore, come to light as an abscess in the buttock which recurs after drainage. A further progression of this local spread may explain the sacral abscess in the present *Case* 6 following actinomycosis in the right iliac fossa.

A special type of anorectal actinomycosis which took the form of an indurated ring at the anorectal junction was described by Morson (1961). He suggested that all rectal strictures should be biopsied to exclude this infection. Finally, a case of primary actinomycosis of the rectum was described by Fry, Martin, Dearing, and Culp (1965) in association with multiple perirectal and perianal fistulae, features which would lead most clinicians to suspect Crohn's disease.

Diagnosis.—Actinomycosis is one of the great imitators in clinical practice, particularly when it occurs in the abdominal cavity. Whilst reviewing cases presented by previous authors one is impressed by the length of time between the onset of symptoms and the final diagnosis. Our series is no exception to the rule as the average time to diagnosis was 18 months, ranging from 1 week to 6 years. Although the modes of presentation were varied there were certain features which, if borne in mind, may lead one to suspect the condition. The majority of cases demonstrates the 'latent' period referred to earlier, the symptoms following weeks or months after an abdominal catastrophe, which often involves perforation of the gut, or abdominal surgery. This may help to distinguish the condition from carcinoma, diverticular disease, and Crohn's disease.

A persistent discharging sinus, particularly following surgery for a perforated viscus, should always suggest the diagnosis, but unfortunately bacteriological study of the discharge may well be negative in the first instance. Even when specifically sought the classic colonies are difficult to culture, particularly as secondary infection of the abscess with such organisms as *E. coli* and staphylococci is so common. If visible macroscopically the 'sulphur granules' are pathognomonic but these are not always present, e.g., in only 5 of 13 cases at Manchester Royal Infirmary. Biopsy of the walls of sinuses or abscesses may also be fruitless, being reported on numerous occasions as showing 'non-specific' inflammation.

Constitutional disturbances, although non-specific as far as diagnosis is concerned, may be particularly severe in actinomycosis. Pyrexia is common in the early stages but is often masked by antibiotic therapy. Microcytic anaemia is a constant feature. Although

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the erythrocyte sedimentation rate is often raised above 100 mm. in the first hour, its value lies in monitoring the response to treatment rather than in diagnosis. Weight-loss usually occurs if the disease is widespread but again is not specific.

The diagnosis of actinomycosis rests almost entirely on the discovery of the typical colonies in pus obtained from the abscesses, but one must not scorn the pathologist for failing to see them initially if the possibility of their presence was not suggested by the clinician.

Treatment.—The first treatment for actinomycosis was surgical extirpation, and surgery still has a place today. Originally the aim was complete extirpation of the disease, which in most cases is impossible. Nowadays surgery is usually limited to incision and drainage with curettage of large abscesses. However, as recently as 1965 Duncan stressed the importance of an aggressive surgical approach in abdominal actinomycosis. Iodine was the first therapeutic agent to be used, and a palatable dosage of 5 minims in milk three times a day was suggested by Chitty (1926). It may still be a useful adjunct to the more usual therapy. The polyvalent actinomyces vaccine has been used as a specific therapeutic agent in the past. Placa, Proca, and Tomas (1966) revived its use in an abdominal case with success, following failure of antibiotic therapy. Its use nowadays lies in diagnosis in cases with negative biopsies. Following intracutaneous injection of 0·1 ml. of graded dilutions of the vaccine a local allergic reaction results in cases of actinomycosis (Bronner and Bronner, 1969). Radiotherapy has been used for its effect of softening fibrous tissue, but is not now used, mainly because of its effects on adjacent viscera.

With the advent of sulphonamides the prognosis of actinomycosis rapidly improved. Walker (1938) was one of the first to describe its use, suggesting a dosage of 1 g. three times a day. Since penicillin was first used no better treatment has been found. If penicillin is administered in the correct dosage it cures virtually every case. All the cases in our series were treated by penicillin with cures in all but 1. When first introduced, a daily dosage of up to 10 MU. intramuscularly was recommended. This was very painful, required prolonged hospitalization, and has recently been shown to be quite unnecessary. A reasonable dosage is 2 MU. daily by intramuscular injection continued for 1–2 months after all clinical evidence of the infection has settled. In fact, our *Case* 1 was treated successfully with a considerably lower dosage, converting to oral penicillin in the later stages of the treatment. A feature of treatment that cannot be overstated is the necessity to continue the therapy for long periods after clinical extirpation of the infection. The cases showing a recrudescence of the disease after short-term therapy are legion.

Recently writers have described the use of other antibiotics in the treatment of abdominal actinomycosis with equally good results (Martin, Nichols, Wellman, and Weed, 1956; Svane, 1966; Halter, 1967). The use of more expensive and more toxic antibiotics appears to be unnecessary unless there is an allergy to penicillin or, as very rarely occurs, a resistant strain of fungus is encountered.

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UNABSORBABLE SUTURE MATERIAL—A RARE CAUSE OF RECURRENT STONES IN THE COMMON BILE-DUCT

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SUMMARY

Three cases are reported in which unabsorbable suture material used to ligate the cystic duct at cholecystectomy was subsequently found within the lumen of the extrahepatic bile-ducts. In 2 cases well-formed gall-stones having a central nucleus of either silk or nylon were removed from the common bile-duct. In the third case two braided nylon sutures were found within the stump of the cystic duct. The use of absorbable suture material for ligating the cystic duct is therefore recommended.

MOST authorities believe that the majority of gall-stones found in the common bile-duct was originally formed in the gall-bladder (Smith and Sherlock, 1964). Thus, following cholecystectomy any stone found within the common bile-duct usually represents either failure to explore the bile-duct or failure to remove all the stones from the bile-duct at the original operation. Such stones therefore are commonly referred to as residual rather than recurrent.

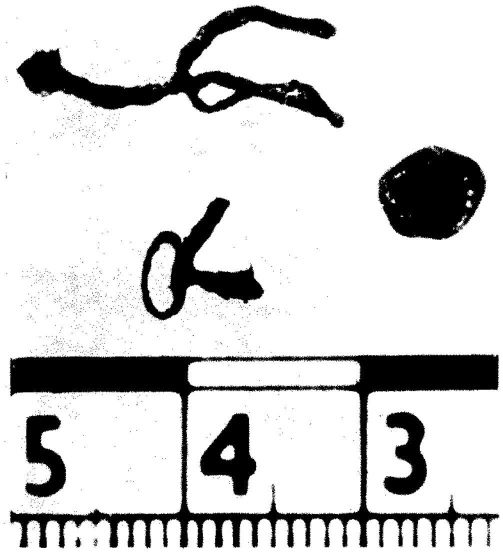

FIG. 1.—*Case* 1. Two braided nylon sutures and residual stone removed following re-exploration of the common bile-duct.

The purpose of this report is to record 3 instances in which unabsorbable suture material used to ligate the cystic duct at cholecystectomy was subsequently found within the lumen of the extrahepatic bile-ducts. In 2 cases a gall-stone formed *de novo* around a nucleus of either silk or nylon, whilst in the third case two nylon sutures encrusted with calcareous material were removed from the stump of the cystic duct.

CASE REPORTS

Case 1.—Mrs. M. J., aged 70 years, presented in 1969 with a 7-year history of recurrent epigastric pain radiating to the back. She had been jaundiced on one occasion and a cholecystogram confirmed the presence of gall-stones. At cholecystectomy numerous stones were palpated in the common bile-duct and a formal exploration was undertaken. The bile-duct was sutured with 000 catgut around a T-tube. The cystic duct, however, was ligated and transfixed with two braided nylon sutures. Her recovery was satisfactory and a postoperative T-tube choledochogram was normal.

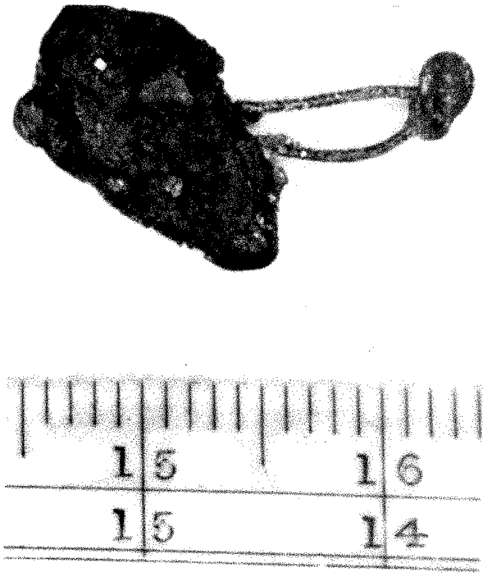

FIG. 2.—*Case* 3. Gall-stone having a central nucleus of monofilament nylon removed from the common bile-duct at the second exploration.

One year later the patient returned complaining of episodic epigastric pain during the preceding 3 months. No abnormality was found on examination and an intravenous cholangiogram demonstrated a dilated common bile-duct but no definite calculi were seen. Re-exploration of the bile-duct was performed and a residual stone was removed from the lower end. In addition, two braided nylon sutures were found within the lumen of the stump of the cystic duct and both were heavily encrusted with calcareous material (*Fig.* 1). A side-to-side choledochoduodenostomy was performed. Her postoperative recovery was smooth. The stone was examined and no suture material was found within it. The patient has remained well since.

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Case 2.—Mrs. E. F., aged 54 years, was admitted to hospital for elective cholecystectomy in 1967 following recurrent bouts of biliary colic over a 10-year period. During one episode she had become jaundiced. At cholecystectomy numerous gall-stones were present in the gall-bladder but a peroperative choledochogram demonstrated a normal narrow segment, free flow of contrast into the duodenum, and no evidence of stone in the common bile-duct. The gall-bladder was removed and the cystic duct was tied with a silk ligature. Her postoperative recovery was satisfactory.

In 1969 the patient was investigated on account of further abdominal pain, and an intravenous cholangiogram demonstrated an enlarged common bile-duct with a suspicious filling defect in the distal portion of the duct. Exploration of the common bile-duct was advised and at operation one stone was removed. The stone was crushed and a silk ligature was found within it. Her postoperative recovery was uneventful and she has had no further symptoms.

Case 3.—Mrs. E. G., aged 73 years, was admitted to hospital as an emergency in December, 1970, with a history of recurrent episodes of epigastric pain radiating through to the back. Six years previously she had undergone cholecystectomy with exploration of the common bile-duct at a military hospital in Germany. Her postoperative recovery had been uneventful and the postoperative choledochogram had demonstrated a normal common bile-duct.

On examination the patient was both febrile and jaundiced but no abnormality could be found in the abdomen. Biochemical investigations confirmed the clinical impression of obstructive jaundice. Subsequently the jaundice resolved spontaneously and an intravenous cholangiogram demonstrated stones within the common bile-duct.

At operation the common bile-duct was enlarged and some monofilament nylon suture material was found adherent to the anterior surface of the duct. A transduodenal exploration of the common bile-duct was performed together with sphincteroplasty; two large and several smaller stones were removed. The two large stones were crushed and in the middle of one a monofilament nylon suture was found (*Fig.* 2). Her postoperative recovery was uneventful and she has remained well.

DISCUSSION

A residual stone in the common bile-duct following cholecystectomy is a distressing but potentially avoidable complication. The importance of operative cholangiography in detecting unsuspected stones in the common bile-duct is now well established (Ferris and Weber, 1956; Le Quesne, 1960), and when operative cholangiography is used routinely in all cases the incidence of residual stones is greatly reduced. Thus, Harvard (1970) reported residual stones in only 5 out of 300 consecutive operations for calculous biliary tract disease. In all 5 cases residual stones occurred in ducts which had previously been explored. This emphasizes the frequent difficulty experienced in interpreting postexploratory cholangiography. The stone removed from the common bile-duct in the present *Case* 1 was faceted (*Fig.* 1) and when crushed no suture material was found. We suggest that this stone was one of the many originally formed in the gall-bladder and that it was thus a residual gall-stone.

Although a previously inadequate operation is undoubtedly the main aetiological factor in residual choledocholithiasis there have been spasmodic reports of recurrent stones forming around unabsorbable suture material (Homans, 1897; Rains, 1961). Despite this there is no unanimity of opinion in surgical textbooks with respect to the most suitable material for ligating the cystic duct. Both Maingot (1969) and Rob and Smith (1969) recommend catgut whereas Gardham and Davies (1963), Rains (1964), and Farquharson (1969) advocate unabsorbable suture material.

The first case reported here was the only instance in which the cystic duct was both transfixed and ligated. Transfixion of necessity introduces the suture material into the lumen of the duct and this may have been a factor favouring the extrusion of the two braided nylon sutures into the cystic duct stump. Once within the bile-duct such material forms an ideal nucleus around which bile, pigment, and cholesterol may aggregate to form a recurrent stone (*Cases* 2 and 3). However, as judged by the scarcity of reports in the literature such stone formation is most unusual. Thus, if ligature extrusion occurs with any frequency it must be assumed that the majority passes harmlessly into the duodenum. Nevertheless the routine examination of recurrent gall-stones may demonstrate that this form of choledocholithiasis occurs more frequently than expected. We suggest that the use of an absorbable suture material for ligating the cystic duct would further reduce the incidence of this rare complication.

Acknowledgements.—We should like to thank Mr. J. W. P. Gummer and Mr. W. W. Slack for permission to publish details about cases who were under their care, and Professor L. P. Le Quesne for his helpful advice.

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OPEN SKIN-GRAFTING IN DEVELOPING COUNTRIES

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SUMMARY

Because of the poor condition of most granulating wounds and the unpredictable and frequently unsatisfactory results of closed skin-grafting, 160 open skin-grafting operations were performed and studied in Egypt and Jordan in order to develop a reliable procedure for use in developing countries. A simple, economical, and successful open grafting method was established. The results are given together with the details of 4 illustrative cases. Important technical points are mentioned. The necessity of the application of open grafts on patients in developing countries is stressed and the advantages of the author's method are discussed.

In some developing countries it is distressing to see many patients with chronic, ungrafted, granulating wounds following deep burns and other forms of traumatic skin-loss. These wounds are frequently associated with cachexia, anaemia, and toxaemia and are often complicated by troublesome deformities and disabling contractures. Such patients occupy hospital beds for months and act as reservoirs for cross-infection.

This unhappy state is mainly due to the poor condition of granulations produced under unfavourable conditions and the prevalence of sepsis. The results of closed grafting techniques are frequently unsatisfactory and, indeed, many patients are denied the benefits of grafting because of the lack of consistently successful grafting procedures under these circumstances.

For these reasons open skin-grafting has been practised by the author in two developing countries (Egypt and Jordan) in an attempt to perfect a reliable method that can be routinely applied even when conditions are unfavourable.

MATERIALS

One hundred and sixty open grafting operations were performed by the author in Egypt and Jordan. About 60 per cent of the cases were due to full-thickness burns; the rest were caused by other forms of traumatic skin-loss. This series includes wounds in all anatomical regions. The trunk was involved in 32 per cent of the cases, the head and face in 6 per cent, the neck in 13 per cent, the upper extremity in 34 per cent, the hand in 10 per cent, the lower extremity in 49 per cent, the scrotum in 1 case, the penis in 1 case, and the orbital socket after exenteration in 1 case. The age of the granulations ranged from 10 days to 3 years; in 37 per cent of the cases the granulations were more than 2 months old.

The patients were operated on in 4 different hospitals in Cairo and Amman. A large number of them were referred from other territories of Egypt and Jordan and therefore this group could be considered to be representative of these two countries.

Clinical infection in the form of purulent discharge was present to a variable extent in almost all the cases. Many patients were referred in poor condition; they had received very little local wound care and were potentially contaminated with many pathogenic organisms. Bacteriological studies were not carried out because facilities were not readily available in most instances, but based on circumstantial evidence and on clinical grounds mixed infection appeared to be prevalent, Gram-negative organisms, particularly *Pseudomonas pyocyaneus*, predominating.

Sepsis, unless obviously severe, was not considered a contra-indication to open grafting, especially when the granulation tissue possessed reasonable vascularity. Complete eradication of sepsis was not usually practical, but when considerable suppuration was present daily cleansing of the wounds and the application of wet Eusol absorptive dressings were carried out before operation to reduce the discharge. When Sulfamylon became available, it proved very helpful in preparing grossly septic cases for grafting. Antibiotics, mostly penicillin, streptomycin, tetracycline, or chloramphenicol, were given before and after operation to help minimize sepsis.

METHODS

Split-thickness skin-grafts were removed under general or local (ethyl chloride) anaesthesia according to the circumstances of each case. When local anaesthesia was used the whole operation was performed as a bedside procedure (Gibraiel, 1971). When general anaesthesia was employed only the process of removal of the grafts was carried out in the operating theatre and the granulating wounds were left undisturbed. The skin thus procured was kept until application in an ordinary refrigerator at above 0° C. After this short procedure of skin removal the patient was returned to his ward, and when he became fully conscious the grafts were applied to the granulating areas to avoid displacement of the grafts during recovery and transport and to gain the patient's co-operation and assistance during their application. This latter process was carried out by a 'clean' but not necessarily sterile technique. The skin was put directly on the raw areas without preparation, i.e., no shaving or curettage of the granulations was done. No sutures or any other devices were used to fix the grafts. The latter were left completely exposed. With simple and reasonable measures it was possible to achieve adequate exposure of almost any region of the body.

After operation the exposed grafts were managed in the usual way (Muir and Barclay, 1962; Blocker, 1964; Converse and Brauer, 1964; Cannon and Murray, 1966; Moncrief, 1966; Artz and Moncrief,

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1969). Dressings were usually applied at about 4–7 days after operation, but in cases with excessive marginal discharge and/or encrustation, exposure was discontinued as early as the third postoperative day without detriment to the taking of the graft.

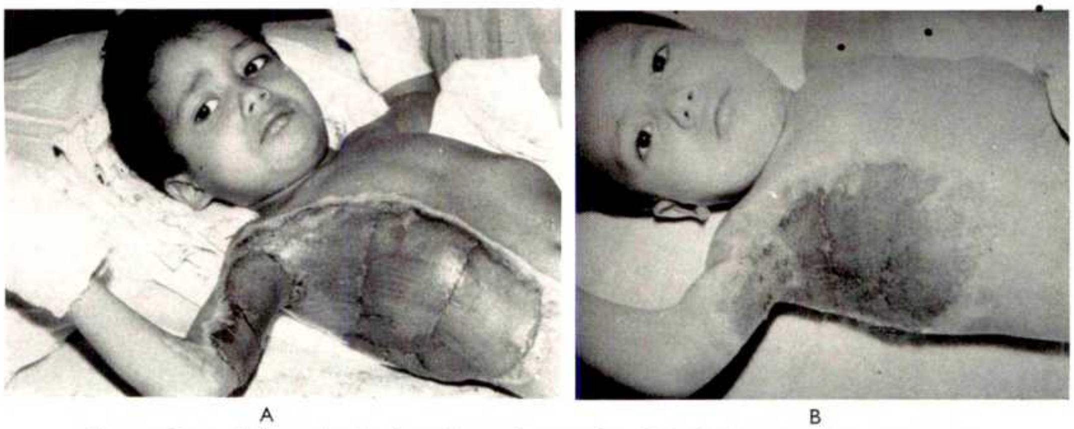
FIG. 1.—*Case* 1. A, Exposed grafts about 48 hours after operation. B, Result about 2 months after operation.

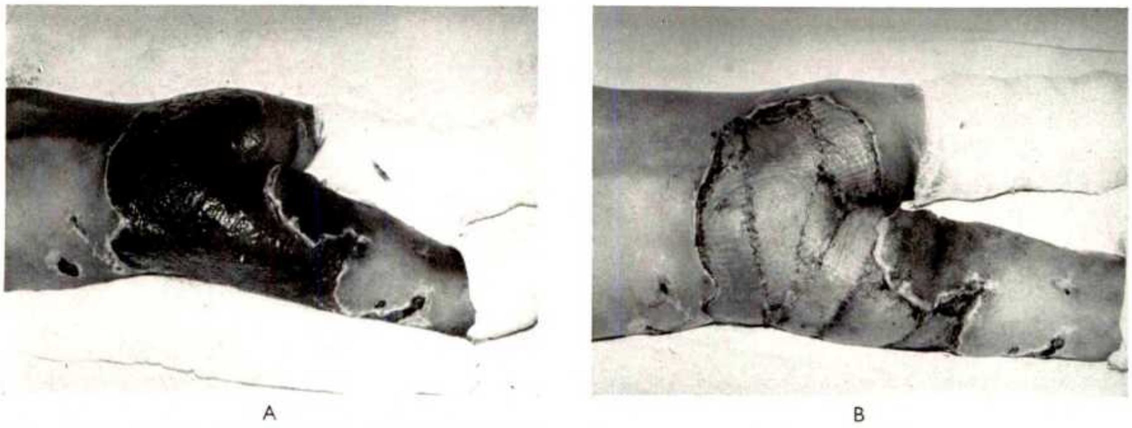
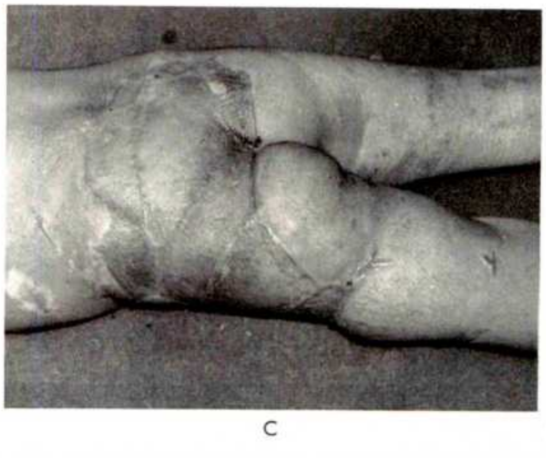
FIG. 2.—*Case* 2. A, Preoperative condition. B, Exposed grafts on the third postoperative day. C, Final result.

Very extensive as well as most circumferential granulating wounds were grafted in stages.

Patients were followed up for a period of 1–6 months after operation.

RESULTS

Grafting was successful in 150 cases (94 per cent). Excellent results (90–99 per cent take) were achieved in 132 cases (83 per cent). Failure occurred in 10 cases (6 per cent), most of these being amongst the early cases. Causes of grafts not taking were recognized in each case and were found to be avoidable with reasonable precautions so that an excellent take was achieved in the following 60 cases. Causes of failure were:—

1. Gross sepsis (5 cases). When the purulent discharge was fairly excessive, it was possible to achieve a good take by the frequent evacuation of the subgraft discharge in the first 48 hours after operation and by the administration of pre- and postoperative antibiotics.

2. Severely fibrotic ischaemic granulations (2 cases). Chronicity *per se* was not a cause of failure since an excellent take was achieved in many cases with chronic granulations of up to 3 years old. Failures due to this reason were later avoided by the application of the homograft test (Moncrief method) to the doubtful chronic cases, and in the event of failure of this test either the whole wounds were excised or the old granulations were pared off and

grafting was performed when young vascular granulations had developed.

3. Mechanical displacement of the grafts (2 cases). Further losses due to this reason were avoided by judicious restraining and proper positioning of patients and by good postoperative care.

4. Growth of numerous epithelial islands under the grafts was responsible for failure in 1 case of a deep partial-thickness burn which had been misdiagnosed as a full-thickness burn.

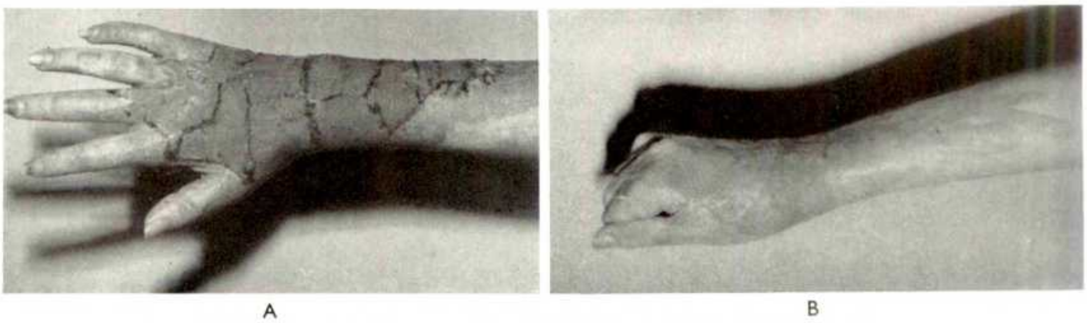

FIG. 3.—*Case* 3. A, Exposed grafts on the fifth postoperative day. B, Final result.

TECHNICAL CONSIDERATIONS

Certain technical points were found of importance for the successful application of open grafting in developing countries.

Vascularity of the granulations as assessed clinically by their colour was found to be the most important factor in determining the success of open grafting. The following methods proved to be very helpful in improving the vascularity of pale granulations before operation: (1) daily wet Eusol dressings, (2) Sulfamylon dressings, (3) improving the general condition of the patient with blood transfusions in particular, and (4), in difficult cases with very poor ischaemic granulations, removal of these granulations and waiting for the development of new vascular granulation tissue.

Because of the prevalence of sepsis the granulations should not be exposed in the operating theatre in order to avoid soiling theatre equipment and contaminating donor sites. Therefore the total surface area to be grafted should be roughly estimated in the ward 1–2 days before operation so that enough skin can be taken at operation. In general it is preferable to take an excess amount of skin-grafts to ensure complete coverage of all the granulating wounds; the rest can be stored in the refrigerator for possible use at a later date.

The grafts should be as thin as possible and in large sheets as these were found to be more suitable for exposure on granulating wounds.

Children and uncooperative patients should be adequately restrained in bed before the application of the grafts. Restraint should be continued as long as the grafts are exposed in order to prevent their displacement. However, if the grafts are dislodged they can be replaced with excellent chances of survival provided that the grafts remain supple and moist.

CASE REPORTS

Case 1.—M. A. K., a male child of 3½ years, was referred to the Cairo Institute for Burns on 14 June, 1970, because of an extensive septic granulating area of his trunk, right axilla, and right upper arm following a burn injury about 2 months previously. The granulations looked adequately vascular despite obvious suppuration. Thin split-skin grafts were removed from both thighs under general anaesthesia, were applied to the raw areas with the patient in bed, and were kept exposed for 1 week. About 48 hours after operation (*Fig.* 1 A) the grafts were well fixed and vascularized. Almost full take of the grafts was finally achieved. *Fig.* 1 B shows the result about 2 months after operation.

Case 2.—O. M. B., a male child of 8 years, was admitted to Ashrafieh Surgical Hospital on 3 May, 1971, following a car accident in which he had sustained a crush injury of his lower back, buttocks, anal and perianal regions, and left thigh with extensive destruction of the skin and soft tissues. The case was managed initially with repeated excisional and débridement procedures. Because of heavy faecal contamination due to partial anal incontinence severe sepsis developed with abundant suppuration. This was partly controlled by systemic non-specific polyvalent antibiotics and by changing the dressings once or twice daily. On 29 May the granulations looked fairly satisfactory (*Fig.* 2 A) in spite of residual sepsis and were grafted. On the third postoperative day the graft take was almost complete (*Fig.* 2 B). *Fig.* 2 C shows the excellent result about 2 months after operation, by which time the patient was also fully continent.

Case 3.—N. A. Gh., a 17-year-old girl, was referred to the Plastic Surgery Service of Ashrafieh Surgical Hospital on 13 May, 1971, because of a granulating area of her right hand and forearm following a burn injury about 1 month previously. As a result of inexpert and inefficient local treatment received elsewhere the granulations were unhealthy and septic and the fingers were stiff in extension. After 2 days' preparation with Sulfamylon application and elevation of the extremity the condition of the wound had improved and open grafting was performed. The patient was encouraged to move her fingers slightly from the first postoperative day. On the fifth postoperative day all the grafts were taking very well (*Fig.* 3 A). Excellent healing was rapidly and simply achieved and good function of the right hand was restored (*Fig.* 3 B).

Case 4.—B. Kh. M., a 15-year-old boy, was admitted to Ashrafieh Surgical Hospital on 3 May, 1971, because of major burn injury. This had resulted in an extensive granulating area involving the chest wall, neck, left axilla, and left upper extremity (*Fig.* 4 A). The whole area was resurfaced in one procedure. An excellent take of all the grafts was achieved. *Fig.* 4 B shows the result of exposure on the fifth postoperative day.

DISCUSSION

Although open grafting is a well-known procedure, it is not popular in Egypt and Jordan because there is an impression that this method is unsuitable when the local and general conditions are unfavourable. However, it is under these circumstances that open techniques are helpful. Exposure of grafts is recommended when there is a poor recipient site (Artz and Moncrief, 1969), in heavily infected cases (Muir and Barclay, 1962), and when the condition of the granulating wound is uncertain (Cannon and Murray, 1966). Therefore the prevalence of sepsis and the poor and uncertain condition of most granulating wounds make exposure of grafts a necessity in developing countries.

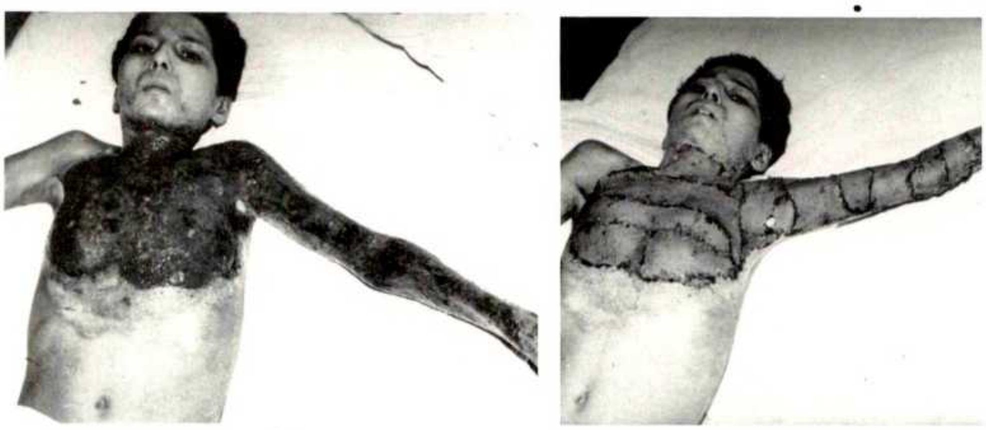

FIG. 4.—*Case* 4. A, Preoperative condition. B, Condition on the fifth postoperative day.

The validity of these statements has been confirmed by the present series. In the experience of the author the results of exposure were better when compared with closed grafting techniques which had been routinely performed before this work was undertaken. This could be attributed to the following reasons:—

1. Sepsis was checked by the open method which provided conditions of dryness, coolness, and exposure to light—factors which are unfavourable to bacterial growth.

2. Exposed grafts were easily observed and any harmful subgraft discharge was readily evacuated.

3. When closed grafting was employed it was necessary to curette or shave the septic granulations, the resultant ooze and possible haematoma formation being responsible for the loss of many grafts.

In general, open grafting is preferred by many authorities. In the experience of Artz and Moncrief (1969) most grafts take better when exposed than when put under a dressing. In describing the method of the United States Army Surgical Research Unit for the treatment of burns Moncrief (1966) states that grafting is better accomplished without covering dressings. Open grafting was mentioned as being used routinely by Blocker (1963). It is particularly indicated for the grafting of granulating wounds of the face, neck, trunk, shoulders, axilla, perineum, and buttocks in order to avoid the displacement of the grafts by the inevitable movement of these parts inside dressings (Muir and Barclay, 1962; Converse and Brauer, 1964).

The grafting method used by the a
following advantages:—

1. It is very well tolerated even b
burned patients and poor-risk indivi
very little anaesthesia is needed and
minimal since no curettage or shaving o
tions is done.

2. The method is very economical; it
time and medical supplies for other pati
them badly so that there is a more econ
hospital facilities which are often limite
ing countries.

3. Contamination of operating thea
equipment, and donor sites from septic
is almost completely avoided by this m
the granulating wounds are not exposed
ing theatre. Thus, cross-infection in th
sepsis in donor sites are reduced to a m

It is my belief that open grafting, part
performed by the method described
represent a revolutionary advance in the
of granulating wounds in developing
satisfactory take can be confidently
almost all cases even under unfavoura
with the minimum of expense.

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VEIN-GRAFT BY-PASS IN AXILLARY AND BRACHIAL ARTERY OCCLUSIONS CAUSING CLAUDICATION

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SUMMARY

Four cases of axillary and brachial artery occlusions which caused claudication in the arm and hand are presented. They demonstrate that the effects of reduced arterial supply are equally disabling in the hand as in the leg. Axillary and brachial artery occlusions can be treated by vein-graft by-pass, in a similar way to arterial disease in the leg, with excellent results.

UPPER-LIMB ischaemia due to arterial disease is much less common than lower-limb ischaemia, but it presents in a similar way, either as rest pain in the hand or as a claudication-type pain on exercise which is felt in the forearm muscles as well as in the small muscles of the hand. There has been a very widely held view that arterial surgery in the upper arm is never or rarely indicated. Martin, Lynn, Dible, and Aird (1956) stated, when considering embolism in peripheral vessels, 'upper limb operation is virtually never required, spontaneous recovery is common even without any treatment at all, for preformed collaterals are more numerous in the upper limb than in the lower'.

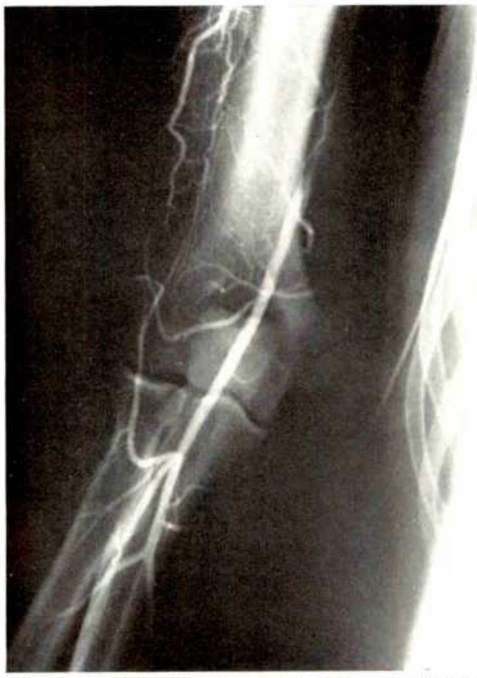

FIG. 1.—*Case* 1. Preoperative arteriogram, showing large collaterals filling the brachial artery distal to the block.

It has been our experience that although severe ischaemia (gangrene) rarely occurs following axillary and brachial occlusions, functional disability (claudication) is more common and can be very severe. It will interfere with work and may make such simple tasks as combing the hair or brushing the teeth extremely difficult. Eastcott (1969) stated, 'reconstructive arterial operation is seldom applicable in cases of upper limb occlusions'. This has not been our experience and we have recently had 4 cases of axillary and brachial occlusions with claudication which were all found to be suitable for a reconstructive arterial operation. They were considerably improved by autogenous vein-graft by-pass.

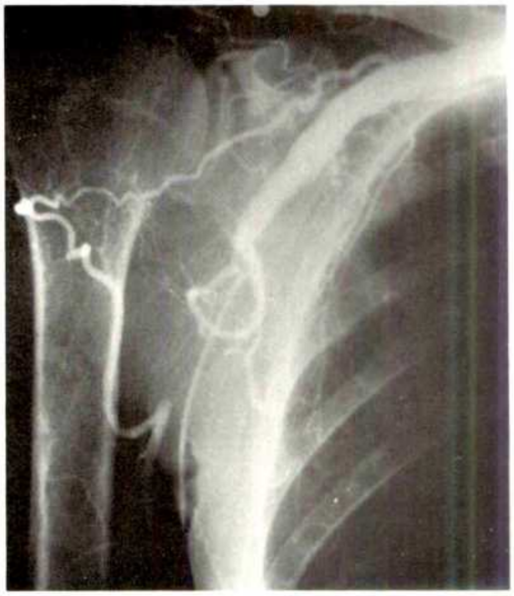

FIG. 2.—*Case* 3. Preoperative arteriogram, showing a block of the lower axillary artery with an excellent collateral circulation around the block.

CASE REPORTS

Case 1.—A 27-year-old man developed an occlusion of the right brachial artery in October, 1969, when his arm was crushed by a fork-lift truck. His work as a butcher was severely limited by claudication. A weak radial pulse was palpable on the right side but this disappeared on exercise. An arteriogram showed a brachial artery block with several large collaterals filling the artery distal to the block (*Fig*. 1). In February, 1970, he had a brachial artery vein-graft by-pass with complete relief of his symptoms.

Case 2.—A 62-year-old man injured the medial side of his right arm in an industrial accident in September, 1969. He developed intermittent claudication in the arm and hand which was sufficient to interfere with his work. Both radial pulses were palpable but the right one was reduced and disappeared on exercise, when the hand became pale. An arteriogram showed a stenosis of the right brachial artery and an irregularity stretching over 6 cm. In September, 1970, he had a brachial artery vein-graft by-pass with complete relief of his symptoms.

Case 3.—A 66-year-old man presented complaining of pain in his right arm on exercise. The pain in his right forearm and hand prevented such simple tasks as brushing his teeth and combing his hair. No pulsation was palpable in the right arm below the axilla. A subclavian arteriogram showed a 5-cm. block in the lower axillary artery with a good collateral circulation around the block (*Fig.* 2). An axillobrachial vein-graft by-pass 3 weeks later resulted in complete relief of his symptoms and the radial pulse was restored.

Case 4.—A 70-year-old man presented with a history of polio affecting both legs at the age of 2½ years. He had used crutches since then. Three months prior to admission he had noticed a pain in the left arm on use, associated with coldness and pallor of the limb. At the time of admission he found it difficult to use his crutches because of the pain. No pulsation was palpable in the left arm below the axilla. A subclavian arteriogram showed a block in the third part of the axillary artery. A left axillobrachial vein-graft by-pass was performed with return of the radial pulse and relief of symptoms. He was discharged on elbow crutches.

OPERATIVE TECHNIQUE

This is essentially similar to that used for saphenous vein-graft by-pass in the lower limb (Taylor, 1962). The brachial and axillary arteries are exposed through a longitudinal incision over the basilic vein. For adequate exposure the insertion of the pectoralis major, and occasionally the pectoralis minor, may have to be divided. A 3-mm. strip of muscle and tendon is left on the humerus for repair of the pectoralis major at the end of the operation. A length of basilic and antecubital vein is freed of its branches. The vein usually empties into several venae comitantes in the upper arm; it is divided immediately below this point. The vein is reversed and anastomosed end to side above and below the occlusion. Arterial spasm during surgery is more of a problem in the brachial artery than in lower-limb arteries; it can be reversed with local papaverine and/or lignocaine. Mechanical dilatation of the artery is sometimes necessary.

DISCUSSION

Upper-limb ischaemia is caused by a wider variety of pathological processes than is found in the lower limb. Of all peripheral arterial emboli, 17 per cent pass to the upper limb and 77 per cent to the lower (Billig, Hallman, and Cooley, 1967). Atherosclerotic occlusions are probably also less common in the upper limb although 1 of our cases would seem to have been a spontaneous thrombosis in an atherosclerotic vessel. Trauma is a major cause of upper-limb ischaemia and 3 of our cases fall into this group. Crutch thrombosis has been a well-recognized entity for some time (Ryle, 1922). Cervical rib can cause claudication, or more commonly rest pain and gangrene, owing to distal embolization. Encroachment of the artery by malignant disease can occur (Knox, Nay, and Blumenthal, 1966). A fibromuscular stenosis of the axillary artery has been recorded (Garrett, Morris, Howell, and DeBakey, 1965). Iatrogenic causes are due to injury secondary either to thoracic and cervical operations or to retrograde brachial artery catheterization. The latter cause is likely to be seen with greater frequency as left-heart catheterization becomes a routine investigation.

Claudication in the arm can be severe even when an excellent collateral circulation is demonstrable by arteriography. The radial pulse may be palpable but the patient could still have claudication. There is a tendency for symptoms to subside as collaterals enlarge but even up to 1 year after occlusion, symptoms may still be severe. It would seem to us that symptoms in the arm are potentially more disabling than similar symptoms in the leg, since active function of the hand is impaired. Right-arm claudication would seem, in general, to be more disabling than left since most people are right-handed. Brachial artery catheterization should not, therefore, be attempted through the dominant arm.

The only other report of revascularization of the upper limb by use of vein-grafts comes from Houston (Garrett and others, 1965). Here an autogenous long saphenous vein was used. The basilic and cephalic veins are readily accessible, however, and their use does not seem to cause any chronic venous insufficiency. All our patients had some minor oedema of the hand in the first few weeks postoperatively but this was never a problem. The long-term results of vein-grafting in the arm have not been recorded, but there seems no reason to suspect they will be different from the excellent results at present being obtained in the leg.

Acknowledgements.—I would like to thank Professor G. W. Taylor and Mr. M. A. Birnstingl for permission to publish details of the patients under their care.

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THE INFLUENCE OF ELECTRICAL STIMULATION OF THE LEG DURING SURGICAL OPERATIONS ON THE SUBSEQUENT DEVELOPMENT OF DEEP-VEIN THROMBOSIS

By L. R. DEJODE, M. KHURSHID, and W. W. WALTHER

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Summary

The effect of galvanic stimulation of the calf muscles during surgical operations on the development of postoperative deep-vein thrombosis was assessed using ^{125}I fibrinogen in 64 patients over 40 years of age undergoing major surgery. Alternate legs were stimulated in alternate patients using the opposite leg as a control. No significant difference in the incidence of deep-vein thrombosis was observed either in the immediate postoperative period or later.

The use of ^{125}I fibrinogen in the detection of deep-vein thrombosis is now a well-recognized method (Atkins and Hawkins, 1965; Flanc, Kakkar, and Clarke, 1968). In a clinical study Doran, White, and Drury (1970) stated that the incidence of post-operative deep-vein thrombosis can be reduced by electrical stimulation of the legs during operation. Browse and Negus (1970), using the ^{125}I-fibrinogen method, came to a similar conclusion. Since the incidence of deep-vein thrombosis is likely to be high in elderly, debilitated, and relatively immobile patients we decided to monitor such cases by the ^{125}I-fibrinogen method to test the contention of Doran and others (1970).

MATERIALS AND METHODS

Patients of both sexes aged 40 years or over undergoing major operations were studied. There were 22 female and 42 male patients and the mean age was 62 years. The operation was a major upper abdominal or thoraco-abdominal procedure in 40 patients, a major lower abdominal or pelvic in 20, and 4 operations fell into neither category.

The method of stimulation of the calf was similar to that used by Browse and Negus (1970) and Doran and others (1970), employing brief intermittent galvanic stimulation every 2 seconds to produce forcible contraction of the calf muscles.

Each patient had one leg stimulated during his operation, the other leg serving as an unstimulated control. Alternate patients had alternate legs stimulated; 33 had their right leg stimulated and 31 the left.

^{125}I fibrinogen, 100 m.c., was given intravenously either just before the operation or at its completion. Thyroid uptake was blocked by 100 mg. of potassium iodide orally 24 hours before operation and continued daily for 1 month. The use of the Pitman 235 Ratemeter (Kakkar, Nicolaides, Renney, Friend, and Clarke, 1970) allowed both legs to be scanned in about 10 minutes.

RESULTS

The total number of thrombosed legs found was 36 in 25 patients, being 39 per cent of the total number of cases.

Table I shows the distribution of deep-vein thrombosis in this study.

Table I.—Occurrence of Deep-vein Thrombosis in the Present Series

Total number of patients	64
Number of patients forming thrombi in legs	25 (39 per cent)
Total number of thrombosed legs	36
Patients with thrombi on unstimulated side only	8
Patients with thrombi on stimulated side only	6
Patients with thrombi on both sides	11
Total number of legs thrombosed on unstimulated side	19 (15 per cent)
Total number of legs thrombosed on stimulated side	17 (13 per cent)

Table II.—Time of First Appearance of Deep-vein Thrombosis

Time of Appearance of Thrombosis	*No. of Patients*
At operation	3
Up to 24 hr. after operation	10
Up to 72 hr. after operation	7
Up to 9 d. after operation	5
Total	25

Table III.—Incidence of Deep-vein Thrombosis in Stimulated and Unstimulated Legs in Relation to the Time of Onset after Operation

Time after Operation		*No. of Patients*
Within first 24 hr.:	Unstimulated	10
	Stimulated	8
Second to ninth days:	Unstimulated	9
	Stimulated	9

Initial evidence of deep-vein thrombosis appeared during the first 9 days following operation. *Table II* shows the distribution in time of the occurrence of deep-vein thrombosis in patients.

Since the possible beneficial effect of leg stimulation during the operation is likely to decrease rapidly with the passage of time we have particularly noted those cases where the deep-vein thrombosis was diagnosed within 24 hours of operation. *Table III* shows the distribution of thrombosis between stimulated and unstimulated legs in relation to the length of time after the operation.

DISCUSSION

The possibility of reduction of postoperative deep-vein thrombosis by the use of calf stimulation is based on the view that thrombosis begins during operation in the majority of cases (Doran and White, 1967).

Our results show that thrombosis was detected in 13 patients in the period between operation and up to 24 hours afterwards whereas in 12 patients this occurred between the second and ninth days. In the latter group the later onset of deep-vein thrombosis would not be expected to be prevented by the use of calf stimulation and is presumably due to factors acting in the postoperative period. It is perhaps significant that our series included a high proportion of elderly, frail patients undergoing very extensive surgery, and in these cases early mobilization was obviously limited or impossible.

These are, however, the very patients most at risk from deep-vein thrombosis and this accords with our overall incidence of deep-vein thrombosis of 39 per cent. Browse and Negus (1970), on the other hand, report a lower incidence of 23 per cent, but no patient in their series had any serious blood-loss or hypotension during or after surgery and most were active within 2 or 3 days.

The evidence for the efficacy of calf stimulation in preventing deep-vein thrombosis should be looked for in the group of patients who developed deep-vein thrombosis during operation or in the first 24 hours after operation. In the 3 patients in our series who developed deep-vein thrombosis during operation this occurred in the stimulated leg in the first, in the unstimulated leg in the second, and in both legs in the third. The distribution of thrombosis between stimulated and unstimulated legs in the first 24 hours after operation does not confirm the value of stimulation; as expected, there is no difference between the groups in the period after 24 hours.

The explanation of the conflict between our failing to demonstrate the protective effect of calf stimulation and the beneficial effect observed by Browse and Negus (1970) may be due to our agreed deliberate selection of cases in whom the likelihood of deep-vein thrombosis was very great. Thus, it may be that in the 10 patients who developed deep-vein thrombosis in the first 24 hours after operation any protective effect of calf stimulation was obscured by the early onset of deep-vein thrombosis in the immediate postoperative period when calf stimulation had ceased and the venous return was still slowed after the long operation and anaesthetic.

On the basis of our results we cannot conclude that stimulation of one leg during operation substantially reduces postoperative deep-vein thrombosis on the stimulated side in elderly patients undergoing major surgery. It remains possible that calf stimulation reduces the risk of deep-vein thrombosis when used in routine operations in elderly patients. In such patients the increased venous return during operation may be sufficient to prevent thrombosis during operation and rapid postoperative mobilization may prevent subsequent thrombosis. We would suggest, however, that in similar studies in the future ^{125}I fibrinogen should be given and the legs scanned initially before operation and that the scan should be repeated immediately after the conclusion of the operation and again the next day, but not thereafter unless ward procedures to reduce deep-vein thrombosis are also being studied.

Acknowledgements.—We are grateful to Mr. N. Veall, B.Sc., F.Inst.P., for the initial supply of ^{125}I fibrinogen and for much useful advice, and to Dr. J. S. Glover of the Radiochemical Centre, Amersham, for a further supply of ^{125}I fibrinogen used in this study. We would also like to thank Mr. E. G. Millwood, F.I.M.L.T., for technical assistance.

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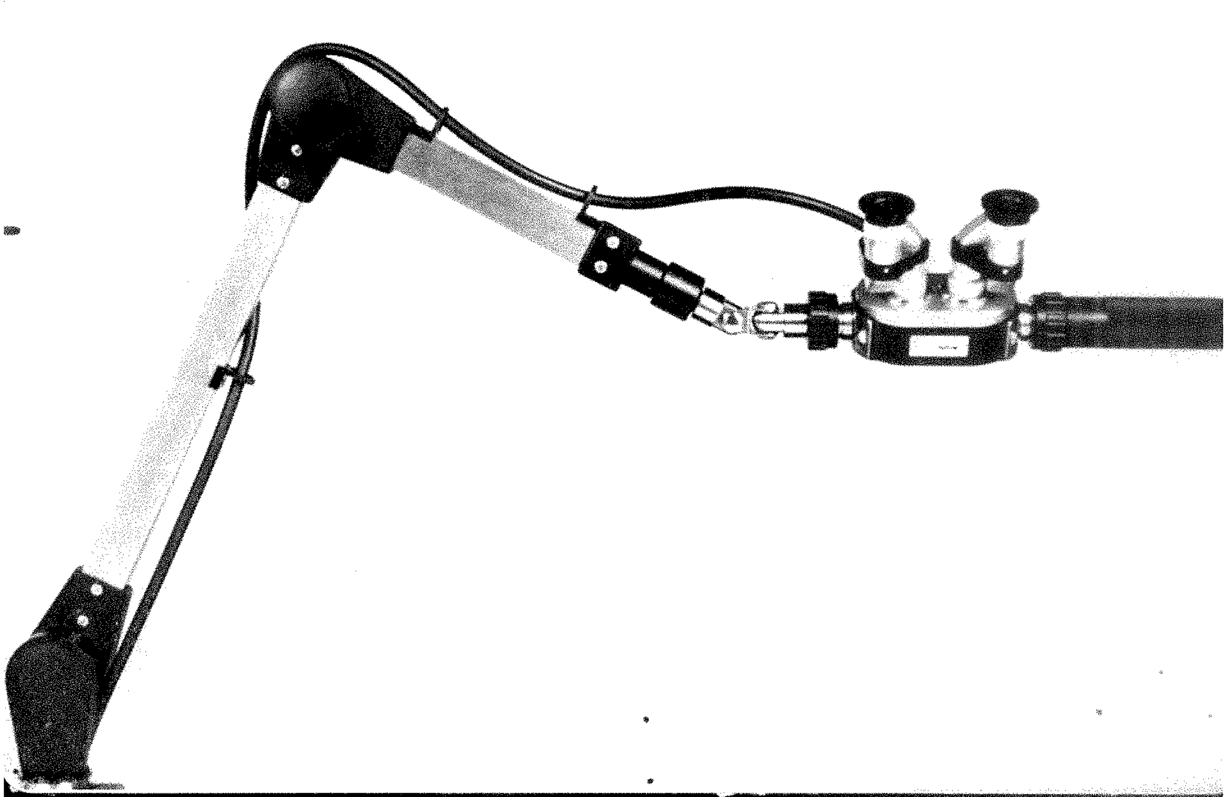

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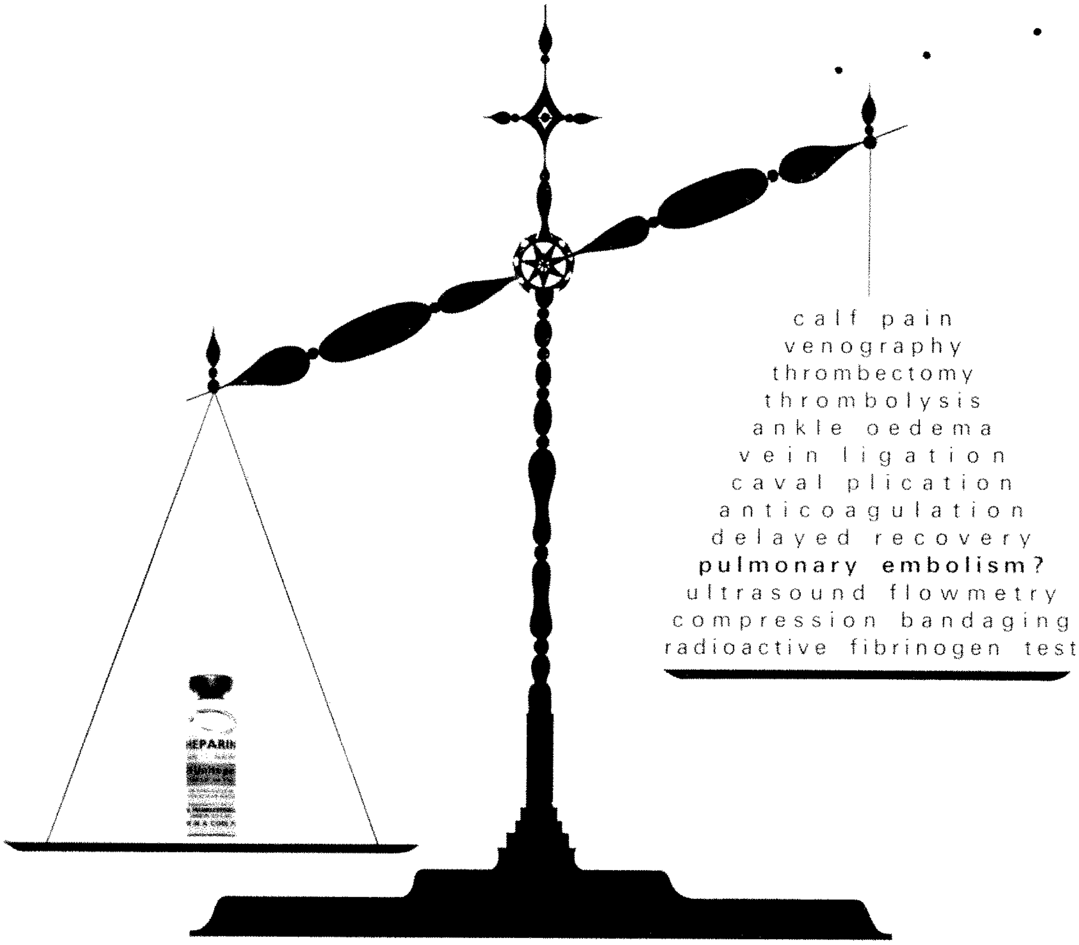

an ounce of prevention is worth a pound of cure!

'by far the most successful [results] recorded for any preventive method hitherto proposed'—Sharnoff, J. G. and DeBlasio, G., Lancet 1970, *ii*, 1006.

'potentially lifesaving'—Kakkar, V. V. et. al., Lancet, 1971, *ii*, 669.

'causes a fall in the frequency of postoperative venous thrombosis'—Williams, H. T., Lancet, 1971, *ii*, 950.

'the incidence of postoperative deep-vein thrombosis is significantly reduced'—Gordon-Smith, I. C. et. al., Lancet, 1972, *i*., 1133.

'frequency of deep-vein thrombosis, determined by the ^{125}I-fibrinogen test, was 42% in the control group and 8% in the patients receiving heparin'.—Kakkar, V. V. et. al., Lancet, 1972, *ii*, 101.

'small doses of subcutaneous heparin are safe and should be given routinely in patients undergoing major general surgery.' —Nicolaides, A. N. et al., Lancet, 1972, *ii*, 890.

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CARCINOMA OF THE AMPULLA OF VATER AND DUODENUM

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SUMMARY

Thirty-one cases of carcinoma of the ampulla of Vater and duodenum have been classified on the basis of pathological criteria.

Two types of tumour were discernible. Nine were polypoid papillary adenocarcinomas occurring at the ampulla of Vater; 19 were adenocarcinomas without a papillary pattern, of which 4 were duodenal tumours and 15 were ampullary. There were 3 ampullary tumours of mixed type. The carcinomas without a papillary structure were more invasive, more often associated with abdominal pain, more frequently misdiagnosed, and were associated with a higher mortality-rate.

The data were insufficient to draw firm conclusions as to the prognosis but the clinical behaviour was related to the pathology of the tumours.

Lesions in the ampullary region were associated with jaundice which was often intermittent. Lesions outside the ampullary area presented early with vomiting of pyloric type but without jaundice.

The importance of a high index of suspicion in dealing with these lesions and the value of barium-meal examinations are emphasized.

It is noted that pancreaticoduodenectomy for ampullary carcinoma has a mortality of less than 25 per cent if performed by an experienced surgeon and can be considerably lower in clinics specializing in this condition.

We suggest that the pathological classification of these tumours used in this paper may form the basis for further investigations into the diagnostic and prognostic problems which these tumours present.

This classification of ampullary tumours is a factor to be considered in assessing the indications for pancreaticoduodenectomy.

PRIMARY carcinomas are uncommon in the small bowel but a high proportion of those which do occur are found in the duodenum (Jefferson, 1916; Bockus, 1964). The literature on carcinoma of the duodenum is now vast and many hundreds of cases have been recorded (Kleinerman, Yardumian, and Tamaki, 1950; Seeley and Campbell, 1954), but the disease still poses a problem for the clinician and a challenge to the pathologist. There is a marked variation in the reported incidence of the various sites of duodenal carcinoma (Berger and Koppelman, 1942; Resnick and Cooper, 1958; Barclay and Kent, 1962), and the information available is difficult to analyse as many authors have not differentiated between carcinomas arising from the duodenal mucosa and those arising from the ampulla of Vater. This distinction can be difficult to make (Lieber, Stewart, and Lund, 1937), and because carcinomas of the duodenum are most frequent in its second part (Kleinerman and others, 1950) failure to make a distinction renders much of the data almost unintelligible.

Authors who have differentiated between these tumours have only regarded a tumour as being of duodenal origin when it has been clearly separated from the ampulla. This accounts for much of the confusion since some carcinomas arising from the duodenal mucosa have been grouped with carcinomas arising from the epithelium of the ampulla simply because of their location.

In this paper we have attempted to classify carcinomas of the ampulla and of the duodenum on the basis of pathological criteria. The possible significance of this classification in the clinical management of these tumours is explored.

MATERIALS AND METHODS

This study is based on a review of 31 surgically treated cases of carcinoma arising in the duodenum, including carcinomas of the ampulla of Vater. All cases in which the malignancy of the lesion was in doubt were excluded. Also excluded were cases in which there was an extensive involvement of the pancreas as the origin of such tumours could not be determined. Of these 31 cases, 4 have been personally treated, and of the remainder, a further 23 have been traced and either personally seen or their clinical records perused. Four cases have been lost to clinical follow-up and for these only pathological data are available.

The pathological material consisted of 20 specimens from a Whipple's type of procedure and 5 from local resections, but only biopsies were available in the rest of the cases. Of the radical resections, the entire specimen was available for study in 7 cases while in the remainder the material consisted of stored paraffin blocks. The pathological material was studied by one of the authors (A. K.) without knowledge of the clinical history and the cases were divided into groups on the basis of the pathology found. Paraffin sections were studied after staining with haematoxylin and eosin, Masson's trichrome PAS with Alcian blue, and Gomori's method for elastic tissue.

PATHOLOGICAL FINDINGS

The majority of the tumours were readily divisible into two main varieties along the lines described by Edmondson (1967). Of the 31 tumours, 9 were papillary adenocarcinomas and took the form of mushroom or button-shaped masses which protruded into the lumen of the duodenum; this type of tumour we have called type I (*Table I*).

Nineteen tumours consisted of ulcerating or stenosing growths which were adenocarcinomas without a papillary pattern. These tumours usually

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produced mucin and had a scirrhous stroma; the term used for this form of tumour in a study conducted at the Mayo Clinic is 'type ordinaire' (Monge, Judd, and Gage, 1964). This type of tumour we have called type II. These could be further divided on the basis of their situation (*Table I*).

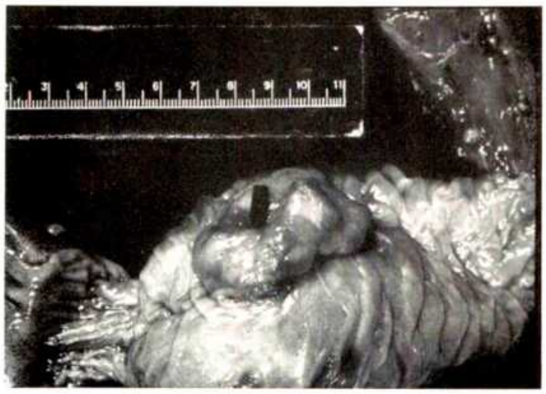

FIG. 1.—An example of a papillary carcinoma at the ampulla of Vater (type I). Note the polypoid shape of this tumour with the central depression which could be seen radiologically (*Fig.* 9). The black rod is in the common bile-duct.

Table I.—A PATHOLOGICAL CLASSIFICATION OF 31 CARCINOMAS OF THE AMPULLA OF VATER AND DUODENUM

PRINCIPAL FEATURES	TYPE	NO. OF CASES
Polypoid papillary tumours of the ampulla	I	9
Non-papillary adenocarcinomas		
Ampullary, ulcerating	IIa	6
Nodules within the ampulla	IIb	9
Duodenal	IIc	4
Tumours of mixed pattern involving the ampulla	III	3

In 3 cases both patterns of growth were present and these have been considered separately as tumours of mixed pattern (type III).

Type I: Papillary Adenocarcinomas.—All of these tumours, and those of mixed pattern, were found at the ampulla of Vater. Eight of the 9 tumours formed a very distinctive type of lesion consisting of a mushroom-shaped tumour which surrounded and replaced the ampulla (*Fig.* 1). The ends of the ducts were buried in the tumour which often appeared to be sprouting out of them. In the remaining case only a biopsy is available and the gross appearance of the tumour is not known.

In size the tumours varied from 0·5 to 3·5 cm. in maximal diameter. The deeper parts of the tumour involved muscle in 7 cases, but clear evidence of complete penetration of the muscle was present in only 2 cases and in no instance was the pancreas involved. Examination of the lymph-nodes was carried out in 5 cases but in none of these was there any metastases.

The tumours were papillary adenocarcinomas (*Fig.* 2); the degree of differentiation was variable, but 5 of the tumours were well differentiated and the papillae were lined by tall columnar cells with eosinophilic cytoplasm and fair
(*Fig.* 3). In 4 cases the cells
pleomorphic and had irregular nu
deeper limits of the tumour, v
being invaded, showed a transitio
pattern of growth sometimes wit
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found in 5 of these tumours bu
marked as in the type-II tumo
tumours had some degree of infla
in the stroma.

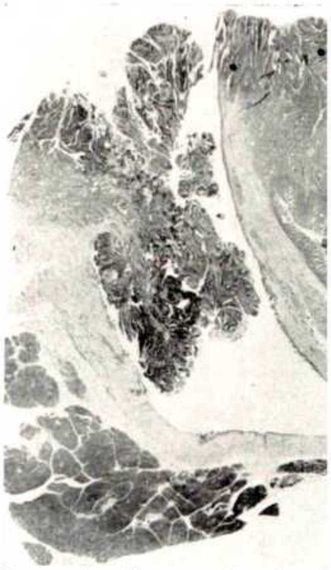

FIG. 2.—A papillary type of carcinoma of the common bile-duct the wall of which part of the field' same case as *Fig.* 1). H. a

Type II: Non-papillary Ade
Nineteen tumours (*Table I*) wer
of these (IIa) were ulcerating les
ampulla. In 9 other cases (IIb)
histologically similar to those of
sisted of a nodule which was no
the ampulla. The remaining 4 t
situated away from the ampull
duodenal carcinomas.

The tumours of type IIa consis
ulcers which varied from 1·5 to
diameter. Unlike the type-I tu
infiltrating growths which extend
duodenal wall and which involved
duct and the pancreatic duct. A
the muscularis propria of the duo
these there was superficial invasi
(*Fig.* 4). The condition of the
known in 4 cases and, of these, met
in 2.

Histologically the tumours pre
ferent appearance from those of ty
ing tumours were scirrhous infiltra
a distinct glandular pattern and o
the production of mucin (*Fig.* 5
more irregular than in the type-I tu
figures were more abundant. Or

group was unusual for the degree of anaplasia and the very marked chronic inflammatory reaction seen. With this exception the cells forming the tumours tended to be large, eosinophilic, and columnar with big vesicular nuclei.

Tumours of type IIb differed only from IIa growths in their lack of ulceration and their situation within the substance of the ampulla. In a number of cases where only a biopsy had been performed it was not possible to place a case in categories IIa or IIb with certainty. Of the 9 cases of type IIb, 5 were definitely submucosal in site and 4 were probably in this position; in 1 case (*Fig.* 6) a small tumour was arising in the duct of Wirsung.

All of these tumours were small in size and some could not be identified before dissecting the specimen (*Fig.* 6); the largest was 1·8 cm. in diameter. In every case there was infiltration of muscle; in 5 cases the muscle had been breached and in 3 the pancreas had been invaded at the edge of the tumour. Lymph-nodes were available in 4 cases, metastases being present in 2 of these.

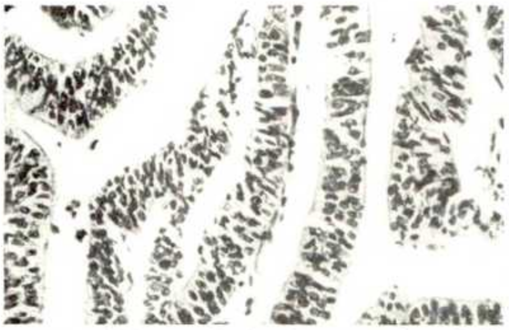

FIG. 3.—A higher magnification of a tumour of type I. The tumour cells are tall and columnar and are arranged on delicate strands of connective tissue. H. and E. (× 145.)

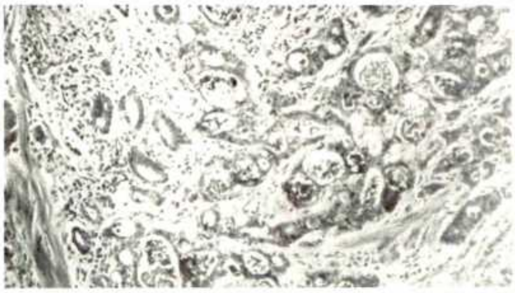

FIG. 5.—A tumour of type II. This is a mucin-secreting adenocarcinoma which is growing in a tubular manner; there is a fibrous stroma which contains a moderate degree of inflammatory reaction. H. and E. (× 50.)

Histologically the tumours closely resembled those of type IIa; all of them were mucin-secreting adenocarcinomas with a marked fibrous reaction.

While types IIa and IIb may be different stages of the same entity the 4 tumours of type IIc differed in that they did not arise at the ampulla, although in 1 case the edge of the tumour did reach the ampullary region, so that all of these tumours are cases of carcinoma of the duodenal mucosa itself (*Fig.* 7). These all occurred in the second part of the duodenum; 3 were proximal to the ampulla and 1 was opposite to the ampulla. In 3 the tumour was a ring stricture and the other was an ulcer (*Fig.* 7). These had all penetrated the muscularis propria but only 1 is known to have invaded the pancreas. The local lymph-nodes were involved in 2 cases and in another case the tumour had spread into the fatty tissue outside the duodenum.

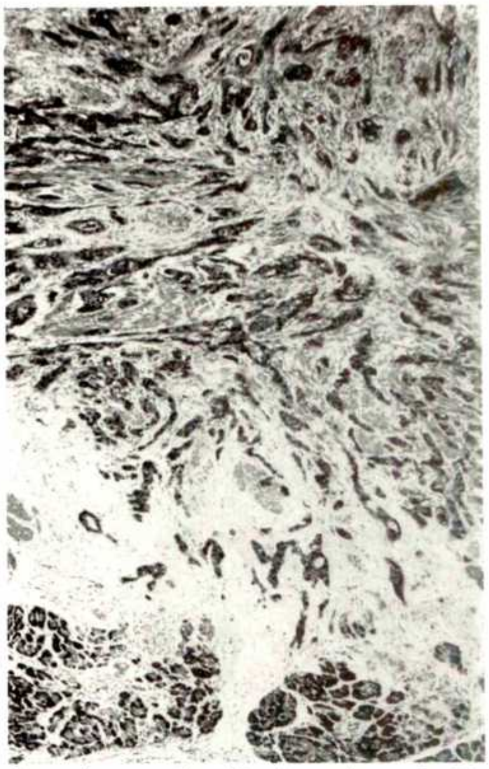

FIG. 4.—A tumour of type IIa arising at the ampulla of Vater. This is a scirrhous adenocarcinoma which has reached the edge of the pancreas in the lower part of the field. H. and E. (× 30.)

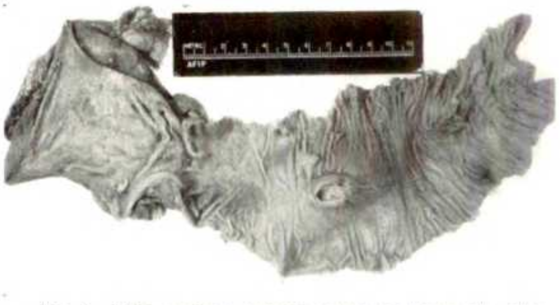

FIG. 6.—This specimen contains a tumour of type IIb. The end of the common duct is widely patent and cup-shaped with an indefinite roughened area on the distal lip. This proved to be a small carcinoma arising at the end of the pancreatic duct.

All of the tumours were moderately or poorly differentiated mucin-secreting adenocarcinomas with a tendency to have a scirrhous stroma which was in 1 instance very dense (*Fig.* 8).

Type III: Tumours of Mixed Pattern involving the Ampulla.—Three tumours could not be placed in either main category, but the study of this small group was hampered by the fact that only biopsies were available. All 3 of the tumours occurred at the ampulla and they contained papillary elements especially in the immediate region of the common bile-duct, while outside the duct the pattern resembled the type-II tumours. The muscle was involved in every case and in 1 instance the pancreas had been invaded.

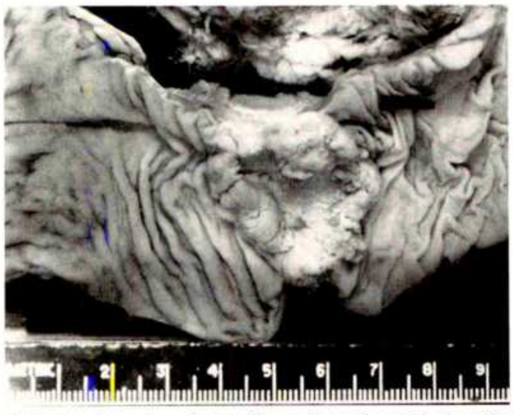

FIG. 7.—A tumour of type IIc; a circumferential ulcerating tumour of the duodenum; the ulcer is completely separate from the ampulla which is marked by the black rod.

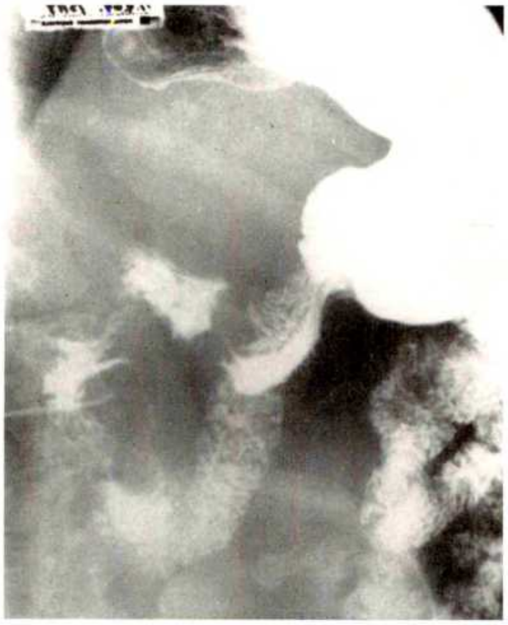

FIG. 9.—A radiograph demonstrating the tumour shown in *Fig.* 1 before it was removed. The tumour can be clearly identified as a type-I carcinoma.

CLINICAL FINDINGS

The clinical follow-up of the 27 patients for whom data were available revealed a number of features previously noted by others but worthy of re-emphasis. More important, it was clear that the classification of the lesions on pathological grounds was to some extent reflected in their clinical behaviour (*Table II*).

There was no significant distinction between the patients with different types of tumour as regards sex. The average age of patients with tumours of types I and III was somewhat younger than that of the patients with type-II lesions (*Table II*). The length of history prior to diagnosis also varied considerably; type-I cases came to operation in an average time of 10·7 weeks from the onset of symptoms, whereas those patients with either type-IIa, type-IIb, or type-III lesions had their operation 22–24 weeks after the onset of their illness. Patients with duodenal lesions outside the ampullary lesion (type IIc), however, presented very early and were submitted to laparotomy in an average of 6·7 weeks from the onset of symptoms (*Table II*).

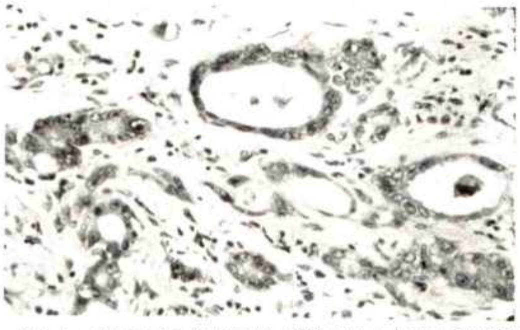

FIG. 8.—A tumour of type II. This was a large ulcerating carcinoma of the duodenum which involved the ampulla at its edge (type IIc). The pattern is similar to that of the ampullary carcinomas of type II (cf. *Fig.* 5). H. and E. (× 50.)

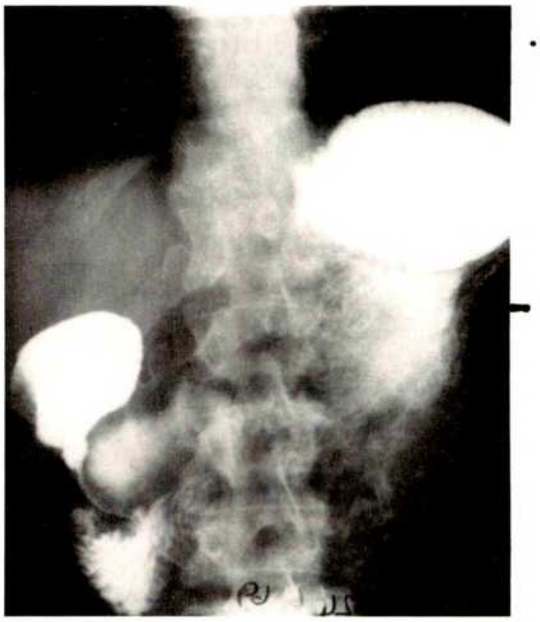

FIG. 10.—In this patient a diagnosis of pyloric stenosis was made, but the barium-meal examination revealed that the obstruction was distal to the pylorus. This was a tumour of type IIc.

Anorexia and vomiting were common presenting features and occurred in 22 of the 27 cases. However, excessive vomiting of a pyloric type associated with a gastric splash was found in only 6 cases. Two of these were patients with a type-I lesion and all 4 patients with duodenal carcinoma (type IIc) presented in this manner.

Jaundice was common and was found in 23 cases, being quite certainly fluctuant in 13 of these. Only the 4 cases with duodenal carcinoma (type IIc) were not jaundiced (*Table II*).

Table II.—CLINICAL FEATURES OF 27 CASES OF CARCINOMA OF THE AMPULLA OF VATER AND DUODENUM

CLINICAL FEATURES	TYPE I	TYPE II			TYPE III
		a	b	c	
No. of cases	8	5	7	4	3
Average age (yr.)	59	65·6	66·6	62·7	52·6
Length of history (wk.)	10·7	24·4	22·3	6·7	22
Anorexia; vomiting	8	4	3	4	3
Vomiting of pyloric type (spash on examination)	2	0	0	4	0
Jaundice	8	5	7	0	3
Pain	1	3	4	0	2
Barium meal done	3	1	0	4	0
Lesion shown	2	0	0	3	0
Misdiagnosis* and delay in diagnosis	1	4	4	1	1

* Other than due to carcinoma of the head of the pancreas.

Pain was frequent and occurred in 10 cases. Nine of the patients with pain had tumours classified as types IIa, IIb, or III, whereas none of the patients with carcinoma of the duodenum (type IIc) experienced any pain at all and only 1 out of 8 cases with type-I lesions gave such a history (*Table II*). The pain was most commonly epigastric or located in the right subchondral region and was occasionally felt in the back. Some patients experienced recurrent attacks of pain.

The gall-bladder was palpable in 19 of the 23 jaundiced patients, and in 2 who were personally observed the gall-bladder, having been initially easily felt, was found impalpable a few days later. In both the jaundice was fluctuant and in 1 the serum bilirubin fell a few days after this observation. One patient who was subsequently found to have a carcinoma arising in the duodenum outside the ampullary region presented initially with deep-vein thrombosis in a leg.

Iron-deficiency anaemia was extremely common but was only severe in 2 cases and there was no difference between the groups in this respect. Overt intestinal haemorrhage occurred on 1 occasion. Faecal occult blood-tests were done in 11 of the 27 cases and were positive on every occasion. Likewise the erythrocyte sedimentation rate was raised in each of the 12 cases in which it was estimated. The reading was often markedly raised, being over 50 mm. in the first hour (Westergren) on 8 occasions. Duodenal cytological studies were undertaken on 1 occasion only and gave a positive diagnosis.

A barium-meal examination was done on 8 occasions and the radiological diagnosis was made on 4 of these (*Fig.* 9). In a further case a preoperative diagnosis of pyloric stenosis was made, but when the radiographs were reviewed postoperatively the lesion was seen clearly demonstrated in the second part of the duodenum (*Fig.* 10).

Misdiagnosis and delay in diagnosis were not infrequent. Where painless jaundice was the presenting feature the most common preoperative diagnosis was carcinoma of the head of the pancreas.

Table III.—OPERATIONS, HOSPITAL MORTALITY, AND SURVIVAL IN 27 CASES OF CARCINOMA OF THE AMPULLA OF VATER AND DUODENUM

OPERATION	SURVIVAL AT TIME OF WRITING					
	Type I		*Type II*		*Type III*	
	Alive	Dead	Alive	Dead	Alive	Dead
Local transduodenal resection	1	1	0	0	0	3
Pancreaticoduodenectomy	4	1	1	10	0	0
Inoperable	0	1	1	4	0	0
Total	5	3	2	14	0	3
Hospital mortality (overall 18·5 per cent)	0		26·3 per cent			
2-year survival (overall 40·7 per cent)	62·5 per cent		31·6 per cent			
5-year survival (overall 11·2 per cent)	25 per cent		5·3 per cent			

Pain appeared to be the clinical feature most likely to lead to diagnostic confusion. An initial diagnosis of gall-bladder disease was made in 7 patients and cholecystography revealed a non-functional gall-bladder in 2 of these. A diagnosis of duodenal ulcer was seriously considered in 1 other case. Yet another patient who was on a variety of drugs for psychiatric disturbance was incorrectly diagnosed as having hepatocellular jaundice, and in 1 patient an initial transient episode of jaundice was ascribed to infective hepatitis. These errors, often leading to delay in diagnosis, were more frequent in cases of types IIa, IIb, and III (*Table II*).

OPERATIVE TREATMENT AND RESULTS

The overall hospital mortality for the entire group of 27 cases was 18·5 per cent with a 5-year survival of 11·1 per cent (3 cases) and a 2-year survival of 40·7 per cent (*Table III*). Seven patients are still alive and well at periods between 2 and 5 years after operation.

Only 1 of the 8 patients with type-I tumours proved inoperable. This patient died after 50 weeks from disseminated cancer. The remaining 7 cases were operable and, of these, 5 underwent pancreaticoduodenectomy and 2 had local transduodenal excision of their growth. Four of the patients who were submitted to pancreaticoduodenectomy are still alive and well and have been followed for periods varying from 2 to 9 years. One of the patients who had a local transduodenal excision died as a result of ischaemic heart disease within 4 months of operation, but the other is alive and well 6 years later. The

5-year survival for type-I cases is 25 per cent and the 2-year survival 62·5 per cent (5 cases) without any hospital mortality (*Table III*).

In contrast, of 19 patients with type-II or type-III tumours, 5 were inoperable. Nevertheless, 1 of these lived 2½ years after a palliative by-pass procedure before dying of metastases, and another aged 70 years* is still alive 3 years after operation. There was only 1 death in the postoperative period in this small group of inoperable cases and the mean survival time was 17 months.

Table IV.—MORTALITY AND SURVIVAL FOR PANCREATICODUODENECTOMY AT THE TIME OF WRITING

TYPE	NO. OF OPERATIONS	HOSPITAL MORTALITY (per cent)	SURVIVAL (per cent)	
			2 years	5 years
I	5	0	80 (4 cases still alive)	20 (1 case still alive)
II	11	36·4 (4 cases)	36·4 (4 cases—3 dead)	9·1 (1 case—dead)
Total	16	25	50	12·5

The remaining 14 cases with type-II or type-III lesions were operable. The 3 cases with lesions of type-III histological pattern underwent local transduodenal excision and all were dead within 2 years of operation. Eleven cases, all of type II, underwent pancreaticoduodenectomy. Only 1 of these patients is still alive 2 years after operation. Two others lived for 2 years and 1 survived 6 years, the latter dying of ischaemic heart disease. All the remaining patients who were submitted to radical operation died within 2 years and 4 of these died in hospital in the postoperative period. The overall 5-year survival for patients with type-II and type-III growths is 5·3 per cent (1 case) and the 2-year survival is 31·6 per cent with a hospital mortality of 26·3 per cent (*Table III*).

Of the entire group of 27 patients, 16 underwent pancreaticoduodenectomy (*Table IV*). The hospital mortality for this operation was 25 per cent with a 2-year survival of 50 per cent and a 5-year survival of 12·5 per cent. However, the patients with type-I lesions had a 2-year survival of 80 per cent (4 cases) without hospital mortality. All 4 of these patients are still alive. This contrasts markedly with a 2-year survival of 36·4 per cent (4 cases of which 3 are dead) and a hospital mortality of 36·4 per cent for pancreaticoduodenectomy in patients with type-II tumours.

DISCUSSION

The clinical features which we have recorded in this series of cases allow comparison with the findings of others and emphasize some of the important points in diagnosis and management. The presenting symptoms underline the importance of jaundice, pain, and vomiting.

Jaundice is an early feature of carcinoma of the ampullary region and a most important manifestation. Our finding that jaundice was clearly fluctuant in over half of the cases is in agreement with that of Monge, Dockerty, Wollaeger, Waugh, and Priestley (1964) and Warren, Veidenheimer, and Pratt (1967). If a clear history of this symptom can be obtained then the diagnosis of a lesion involving or close to the ampulla of Vater is highly likely. This contrasts with carcinoma of the pancreas where fluctuant jaundice is rare. Our observation that the gallbladder may be intermittently palpable is a useful physical sign and if combined with fluctuant jaundice is highly suggestive of an ampullary neoplasm.

Anorexia, nausea, and vomiting were very common and the finding that cases of duodenal carcinoma arising outside the ampullary region present with vomiting as the major symptom is similar to that of Devlin, Platten, and Corrin (1968) and Craig (1969). The importance of bearing in mind the possibility of a duodenal lesion in cases with symptoms suggestive of pyloric stenosis is clearly indicated.

The common occurrence of iron-deficiency anaemia and positive faecal occult blood-tests is an important feature and if associated with jaundice and a high erythrocyte sedimentation rate is highly suggestive of an ampullary lesion (Hall and Krementz, 1968). It is interesting that frank haemorrhage occurred on only 1 occasion.

A striking feature of this series is the early presentation and diagnosis in cases of duodenal carcinoma (type IIc) and of the painless jaundice occasioned by the tumours of type I. By contrast, diagnosis in cases with tumours of types IIa, IIb, and III was much later and pain appeared to be the symptom most likely to cloud the issue, particularly if the jaundice was fluctuant in type.

We would agree with other workers (Barclay and Kent, 1962; Hall and Krementz, 1968; Craig, 1969) in their plea for a high index of suspicion in regard to these lesions. It is only by early diagnosis that the prognosis can be improved. Of the diagnostic procedures available the barium meal is a most important aid and it is vital to obtain good visualization of the duodenal loop (Barclay and Kent, 1962). In 1 example of a type-I tumour the gross form of the tumour was clearly outlined in this way.

Hypotonic duodenography may be a most useful aid. Nevertheless, we would agree with Warren, Braasch, and Thum (1968) in emphasizing that too much reliance should not be placed on negative gastro-intestinal radiology since a small periampullary lesion may not be demonstrable.

Duodenal intubation with aspiration of the duodenal contents and subsequent cytology for malignant cells may also be useful and gave positive results in the 1 case in which it was utilized. However, it should be noted that a negative result does not rule out the diagnosis and false positives have been reported (Rankin and Brown, 1964).

The recent introduction of fibreoptic duodenoscopy (Takemoto, 1968) with facilities to carry out ampullary biopsy and endoscopic pancreatocholedochography (Ogoshi, Tobita, and Hara, 1970) holds out considerable promise for the more accurate diagnosis of lesions in the region of the ampulla of Vater.

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* This case is classified here as inoperable since although the lesion was small and technically operable the diagnosis was missed at operation and only an incomplete wedge biopsy was taken from a segment of the ampulla.

A striking feature of the cases in this series was the rarity of accurate preoperative diagnosis. It would seem that recognition of the lesion before operation would allow better preoperative preparation for major surgery. However, in cases with clearly established obstructive jaundice or when obstruction cannot definitely be excluded by any other means, laparotomy should be proceeded with.

The 5-year survival for the whole group of 27 patients in this series was 11·1 per cent. However, those patients with type-I tumours had a 5-year survival of 25 per cent (*Table III*). It is difficult to compare these figures with those reported by others since our series is composed of patients with ampullary and duodenal tumours and no pancreatic cancers are included. Furthermore the figures relate to the whole group of cases and include both operable and inoperable patients.

Comparison with the mortality and survival for radical surgery is, however, possible. Hall and Krementz (1968) suggest that when a precise diagnosis of carcinoma of the ampulla or duodenum can be made then a 5-year survival of 30–40 per cent can be expected. They report a hospital mortality of 50 per cent, although most mortality-rates for pancreaticoduodenectomy lie between 20 and 30 per cent (Child and Frey, 1966). It should be noted that surgeons with a special interest in periampullary cancer have achieved 5-year survival-rates of 30–40 per cent with a hospital mortality as low as 13·5 per cent (Warren and others, 1968; Monge, Judd, and Gage, 1964), and recently a mortality-rate of only 2 per cent has been recorded for pancreaticoduodenectomy performed for periampullary cancer (Smith, 1970).

The patients whom we have reported were operated on by a number of surgeons none of whom had a special interest in the treatment of this disease, but the mortality for pancreaticoduodenectomy (25 per cent) compares favourably with that of other series (Child and Frey, 1966; Crile, Isbister, and Hawk, 1970). It is of interest to note that none of the 5 patients with type-I tumours who underwent pancreaticoduodenectomy died postoperatively. The 5-year survival for pancreaticoduodenectomy (12·5 per cent) is low by modern standards (Warren and others, 1968; Smith, 1970), but it is noteworthy that 5 patients who were submitted to this operation are still alive. The 2-year survival is 50 per cent and is 80 per cent (all 4 patients are still alive) for the patients with type-I tumours (*Table IV*). This compares favourably with the 50 per cent 3-year survival recorded recently by Smith (1970). It would seem from the evidence we have presented that the mortality for the operation should not exceed 25 per cent and indeed can be considerably lower. These figures should be compared with the short duration of life following palliative surgery and the fact that such surgery is not itself free of mortality. In our series of cases 1 patient died following a by-pass procedure and the average duration of life after such operations was 17 months; similarly the average survival following biliary by-pass procedures was only 6·5 months and 16 months in two large series of cases recorded by Warren and others (1968), Monge, Docherty, and others (1964), and Monge, Judd, and Gage (1964).

Although at first sight it seems that the cases with type-I lesions fared a lot better than those with type-II or type-III tumours the number of different surgeons involved, the large number of postoperative deaths among patients with type-III lesions, and the small total number of patients make it impossible to differentiate the groups on the grounds of prognosis. Nevertheless, our observations lend some support to the suggestion (Crile and others, 1970) that radical surgery is more frequently indicated in cases with polypoid ampullary lesions.

Several aspects of the pathology of these tumours require comment. In particular there is the question of the validity of the separation of these tumours into two main types. It is probable that, as stated by Edmondson (1967), all the tumours are shades of a continuous spectrum and the presence of the small group of mixed pattern (type III) would support this, but at least the ends of the spectrum can be distinguished from each other. Several tumours of type I had small infiltrating areas in their deep aspects which resembled the type-II pattern of growth. It may be that all of these tumours are basically the same but that the histological pattern is dependent on the surrounding tissue, so that a tumour may excite a dense scirrhous reaction where it is infiltrating muscle but grows as delicate papillae in the duodenal lumen. This interpretation merely reflects the invasiveness of type-II tumours as compared with type-I lesions.

The evidence does not suggest that one variety of tumour is an earlier stage of the other, for the type-II tumours were often smaller than those of type I although the type-I lesions appeared to be less advanced in terms of invasiveness. As far as invasion is concerned, there seems little doubt that the type-II tumours were much more aggressive. If a modified Duke's classification (Astler and Coller, 1954) is applied to those specimens for which all the necessary data are known, of 4 type-I tumours, 1 was stage A, 2 were B_1, and 1 was B_2. By contrast, in 10 type-II tumours 4 were B_2 and 6 were C_2. Furthermore, cytological evidence of anaplasia was much more prominent in the type-II lesions.

Taking this series of cases in isolation, it could be argued that the type-I tumours are carcinomas of the ampulla while the type-II tumours arise from the duodenal mucosa, for all 4 of the tumours which arose away from the ampulla were scirrhous carcinomas (type IIc) and those of type II which arose at the ampulla may have arisen from its overlying duodenal epithelium. Simple and attractive though this hypothesis is it may not be valid, for some of the type-II tumours were arising beneath the duodenal mucosa (type IIb) from the termination of the ducts. Furthermore, some authors have described papillary adenocarcinomas occurring in sites away from the ampulla (Meyer and Rosenberg, 1931; Lieber and others, 1937; Stewart and Lieber, 1937; Miller, Dockerty, Wollaeger, and Waugh, 1951, Monge, Dockerty, and others, 1964). Nevertheless, numerous authors have recognized polypoid, ulcerating, and stenosing varieties of carcinoma in the duodenum and many have commented that ampullary and periampullary lesions are often of the polypoid form (Pic, 1895; Meyer and Rosenberg, 1931; Baggenstoss, 1938; Hoffman and Pack, 1937; Felsen and Wolarsky, 1943; Brenner and Brown, 1955; Burgerman, Baggenstoss, and Cain, 1956; Monge, Docherty, and others, 1964; Edmondson, 1967), so that this type of carcinoma (type I) is a distinctive variety even if it may not be peculiar to the immediate region of the ampulla.

Acknowledgements.—One of us (L. H. B.) operated on some of the cases in this series whilst Senior Registrar to Mr. Clifford D. P. Jones at the Sheffield Royal Infirmary. We would like to record our thanks to him and to Professor H. L. Duthie, Mr. D. H. Randall, Mr. C. H. Talbot, and Mr. J. Lyttle for allowing us to study their cases.

The photography is the work of Mrs. M. Row and the Photographic Department of the United Sheffield Hospitals.

The work was supported in part by funds from the British Empire Cancer Campaign.

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LOCAL RECURRENCE IN PRIMARY OSTEOSARCOMA OF THE FEMUR

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Summary

Cases of primary osteosarcoma of the lower femur treated by through-femur amputation and reported to the Bristol Bone Tumour Registry have been reviewed from the viewpoint of local recurrence.

There were 2 recurrences within the stump and 4 cases with metastases in the ilio-inguinal region.

It is argued that these figures do not justify the routine use of hip disarticulation with its necessarily cumbersome prosthesis in the primary treatment of these tumours.

A large proportion of osteosarcomas arising in previously normal bone occur in the lower end of the femur, quoted figures varying between 35 and 50 per cent (Jaffe, 1958; Coley, 1960; Lichtenstein, 1965; Dahlin and Coventry, 1967). If these are treated primarily by amputation the effectiveness of through-femur amputation compared with hip disarticulation must be considered in relation to the incidence of local recurrence within the stump. The only figures available for such a comparison are those of Sweetnam (1969), who quotes 9 instances of stump recurrence in 42 cases in a survey prepared for a Medical Research Council Report (1969). Cases of primary osteosarcoma in the lower femur treated by through-femur amputation and reported to the Bristol Bone Tumour Registry were therefore reviewed.

MATERIALS AND METHODS

Bristol Bone Tumour Registry files contain 168 cases of primary osteosarcoma presenting up to 1968. Of these, 55 (30 per cent) occurred in the lower femur. Thirty-three cases were treated by amputation through the femur in the apparent absence of metastases. Thirty-one patients have been reviewed, 2 being excluded because there was inadequate information for assessment, both being cases treated overseas.

Each case had been reviewed by the Registry Panel of pathologists, radiologists, and surgeons and the diagnosis agreed on the basis of a primary malignant bone tumour forming osteoid and/or bone. The incidence and site of local recurrence were decided by reference to Registry records and by correspondence with the hospital, surgeon, and general practitioner involved. In cases where uncertainty still existed the full hospital records were consulted but in only a few instances were radiographs available.

RESULTS

There were 9 survivors and all had survived for more than 5 years. The remaining 22 patients had died at periods between 4 and 86 months after amputation (average, 26 months). Thus, all the cases are accounted for and a local recurrence in the survivors is extremely unlikely.

There were 2 recurrences in the amputation stump, noted at 19 and 11 months after amputation respectively. In addition, there were 4 instances of tumour metastases in the neighbouring ilio-inguinal region at 4, 6, 8, and 19 months after amputation respectively. All those with local recurrence died within a few months of this being noted except for 1 patient with a groin recurrence who survived a further 39 months with local radiotherapy.

DISCUSSION

There appears to have been a swing recently in favour of hip disarticulation rather than primary amputation for the treatment of patients with osteosarcoma of the lower end of the femur. Of such cases reported to the Bristol Bone Tumour Registry in the past 4 years, 6 out of 8 were amputated at hip level. Opinions on the necessity for this vary. Lee and McKenzie (1964) favour hip disarticulation while Jaffe (1958), Coley (1960), Lichtenstein (1965), and Dahlin and Coventry (1967) favour amputation through the femur, although Coley (1960) specifies histological examination of the stump marrow at operation.

A femoral stump, even if short, forms the basis for a prosthesis which is greatly superior to that fitted after hip disarticulation, both in the rapidity and ease with which it is fitted and in the eventual level of function obtained. The first point is of particular importance to those who eventually succumb to their disease (in this series this occurred 27 months, on average, after amputation).

Sweetnam (1969) states that femoral amputation is frequently followed by stump recurrence, quoting 9 such instances in 42 cases (or 7 of 28 who had no other treatment), and suggests that hip disarticulation would eliminate the presenting lesion more completely. This may apply to 1 of the 2 recurrences in the stump in the present series, but in the other further metastases were present when the femoral recurrence was first noted and therefore overall survival would not have been affected although an often troublesome and painful local recurrence would have been avoided.

The 4 ilio-inguinal lesions were almost certainly lymph-node involvement. In 2 cases radiographs of the pelvis and hip showed no bony involvement, while a third was described as 'inguinal nodes'. This frequency of lymph-node involvement is not generally acknowledged although McKenna, Schwinn, and Soong (1966) in a series of autopsy examinations found such spread in 30 per cent of cases. These might appear clinically to be stump recurrences, particularly if the remaining femoral fragment was short. They would, nevertheless, not have been cleared by hip disarticulation unless this had been combined with ilio-inguinal node excision. Even this more major procedure would probably not have affected overall survival in 2 of the 4 patients since these had other metastases at the time of the groin recurrence.

Hence, in this group of 31 patients the life of 1 patient might have been saved if hip disarticulation had been undertaken in every case and a second patient would have been spared the local stump recurrence although his fate was sealed by widespread recurrences and he died within 5 months of the appearance of the stump recurrence. The remaining 29 patients, particularly the nine 5-year survivors, would have been adversely affected to a marked extent.

When considering the outcome of treatment for osteosarcoma of the lower end of the femur in these 31 patients we must give due weight to the quality of life of all these young people, both the fortunate who will survive and the unfortunate majority who will die. We must remember that the seed and the soil are more important than the surgery and not extend the mutilation in the mistaken idea that the surgeon's role can be more effective than is, in fact, unfortunately the case.

These results suggest that in osteosarcoma of the lower end of the femur, as in other more common types of malignant disease, the more major excisions are not necessarily the more effective.

Acknowledgements.—I wish to thank Mr. A. L. Eyre-Brook as a result of whose advice and encouragement this study was made, and also Dr. C. H. G. Price and Mrs. L. E. Nutt of the Bristol Bone Tumour Registry for their great help in dealing with the Registry records.

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SUBTOTAL COLECTOMY AND CAECOPROCTOSTOMY

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Summary

The technique of subtotal colectomy with caecoproctostomy is described, together with clinical details of 6 patients in whom it was performed. An important feature of the operation is retention of the ileocaecal sphincter which helps to maintain almost normal bowel function.

THE operation of subtotal colectomy and caecoproctostomy is little known among abdominal surgeons. The indications for the operation are few, but include all extensive colonic diseases which have spared the ascending colon and the rectum. The aim of the procedure is to remove all the diseased areas with preservation of as much healthy colon as is feasible; continuity can be achieved by anastomosing the inverted, proximal, ascending colon to the rectal stump.

The operation was described by Wangensteen, Lewis, Arhelger, Muller, and MacLean (1954) as a primary procedure in radical surgery for carcinoma of the colon. Lillehei and Wangensteen (1955) stressed the importance of preservation of the ileocaecal valve in water absorption. Rosi and Cahill (1962) reported 15 patients with polyposis coli in whom subtotal colectomy with caecorectal reconstitution was employed, leaving only 25 cm. of large bowel which they felt they could keep under observation by sigmoidoscopy. In this country Thompson (1971) has used the procedure in several situations, including cases of colitis where the caecum has appeared normal, diverticular disease with complications, multiple adenomata of the large intestine, and multiple malignancies of the colon.

In Oxford limited experience of the operation over a period of years has led us to believe that provided the indications are correct the functional results are outstandingly good.

SURGICAL TECHNIQUE

Selection of patients is made on clinical grounds and the findings of barium studies and sigmoidoscopy. The last must show no evidence, or only minimal evidence, of proctitis.

After standard bowel preparation, the abdomen is explored through a long left paramedian incision and the extent of the disease confirmed. The ascending colon is then mobilized and the bowel divided at a point 10–15 cm. from the base of the caecum. The ileocolic artery and its branches to the proximal ascending colon are preserved with care.

Subtotal colectomy is then performed, removing the distal ascending colon, transverse colon, left colon, and sigmoid. The greater omentum is removed in continuity and the main blood-vessels, including the inferior mesenteric, are divided where suitable. The point of division of the inferior mesenteric artery will be determined by the nature of the sigmoid disease, that is, near the bowel in inflammatory disease but near the aorta in malignant disease. The presacral space is then opened to allow the rectum to be straightened, so that the anastomosis can take place at the level of the sacral promontory. The rectosigmoid is divided between clamps and the colon removed.

The ascending colon is then rotated *counter-clockwise* so as to lie in the midline or the left iliac fossa above the rectal stump. This is an important manœuvre in ensuring the correct lie of vessels in the pedicle.

An end-to-end anastomosis is performed in two layers without clamps, ensuring that both bowel ends bleed. The outer layer consists of interrupted sutures of 00 thread or silk and the inner of continuous 00 or 0 chromic catgut.

Finally, appendicectomy is performed, and after experience with 1 case where caecal ileus developed an appendicostomy tube is inserted through the appendix stump, a small Malecot or Foley catheter being employed. The anorectal ring is dilated and a large-bore flatus tube stitched in situ. *Fig.* 1 shows a diagrammatic representation of this procedure.

The postoperative course is usually smooth. The flatus tube is removed after 48 hours. The appendicostomy tube is left on continuous open drainage initially and occasionally washed gently with saline to ensure that it has not become blocked. It is removed on the fourteenth postoperative day. One case in our series developed a faecal fistula after early removal of the tube because of wound infection but this soon closed.

Recovery is complete by the third postoperative week, by which time the patient is passing three to four semiformed stools a day with control.

A late postoperative barium-enema film is shown in *Fig.* 2.

CASE REPORTS

Case 1. Male, born in September, 1940. This patient was diagnosed as suffering from ulcerative colitis in 1958. He was treated by blood transfusions, steroids, and retention enemas. In 1963 he was admitted to hospital because of progressive anaemia, and later in the same year he was readmitted urgently with a further relapse and severe anaemia. A barium-enema examination at this time showed gross polyposis extending from the sigmoid colon to the hepatic flexure, but on sigmoidoscopy the rectum showed only minor inflammatory changes. Some doubt was expressed as to the precise diagnosis, and despite the absence of a family history the possibility of the case being one of familial polyposis coli was raised. In February, 1964, a caecoproctostomy was performed. The excised colon was extremely bulky owing to polyps, but the rectum and ascending colon were grossly normal. Histological examination showed that the polyps were of the inflammatory type and that the original diagnosis of ulcerative colitis was correct.

During the early postoperative period the patient experienced persistent lower abdominal pain which was almost certainly caused by gaseous distension of the inverted caecum. This gradually settled and he was allowed home on the twenty-fifth postoperative day, by which time he was passing only two stools daily. An interesting feature was that the faecal fat excretion was 18·8 g. in a 24-hour period preoperatively, but by the time of the patient's discharge this figure had fallen to 7·7 g.

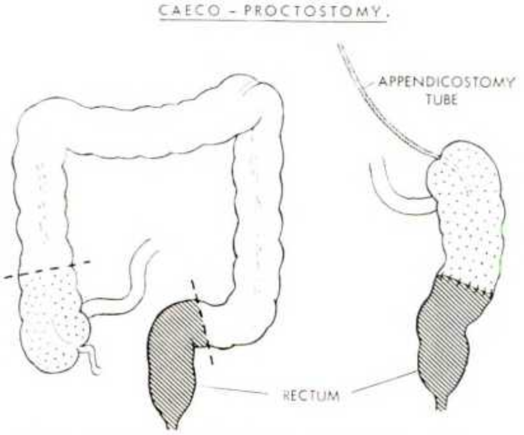

FIG. 1.—Diagrammatic representation of caecoproctostomy.

In November, 1966, by which time the patient was extremely well, he developed an adhesive small-bowel obstruction which required laparotomy. The present situation 6 years after surgery is that he has one bowel action a day which is usually formed. He occasionally has to control his excessive weight-gain by dieting. A recent sigmoidoscopy showed normal rectal mucosa; the haemoglobin is 110 per cent and the sedimentation rate 4 mm. per hour. He is fully employed as an engineer and has fathered 2 children since operation.

Case 2.—Female, born in March, 1915. This single woman who held a responsible post as a secretary was admitted to hospital in 1963 for investigation of diarrhoea, weight-loss, and erythema nodosum. A barium-enema examination showed gross disease extending from the sigmoid to the transverse colon and was suggestive of Crohn's disease. She was treated with oral steroids and retention enemas, and although she gradually improved her skin lesions recurred when the steroids were stopped. In 1965 she relapsed whilst still under treatment and a further barium-enema examination showed stricture formation in the distal transverse colon. In October, 1965, a subtotal colectomy and caecoproctostomy was performed and on this occasion, because of experience with *Case* 1, after appendicectomy a Malecot catheter was introduced so that the caecum could be deflated if necessary. The patient's postoperative recovery was very smooth and she was allowed home on her nineteenth postoperative day, but she continued on steroids and Salazopyrin. The pathology confirmed that the colonic disease was of the Crohn's type.

By June, 1966, the steroids were discontinued, but she continues on small doses of Salazopyrin. She has one bowel action per day with good control, is working full time, and remains in good health 4 years after surgery.

Case 3.—Male, born in March, 1909. This patient who held a post as borough treasurer in a large town developed granular proctitis in 1955. In 1961 a stricture of the sigmoid colon occurred. A defunctioning ileostomy was performed and subsequently the stricture was excised. The isolated colon was treated with steroids for 2 years, but during the course of treatment he developed a large polyp in the left colon. In June, 1963, the polyp was removed by colotomy and the ileostomy was closed. The polyp proved to be of the inflammatory type. However, by 1965 he had developed polyps in the left and transverse colon which radiologically were broad-based and probably adenomatous. He also had mild recurrent symptoms and was advised to undergo further surgery. Having experienced an ileostomy for 2 years, the patient was anxious to avoid a permanent ileostomy, and as his right colon was apparently normal and the rectal changes very minor a caecoproctostomy was performed in November, 1965. The patient was discharged on his twenty-first postoperative day, and when last seen in March, 1969, he was extremely fit. He had three bowel actions a day and on sigmoidoscopy there were only very minor mucosal changes. He has now emigrated to Zambia, having taken up further employment following his retirement in this country. The specimen removed at colectomy showed evidence of ulcerative colitis but with hyperplastic adenomatous polyps in the left colon and splenic flexure.

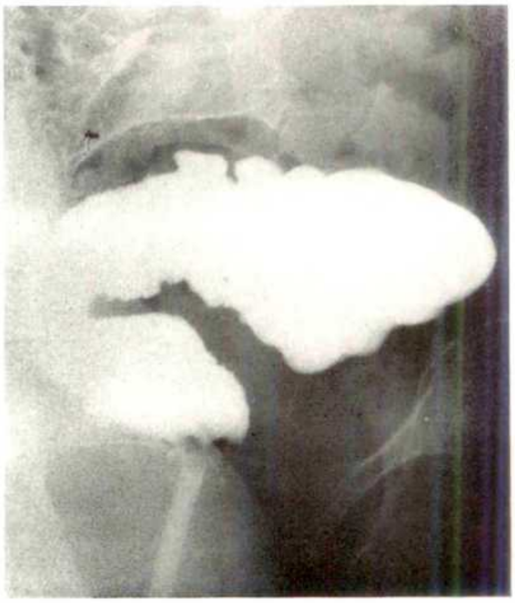

FIG. 2.—Barium-enema film, showing the rectum and inverted caecum.

Case 4.—Male, born in November, 1942. This young garage mechanic originally attended the Radcliffe Infirmary in 1962, giving a 2-year history of left-sided abdominal pain and diarrhoea. A barium-enema examination was consistent with the diagnosis of Crohn's disease of the colon with gross disease from the proximal transverse colon to the sigmoid. Sigmoidoscopy, however, was normal up to 15 cm., at which point the mucosa became cobble-stoned. The patient was treated with systemic and local steroids and Salazopyrin, and he kept reasonably well until late 1965 when he was admitted as an acute case. He was then gravely ill with weakness, prostration, dyspnoea, increasing diarrhoea, and nausea. There was a recorded recent weight-loss of 25 kg. and investigation showed evidence of both gastrocolic and jejunocolic fistulae.

Operation was performed in February, 1966, when the patient weighed 38 kg. He was found to have one gastrocolic, two jejunocolic, one colocolic, and one vesicocolic fistulae. The disease, however, was still confined to the transverse and left colon down to the sigmoid and accordingly, after patching the stomach and the jejunum, a subtotal colectomy and caecoproctostomy was performed. The appendix was removed and a Malecot catheter inserted. The patient was discharged on his forty-first postoperative day to continue on oral prednisolone and Salazopyrin, but by this time he was extremely well, having gained 13 kg. in weight. Within 2½ months of operation his weight had risen to 63 kg. He discontinued taking steroids after 6 months, but continued on Salazopyrin.

The hospital lost touch with this patient in May, 1967, but contact was regained in January, 1970. A recurrence of Crohn's disease had developed in the upper rectum, but this was rapidly controlled by systemic steroids and Salazopyrin. He is fully employed.

Case 5.—Female, born in February, 1910. This woman was a chronic invalid, suffering from hypertension, myxoedema, and a right hemiparesis. In 1967 she developed faecal incontinence and on investigation was found to have a megacolon with colonic inertia and a rectovaginal fistula.

In January, 1968, an extensive sigmoidectomy was performed with a left inguinal colostomy and exteriorization of the rectal stump. The pathological report of the sigmoid colon suggested that the lesion was an acquired idiopathic megacolon, there being no reduction in ganglion cells. In February, 1968, the rectovaginal fistula was repaired and the colostomy was closed. Bowel control following this was poor and her diarrhoea became worse. Her family considered that she was better with a colostomy, but the patient was anxious to avoid this. Barium studies performed in January, 1969, suggested that the left colon, which had become tubular, was the site of ischaemic colitis.

Ultimately, on 31 Jan., 1969, the abdomen was re-explored and subtotal colectomy and caecoproctostomy were performed. The wound around the appendicostomy catheter became infected and as a result the catheter was withdrawn early. A faecal fistula developed which closed in 3 weeks. The pathological report confirmed the presence of ischaemic colitis. The patient's present situation is that her bowel control is better, incontinence is quoted as 'slight' by the district nurse, and she usually passes one formed stool per day. She gets occasional attacks of diarrhoea which are readily controlled by codeine phosphate and at present is attending a day hospital on 2 days a week.

Case 6.—Female, born in August, 1927. This housewife was referred to hospital with a 3-month history of progressive diarrhoea and anaemia. A barium-enema examination showed an irregular sigmoid stricture which was presumed to be a carcinoma. Laparotomy was performed on 13 March, 1969, revealing an advanced sigmoid carcinoma which had infiltrated the transverse colon and mesocolon and the left ovarian tube. A subtotal colectomy was performed with appendicectomy and removal of the left tube and ovary. Continuity was re-established by caecoproctostomy with a Malecot catheter as an appendicostomy tube. The patient was allowed home on her twenty-second postoperative day, and 2½ years after surgery she was well with two or three bowel actions a day and good control. She has no other symptoms.

DISCUSSION

Function.—The most attractive feature of this operation is that, despite removal of most of the colon, almost normal bowel function is retained. Following recovery most patients pass one or two stools per day and these are of normal consistency. This compares favourably with the functional results of ileorectal anastomosis (Baker, 1970; Watts, 1969).

We believe that the ileocaecal sphincter plays an important role in this good functional result. As early as 1931 Ogilvie was led to attempt preservation of the ileocaecal sphincter when resecting the right half of the colon for non-malignant disease, stressing its importance in absorption. Kremen, Linner, and Nelson (1954) showed the value of retaining the ileocaecal sphincter in nutritional adjustment to lower small-bowel excision. More recently, Gazet (1968) has demonstrated that removal or by-pass of the ileocaecal sphincter results in an apparent defect of vitamin-B_{12} absorption and may have a harmful effect upon the animal as a whole. Wangensteen (1943) and Lillehei and Wangensteen (1955) have described the terminal ileum and caecum as the 'water-wringer' of the gut and commented on the absence of diarrhoea following caecorectal anastomosis compared with the persistence of diarrhoea following ileorectal anastomosis.

Indications and Selection.—This operation is particularly suitable for patients with Crohn's disease or ulcerative colitis with sparing of the caecum and rectum, and may also be suitable in ischaemic colitis. It is not the technique of choice for those with carcinoma of the right side of the colon, as adequate excision of lymphatic drainage for this area is not performed. Some patients with multiple or extensive malignancy of the transverse or left colon may be appropriately treated by this procedure. Individual case selection is based upon the results of barium-enema and sigmoidoscopic examination, together with appropriate histological findings on biopsy.

Appendicostomy.—Special attention is drawn to this point for two reasons. The first is that removal of the appendix prevents the possible difficulties of diagnosis and treatment of what would be 'very atypical' appendicitis!

The second reason is that experience with *Case* 1 showed the danger of caecal distension which is readily avoided by this simple means.

Acknowledgements.—We wish to thank Dr. S. C. Truelove for helpful criticism and also Mrs. Linda Ealey and Miss D. Pollard for the typescript.

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PSEUDOCYST OF THE PANCREAS

BY ALAN SIMPSON AND V. K. SRIVASTAVA
WEST BROMWICH AND DISTRICT GENERAL HOSPITAL, STAFFORDSHIRE

SUMMARY

An account of pseudocyst of the pancreas, which is a less common cause of abdominal swelling, is given. Various methods of treatment are described. A series of 8 patients with pseudocyst of the pancreas is reported. The treatment in each case is described.

PSEUDOCYST of the pancreas is an unusual cause of abdominal swelling. The first recorded surgical treatment of the condition was by aspiration (Le Dentu, 1862). Since that time many attempts have been made to find a more satisfactory method of treatment. The methods used have ranged from simple drainage techniques to complete excision of the cyst. Even a century later pseudocyst still presents a surgical problem. The literature contains few reports of this condition and only small series of cases have been recorded, from which it is difficult to draw any definite conclusions. Some aspects of pseudocyst of the pancreas with particular regard to management are discussed in the present paper.

INCIDENCE

Pseudocyst accounts for about 80 per cent of all cases of pancreatic cyst. In 72 patients with acute pancreatitis collected from 1959 to 1969 we have only been able to diagnose pseudocyst in 8 cases. In a similar series described by Louw, Marks, and Bank (1967) the incidence of pseudocyst was 20 per cent.

AETIOLOGY

The main causes of pseudocyst in order of frequency are: (1) acute pancreatitis (and chronic relapsing pancreatitis), (2) upper abdominal trauma, and (3) neoplasm (rare).

Whilst acute pancreatitis accounts for most of these cysts, patients sustaining blows in the upper abdomen (probably in the form of blunt upper abdominal trauma) also account for a considerable number of cases. As early as 1892 Lloyd recognized this association. In a series of 20 patients with a history of upper abdominal trauma quoted by Warren and Hardy (1968) no less than 13 of these patients developed pseudo-pancreatic cyst.

From our observations acute pancreatitis has been the forerunner and the main aetiological factor of pseudocyst in most patients. One case, a child of 14 years, developed pseudocyst after an attack of pancreatitis due to mumps. This cause has also been reported by Attard (1969). We have had no incidents of acute pancreatitis or pseudocyst following blunt upper abdominal trauma. Chronic relapsing pancreatitis has also been mentioned as an important cause of pseudocyst, although no such case occurred in our series. Neoplasm appears to be a rare predisposing cause and only a few incidents have been reported where the cyst was associated with a pancreatic neoplasm.

PATHOGENESIS AND PATHOLOGICAL ANATOMY

During the acute phase of an attack of pancreatitis or, in some cases, following pancreatic trauma considerable quantities of pancreatic exudate rich in digestive enzymes are discharged into the retroperitoneal tissues. Sometimes (probably in the more severe cases when necrosis of the peripancreatic tissue occurs) this exudate is discharged into the lesser sac itself.

We believe that under normal conditions this fluid finds an escape via the foramen of Winslow into the greater sac, thus accounting for the characteristic findings at laparotomy in cases of acute pancreatitis, i.e., blood-stained ascites and fat necrosis. In some cases this ascitic fluid becomes encysted in the lesser sac as a result of blockage of the foramen of Winslow. It probably takes several days for the products of autodigestion to occur in sufficient quantity to form enough sludge to seal the outlet, thus accounting for the delay between an attack of pancreatitis and the appearance of a pseudocyst (*Figs.* 1–4).

In a proportion of cases of pseudocyst a direct connexion between the cyst and the pancreatic duct system becomes established. Such a fistula would explain the fluctuation in the size of some of these cysts affected by a proximal blockage of the pancreatic duct system, this blockage being caused by either scarring or spasm at the sphincter of Oddi or blockage of the actual pancreatic duct system itself or both. We have tried to explain this mechanism in *Fig.* 5. Doubilet and Mulholland (1953) believe that the primary cause is spasm of the sphincter of Oddi which gives rise to pancreatitis and the resulting pseudocyst. The persistence of spasm raises the intraductal pressure and causes the cyst to swell more until the pressure in the cyst increases, owing to pressure transmitted by the neighbouring viscera, and overcomes the intraductal pressure. In this case the cyst will drain once again into the duodenum and spontaneous decompression will occur. On this basis Doubilet and Mulholland (1953) recommend a sphincterotomy as the primary treatment for pseudocyst. This explanation sounds attractive, but fails to answer how a block distal to the sphincter of Oddi could be satisfactorily treated by sphincterotomy since this would not relieve the obstruction and could not therefore reduce the size of the cyst.

DIAGNOSIS

In 72 cases of acute pancreatitis we have adopted the following clinical and radiological criteria in the diagnosis of pseudocyst.

1. History.—*Tables I* and *II* show the type of history obtained in our patients with pseudocyst.

2. Physical Signs.—The main physical sign was that of an intra-abdominal cyst, though in 1 patient ascites was mimicked and in another a brown discoloration of the skin appeared over the cyst (*Fig.* 6).

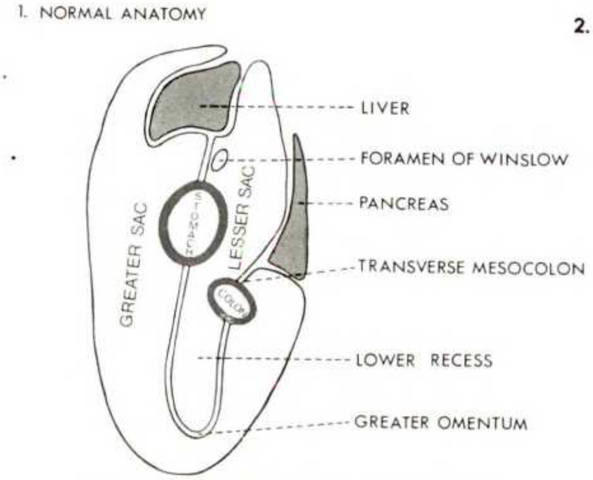

FIG. 1.—Normal anatomy of the pancreatic region.

3.

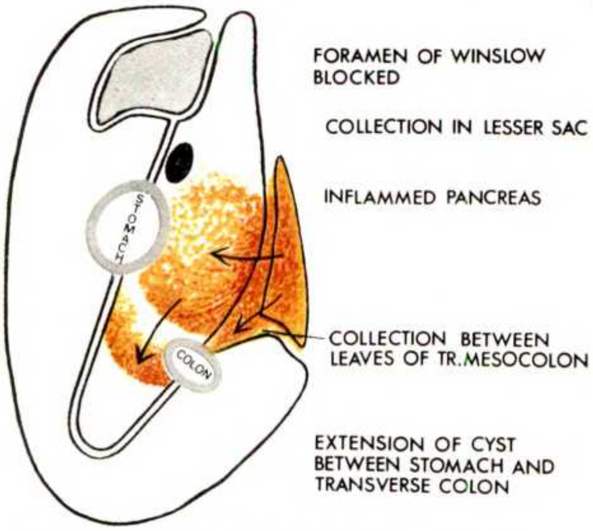
FORAMEN OF WINSLOW BLOCKED
COLLECTION IN LESSER SAC
INFLAMMED PANCREAS
COLLECTION BETWEEN LEAVES OF TR.MESOCOLON
EXTENSION OF CYST BETWEEN STOMACH AND TRANSVERSE COLON
STOMACH
COLON

FIG. 3.—Blockage of the foramen of Winslow causes exudate to become encysted in the lesser sac.

3. Radiographic Aids.—It would be ideal to screen all probable cases of pseudocyst. In our series several patients missed this investigation as a result of diagnosis not being made until abdominal section, or diagnosis had already been made, or the patient's general condition did not warrant this investigation.

However, screening was done in 3 cases and in 2 of them it considerably helped the diagnosis. The most useful findings were: (*a*) distortion of the stomach and transverse colon and an increase in the vertebro-gastric distance, (*b*) displacement of the duodenal cap towards the left of the midline in the antero-posterior view, and (*c*) widening of the duodenal sweep.

4. Intravenous Pyelography.—This was done in some cases where the diagnosis was uncertain. In our series no abnormalities were detected on pyelography (although occasionally a pseudocyst may have to be differentiated from a renal cyst).

2.

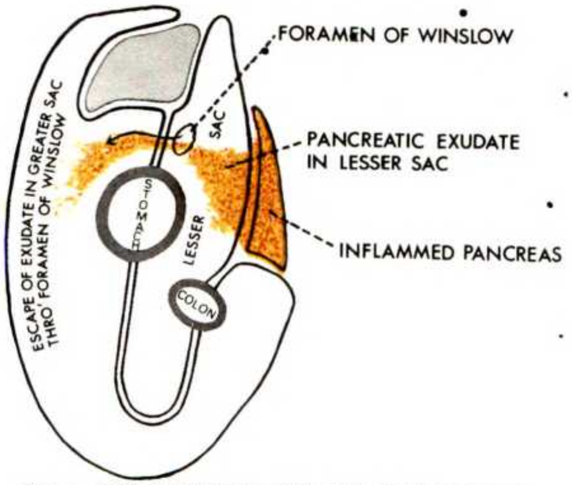
FORAMEN OF WINSLOW
PANCREATIC EXUDATE IN LESSER SAC
INFLAMMED PANCREAS
ESCAPE OF EXUDATE IN GREATER SAC THRO' FORAMEN OF WINSLOW
SAC
STOMACH
LESSER
COLON

FIG. 2.—Acute pancreatitis in which pancreatic exudate escapes from the lesser sac via the foramen of Winslow into the greater sac.

4.

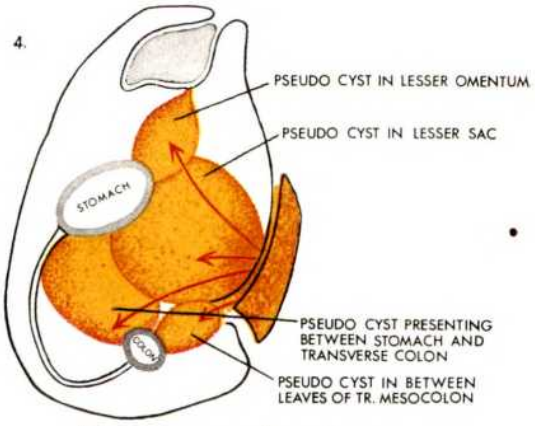
PSEUDO CYST IN LESSER OMENTUM
PSEUDO CYST IN LESSER SAC
STOMACH
COLON
PSEUDO CYST PRESENTING BETWEEN STOMACH AND TRANSVERSE COLON
PSEUDO CYST IN BETWEEN LEAVES OF TR. MESOCOLON

FIG. 4.—Appearance of a pseudocyst.

Table I.—PRESENTING HISTORY OF PATIENTS WITH PSEUDOCYST OF THE PANCREAS

History	*No. of Cases*
Recent attack of acute pancreatitis	6
Chronic relapsing pancreatitis	Nil
Blunt upper abdominal trauma	Nil
Operative procedure on pancreas and/or adjacent organ	Nil
Miscellaneous	
None of the above	1
Mumps causing pancreatitis	1

5. Chest Radiography.—This was done routinely. No evidence of extension of the cyst into mediastinum was found in any of our patients.

6. Serum Amylase.—This investigation was done shortly after admission in 6 out of the 8 patients.

In 5 patients the serum amylase was elevated to a figure of 1600 Somogyi units and in the remaining case to 800 Somogyi units. Serum amylase seems to be often markedly elevated in cases of pseudocyst.

TREATMENT

As there is invariably an obstructive element present in pseudocyst, inadequate free drainage is present and almost always requires some form of surgical drainage procedure. This is necessary not only to cure the condition but also to prevent the dangerous complications which may follow conservative policies. These complications include spontaneous rupture of the cyst giving rise to severe peritonitis, gastro-intestinal haemorrhage, and pancreatic abscess, and there is also the possibility of association of carcinoma of the pancreas.

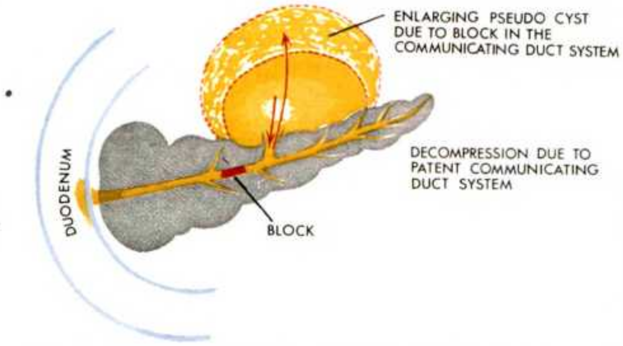
ENLARGING PSEUDO CYST DUE TO BLOCK IN THE COMMUNICATING DUCT SYSTEM
DECOMPRESSION DUE TO PATENT COMMUNICATING DUCT SYSTEM
BLOCK
DUODENUM

FIG. 5.—Fluctuation in size of a pseudocyst owing to a fistulous connexion with the pancreatic duct system.

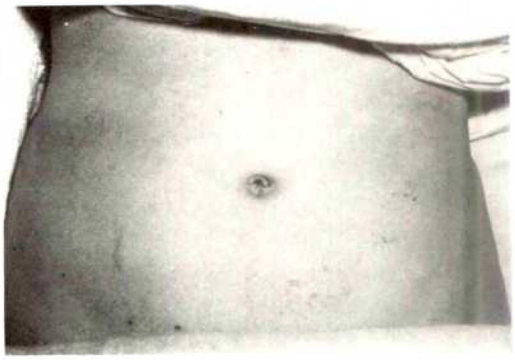

FIG. 6.—Brown discoloration of the skin of the area over the pseudocyst.

The only satisfactory surgical treatments that have been used so far fall under the heading of some form of drainage procedure. It is rarely possible to excise the cyst because of anatomical difficulties and the nature of the pathology.

Surgical Treatments.—

- *a*. External drainage.
  - i. Marsupialization.
  - ii. Drainage through a catheter or tube.
- *b*. Internal drainage.
  - i. Cystogastrostomy.
  - ii. Cystojejunostomy.
  - iii. Cystoduodenostomy.
  - iv. Drainage through a Roux-en-Y-type of procedure.
- *c*. Combination of internal and external drainage through a T-tube put in a cystogastrostomy wound.
- *d*. Excision is rarely possible, but should be attempted in the following circumstances:—
  - i. When there is the possibility of a carcinoma.
  - ii. If the cyst is easily accessible, such as when a cyst arises from the wall of the pancreas.

External Drainage.—External drainage has been fairly widely used for the management of pseudocyst but it has the disadvantages of prolonged leakage, the occasional establishment of a pancreatic fistula (both being associated with skin necrosis), and sometimes the occurrence of gastro-intestinal haemorrhage. External drainage by marsupialization was first introduced successfully by Gussenbauer in 1882, though Warren and Baker (1962) reported satisfactory results from simple drainage using a Depezzer catheter and they considered this method to be not only superior to marsupialization but also particularly suitable for deeply situated cysts. Louw and others (1967) reserved this procedure for desperately ill patients and for cases where the cyst wall is friable and unsuitable for suturing. It is interesting to note that Louw and his colleagues reported no less than 2 deaths out of 6 patients whom they treated by this method, both patients dying from severe gastro-intestinal haemorrhage. A further 2 patients developed chronic pancreatic fistula and in the light of these experiences they now avoid external drainage procedures wherever possible.

Table II.—PRESENTING SYMPTOMS IN PATIENTS WITH PSEUDOCYST OF THE PANCREAS

Symptom	*No. of Cases*
Upper abdominal pain	7
Swelling in upper abdomen	8
Dyspepsia	2
Motor disturbances of upper gastro-intestinal tract due to mechanical effects	2
Miscellaneous, such as fever and chills	Nil

Internal Drainage.—Internal drainage for a pseudocyst was first reported in 1915 by Jedlicka. At least four types of internal drainage have been used:—

Cystogastrostomy: This is a popular method and is particularly suitable for dealing with cysts in the lesser sac. Louw and others (1967) recently reported this form of management in 15 of their patients and were successful in obtaining satisfactory results in all but 2 of them.

Cystoduodenostomy: This method of internal drainage is suitable for dealing with pseudocysts which are adjacent to the head of the pancreas.

Cystojejunostomy: This was first introduced by Heme and Hann in 1927. It is probably the best method of internal drainage for managing pseudocysts and has been most successfully used by Hoxworth, Mattheis, Coith, and Altemeier (1963) and Parshall and Remine (1965) in their series. Louw and others (1967) reserve this method for cysts presenting to the left of the stomach or between the leaves of the transverse mesocolon.

Drainage through a Roux-en-Y-type of procedure: In 1946 Konie described a method using a Roux-en-Y-type of procedure. He made a formal anastomosis to a Roux-en-Y segment of jejunum or to a loop of jejunum defunctioned by entero-enterostomy, and in 3 patients who were treated by this method excellent results were obtained.

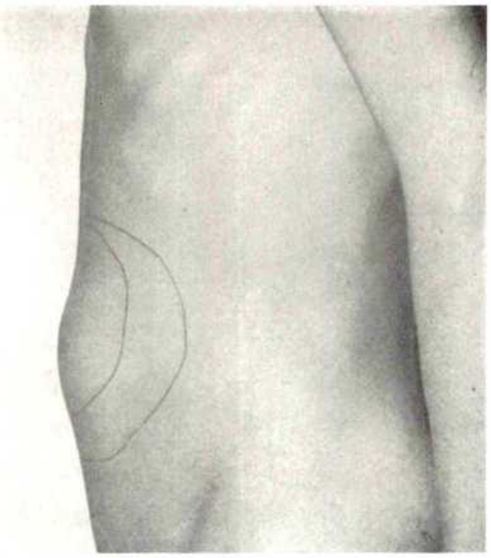

FIG. 7.—*Case* 2. Central abdominal swelling on presentation.

The chief advantage of these internal drainage procedures is avoidance of external fistula and its associated problems, and the main disadvantage is that when the cyst is friable, thin, and often indefinable it is impossible to do a satisfactory anastomosis.

Warren and Baker (1962) have reported 5 cases where internal drainage was complicated by massive gastro-intestinal haemorrhage.

Excision.—Simple excision of a pancreatic cyst is seldom feasible. It has a limited application to patients where the cyst is in the tail area of the pancreas and also where there is a possibility of a neoplasm. As early as 1882 Bozeman did a successful excision.

In our series most of these methods of treating a pseudocyst have been used. The 8 cases of pseudocyst which form the present series are briefly described below, mentioning their subsequent progress and the results of treatment.

CASE REPORTS

Case 1.—A 75-year-old woman was admitted to hospital with typical acute pancreatitis. Ten days after the onset of the attack when the severe symptoms had subsided abdominal distension began, and in 2–3 days' time an ascites-like picture had formed. The serum amylase was raised to 1600 Somogyi units and in view of enlarging ascites it was decided that laparotomy was now necessary. Owing to her poor general condition external drainage by marsupialization was performed. She recovered from the operation quite well but it took several weeks for the discharge to subside, and during this time she was considerably troubled by skin necrosis. During the fifth week she developed a further mild attack of acute pancreatitis, but finally after about 7 weeks the cyst dried up and she was discharged from hospital.

Case 2.—A 14-year-old boy presented at the surgical out-patients' department with a central abdominal swelling (*Fig.* 7). He gave no clear history of pancreatitis but 6 weeks previously he had had an attack of mumps. He was admitted to hospital for diagnostic purposes, and a barium-meal examination, an intravenous pyelogram, and a cholecystogram were all negative. Owing to the rapid enlargement of the swelling it was necessary to carry out a laparotomy, when a large pseudocyst was found to be present between the stomach and the transverse colon. The wall of the cyst was thick and it was possible to do a cystogastrostomy (*Fig.* 8 A). He made a good recovery from this procedure until some 6 months later when he developed further upper abdominal pain and tenderness. At this stage it was decided that a further drainage procedure should be performed. A second internal drainage operation, involving anastomosis of the cyst via a Roux-en-Y loop to the jejunum, was performed. Following this the patient made an uneventful recovery (*Fig.* 8 B).

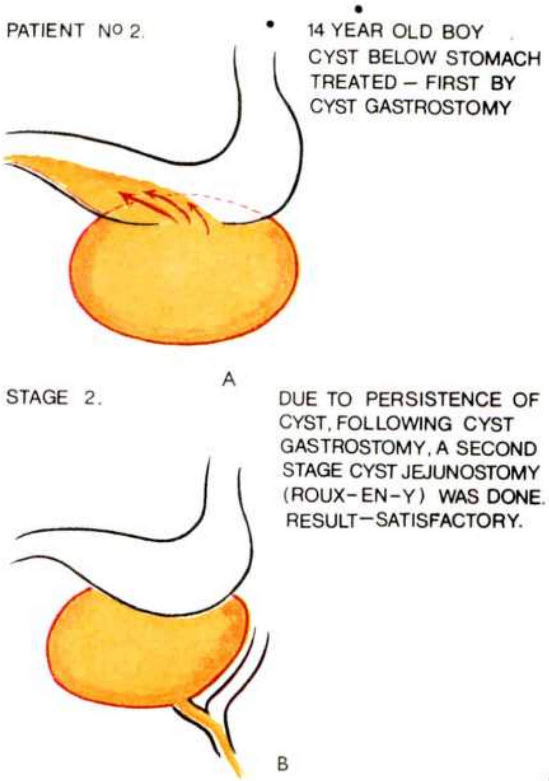

FIG. 8.—*Case* 2. A, Initial treatment by cystogastrectomy. B, Six months later a cystojejunostomy was carried out for persistence of the pseudocyst. A satisfactory result was achieved.

Case 3.—A 45-year-old man was admitted with acute pancreatitis. He was desperately ill for several days and just as he started to recover it became obvious that he was developing a pseudocyst. This cyst rapidly enlarged and it was necessary to do a laparotomy. At operation the wall of the cyst was friable and almost indefinable, and the only possible way of managing the case was by external drainage, this time using a Foley catheter. His general condition gradually improved but he then developed a pancreatic fistula. The skin was becoming increasingly digested and it was decided to try to implant the fistula into the jejunum, forming a type of Roux-en-Y procedure. This was done with an excellent result.

Case 4.—A 34-year-old woman had a typical attack of acute pancreatitis and several days later developed a pseudocyst which rapidly expanded, necessitating operation. At laparotomy the cyst was found lying in the usual position, i.e., it had formed in the lesser sac, and was thick-walled. It was possible to do a cystogastrostomy very easily, following which the patient made a good recovery.

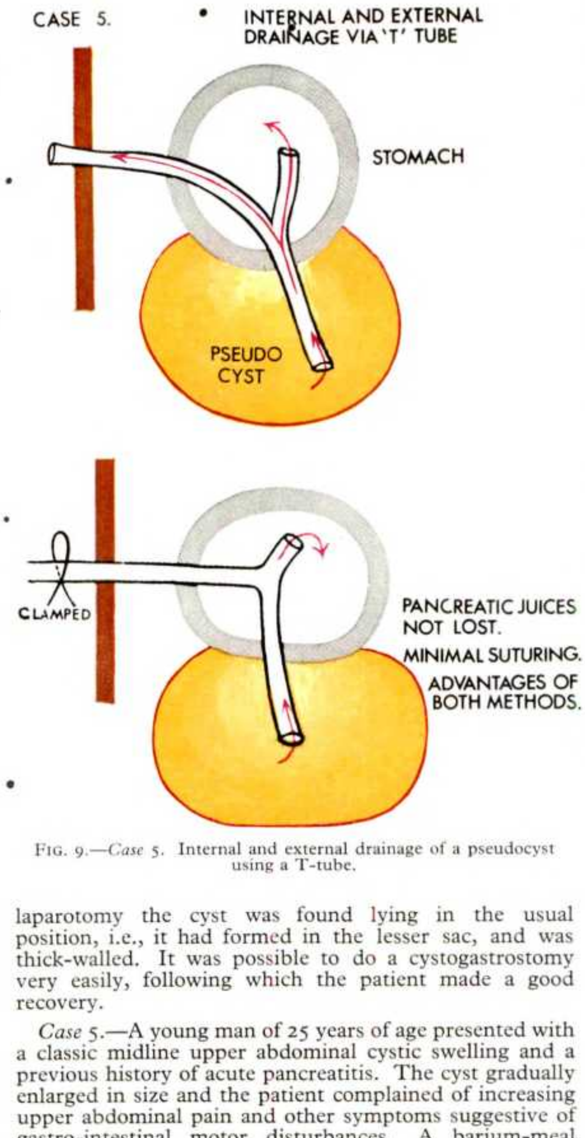
CASE 5.
INTERNAL AND EXTERNAL DRAINAGE VIA 'T' TUBE
STOMACH
PSEUDO CYST
CLAMPED
PANCREATIC JUICES NOT LOST.
MINIMAL SUTURING.
ADVANTAGES OF BOTH METHODS.

FIG. 9.—*Case* 5. Internal and external drainage of a pseudocyst using a T-tube.

Case 5.—A young man of 25 years of age presented with a classic midline upper abdominal cystic swelling and a previous history of acute pancreatitis. The cyst gradually enlarged in size and the patient complained of increasing upper abdominal pain and other symptoms suggestive of gastro-intestinal motor disturbances. A barium-meal examination was suggestive of pancreatic pseudocyst. His serum-amylase level was markedly elevated. A laparotomy was carried out and the diagnosis was confirmed. The cyst was large and so friable that any type of formal anastomosis was quite out of the question. Drainage of the cyst was effected by means of a T-tube placed into the cyst via the posterior wall of the stomach (one arm of the T into the cyst, the other arm of the T was left in the stomach, the long arm of the T being brought out through the abdominal wall). This method offered internal drainage from the cyst into the stomach and also an external means of drainage, thus allowing qualitative and quantitative assessment of the cyst as well as radiographic assessment of the cyst cavity. Gradually the external drainage reduced to a minimum and the long arm of the T-tube was clamped off. This caused neither pain nor discomfort to the patient. One week after clamping the T-tube a quantity of Gastrografin was introduced into the T-tube, but this showed no entry of dye into the cyst cavity, probably indicating complete decompression and obliteration of the cyst. The T-tube was then removed and the patient made an excellent recovery. Several months have now gone by and he has had no further trouble (*Fig.* 9).

Case 6.—A 50-year-old woman presented with a cystic mass in the epigastrium. A diagnosis was not made prior to laparotomy, at which a retrogastric pseudocyst was found. A cystogastrostomy through the posterior wall of the stomach was easily performed, since which she has made a satisfactory recovery.

Case 7.—A 53-year-old woman presented with a large mass in the epigastrium. A provisional diagnosis of carcinoma of the head of the pancreas was made and at operation this was confirmed, but the mass was found to be of multiple cystic origin arising from the head of the pancreas. A subtotal pancreatectomy was performed, the patient making a satisfactory recovery until the tenth postoperative day when she died from a coronary thrombosis. The histology report confirmed the diagnosis of a multiple cyst arising from the head of the pancreas.

Case 8.—A 28-year-old woman presented in the first instance with a very severe attack of acute pancreatitis. After a very stormy period she gradually improved and was discharged home. Later she developed a central abdominal swelling which gradually enlarged and suddenly underwent spontaneous rupture while she was at home. She was admitted to hospital in a moribund condition and at this time we felt that she was too ill to be subjected to laparotomy. After several days her condition improved sufficiently to undergo exploration, when there was evidence of oedema of the pancreas and a recent peritonitis. The gall-bladder was full of gall-stones and a cholecystectomy was performed. Following this she made an uneventful recovery.

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INTRACRANIAL SUBDURAL ABSCESS

By D. I. ANAGNOSTOPOULOS AND PETER GORTVAI

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SUMMARY

Thirty-two cases of intracranial subdural abscess were treated between 1947 and 1969 in two neurosurgical centres. Five patients (15·6 per cent) died. When an E.N.T. focus is detected clinically or radiologically the abscess is always related to it. Four of the 5 fatalities harboured pus along the falx cerebri. Angiography is used to aid localization and to detect further collection of pus. Limited experience in the use of gamma scanning for localization is encouraging. Pus in the subdural space is drained through bur-holes and antibiotics are administered locally. Broad-spectrum bactericidal antibiotics are used in high dosage as the initial treatment and cerebral oedema is controlled by mannitol and dexamethasone in the drowsy or unconscious patient. Surgical decompression should be considered when comatose patients do not respond to bur-hole drainage of the pus and medical measures.

SUBDURAL abscess is one of the types of intracranial suppuration. Pus forms in the potential space between the dura and arachnoid as a consequence of bacterial infection from the surrounding structures or from distant sites by spread via the blood-stream.

Kubik and Adams reviewed the literature in 1943 and described 14 cases. Antibiotics were not in use at that time and 12 patients died.

Schiller, Cairns, and Russell (1948) reported on the use of penicillin in subdural abscess, and recorded a mortality of 30 per cent in patients who received penicillin both locally and systemically. Hitchcock and Andreadis (1964), using local and systemic broad-spectrum antibiotics, reported a similar mortality-rate: 10 dead out of 29 cases. Garfield (1969) had an overall mortality of 38 per cent in 38 cases; local penicillin and streptomycin were employed with systemic antibiotics. Mortality was higher in patients whose systemic antibiotic treatment was considered inadequate or inappropriate in retropsect. Further recent series have been published by Bhandari and Sakkari (1970) and Torres, Yarzagary, and West (1970).

CLINICAL MATERIAL

Thirty-two cases of subdural abscess were seen between 1947 and 1969 at Oldchurch Hospital, Romford, and at the Derbyshire Royal Infirmary.

The age and sex distribution is given in *Table I.* More than half the cases were in the 10–30 years age-group. Males outnumbered females in a ratio of 3 : 1.

The primary site of infection is set out in *Table II.* In two-thirds of the cases sepsis originated in the paranasal air sinuses or the middle ear. Cases of intracerebral abscess which ruptured into the subdural space have been excluded from this study.

The presenting signs and symptoms are summarized in *Table III.* Fever was invariably present and temperatures ranged from 38 to 39° C. Hemiparesis, associated with dysphasia when the dominant hemisphere was affected, was a common feature. Headache, vomiting, and papilloedema—the classic triad of raised intracranial pressure—were also often seen. Epileptic attacks occurred in half the cases.

Table I.—AGE AND SEX DISTRIBUTION OF PATIENTS WITH INTRACRANIAL SUBDURAL ABSCESS

Age	*Male*	*Female*
1 mth.–10 yr.	2	—
10–30 yr.	18	5
31–51 yr.	3	1
51 yr. and over	1	2
Total	24	8

Table II.—PRIMARY SITE OF INFECTION IN PATIENTS WITH INTRACRANIAL SUBDURAL ABSCESS

Primary Site of Infection	*No. of Cases*
Paranasal sinuses	18
Frontal sinus	11
Sphenoidal sinus	1
Multiple	6
Otitis	6
Meningitis	2
Trauma (fractured skull)	1
Treatment of subdural haematoma	1
Upper respiratory tract	3
Orbital cellulitis	1

Table III.—PRESENTING SYMPTOMS AND SIGNS IN PATIENTS WITH INTRACRANIAL SUBDURAL ABSCESS

Symptoms and Signs	*No. of Cases*
Fever	32
Neck rigidity	32
Headache	28
Vomiting	19
Epilepsy	16
Hemiparesis	23
Papilloedema	18
Dysphasia	10
Homonymous hemianopia	4

The level of consciousness on admission was classified as follows:—

Category A: alert and correctly orientated (5 cases).

Category B: drowsy and disorientated (21 cases).

Category C: responding only to painful stimulation (6 cases).

These categories correspond to those used by Garfield (1969).

Investigations.—Skull radiographs were available for examination in 16 cases. In 13 there was opacity of one or more of the paranasal air sinuses. The sutures were widened in 2 cases and in 1 case there was osteomyelitis of the skull. In 2 cases with a history of trauma the skull radiograph showed a fracture.

The white-cell count in the peripheral blood was increased in all the cases, the total count ranging from

10,000 to 17,000 per c.mm. with an increase in the number of polymorphonuclear cells. The erythrocyte sedimentation rate was increased in most cases. The range observed was 7–140 mm. (Wintrobe).

An electro-encephalogram was obtained in 13 patients preoperatively. Correct localization of the abscess was given in 3 cases only, and the localizing feature in these cases was the presence of delta waves.

Carotid angiography was performed in 19 cases. In 11 correct localization of the abscess was possible; in 3 a shift of the midline structure was observed. A collection of pus beside the falx was demonstrated in 3 cases. In 5 cases the angiogram was normal.

In all 18 patients where the primary site of infection was E.N.T. sepsis correct localization was possible in retrospect on considering the site of the sepsis.

Gamma scan of the brain was undertaken in 2 patients and in both the increased peripheral uptake was suggestive of a subdural abscess.

Preoperative ventriculography or air encephelography was not used in this study.

Lumbar puncture was performed preoperatively in 22 cases. The pressure was always raised to 200–300 mm. of cerebrospinal fluid. The total protein content was elevated in every case, the range being 60–220 mg. per ml. The cell count was also increased in every case. Culture of the cerebrospinal fluid yielded no growth in 19 of the 22 cases. Streptococci, staphylococci, and *Proteus vulgaris* were each isolated on a single occasion.

Table IV.—RESULTS OF CULTURING THE SUBDURAL PUS FROM PATIENTS WITH INTRACRANIAL SUBDURAL ABSCESS

Organisms cultured	*No. of Cases*
Haemolytic streptococci	2
Non-haemolytic streptococci	4
Anaerobic streptococci	1
Coagulase-negative staphylococci	2
Coagulase-positive staphylococci	2
Proteus vulgaris	2
Fusiform bacilli	1
No growth	16

Isolation of Organisms.—Lumbar puncture, when performed before referral to the neurosurgical unit, usually gave a picture of sterile meningitis. The offending organisms, when isolated, were cultured from pus obtained at operation. The results of culture from subdural pus in 30 cases are given in *Table IV*. In just over a half of the cases the pus was sterile. Streptococci and staphylococci were isolated from most of the remainder.

TREATMENT

All the cases were treated by making multiple burholes over the affected region and evacuation of the pus. Catheters were left in the subdural space. Penicillin, 20,000 U., with streptomycin, 50–100 mg., were instilled daily. Broad-spectrum antibiotics were prescribed systemically in every case. One of the following antibiotics was used as the initial treatment: penicillin 4–6 MU. with streptomycin 1 g., daily; chloramphenicol 2–3 g. daily; cephaloridine 4 g. daily. Further appropriate antibiotics were given if indicated by the results of the culture or if the clinical condition of the patient failed to improve.

Epileptic seizures, when present, were controlled by the administration of phenobarbitone and phenytoin. Valium was used intramuscularly or intravenously in a few cases for status epilepticus.

Medical measures were taken to combat cerebral oedema in drowsy and unconscious patents (categories B and C); 500 ml. of 10 per cent mannitol solution were given initially and repeated 6-hourly if there was no improvement. Most of the more recently treated patients were also given dexamethasone intramuscularly, 10 mg. initially and 4 mg. 6-hourly.

No improvement in the patient's conscious level after 24 hours was considered an indication for a wide craniotomy and decompression, combined with a limited frontal or temporal lobectomy when there was massive herniation of the brain after opening the dura. Craniotomy was performed in 4 cases.

CLINICAL RESULTS

Of the 32 cases presented here, 27 survived and 5 patients (15·6 per cent) died. Sixteen of the patients suffered epileptic attacks before operation. Twelve of these continued to have fits postoperatively. Sixteen of the survivors suffered epileptic attacks of a greater or lesser severity 1–2 years after operation. Nine patients were hemiparetic but only 1 was severely disabled. Some dysphasia was discernible in 6 cases. In 1 patient the presenting homonymous hemianopia persisted.

Of the 5 patients who died, no less than 4 had a sizeable extension of the subdural pus along the medial surface of the affected cerebral hemisphere next to the falx cerebri.

DISCUSSION

Age and Sex Incidence.—More than half the cases occurred in the 10–30-year age-group. Such a finding is not general and the relative youth of the case material may have contributed to the low mortality. However, the age of the patient had no significant effect on the mortality-rate in Garfield's (1969) survey of cerebral abscesses.

Males outnumbered females by 3 : 1 in this series. We feel that the preponderance of males is significant and may be related to the larger incidence of E.N.T. sepsis in the male.

Diagnosis.—A glance at *Table III* suffices to see that a certain differential diagnosis from meningitis or meningo-encephalitis is not possible on the grounds of clinical signs and symptoms alone. The incidence of focal neurological signs and of epilepsy is higher than is normally expected in meningitis, and therefore the diagnosis of intracranial pus can be suspected.

Lumbar puncture was performed in many of the cases because meningitis was suspected. We were not able to ascertain the degree of risk, but we would agree with previous authors (Gregory, Messner, and Zinneman, 1967; Duffy, 1969; Garfield, 1969) that lumbar puncture causes deterioration in the clinical state of the patient with a space-occupying lesion in the cranium. Neurosurgical investigations should be instituted without lumbar puncture if an intracranial abscess is suspected on the grounds of meningitis complicated by hemiparesis, raised intracranial pressure, or fits.

Epilepsy.—Half the cases had epileptic seizures before operation, a figure comparable to that of Hitchcock and Andreadis (1944). During the follow-up 16 of the patients suffered from epilepsy, 12 of whom had had preoperative seizures. Epilepsy is a common complication amongst the survivors of subdural abscess and postoperative epilepsy is three times more frequent in patients who had attacks before operation.

Localization of the Abscess.—When the source of the infection is sinusitis or middle-ear disease, the site of the abscess is closely related to the primary infection. Angiography localized the abscess 11 times in 19 cases, a moderately high success rate, against which must be balanced the fact that in 5 cases the angiogram was normal. The angiographic findings in subdural empyema have been fully discussed by Torres and others (1970). On the anteroposterior projection there is often a crescentic avascular area over the surface of the cerebral hemisphere and the medial edge of this area is often scalloped, which differentiates subdural empyema from the rather similar picture of a subdural haematoma. In subdural haematoma the medial edge of the avascular area is smooth.

Our limited experience with gamma scanning is highly encouraging, but there seems to be no doubt at the present time that a bur-hole judiciously placed near the primary site of infection should be made when the clinical picture is suggestive of an abscess, even when the angiogram is negative. A gamma scan is a useful adjunct but treatment must not be delayed if scanning is not available within a few hours.

Bacteriology and the Use of Antibiotics.—The sensitivity pattern of the organisms cultured from pus could not be accurately analysed from the available data. We would hazard a guess that of the 14 instances of positive culture listed in *Table IV*, some organisms would certainly be resistant to penicillin and some of the cocci would be likely to be resistant. We therefore do not agree with Gregory and others (1967) and Garfield (1969) that penicillin alone in a high dosage is a suitable primary treatment. We favour the systemic use of bactericidal broad-spectrum antibiotics in high dosages.

Mortality.—The mortality of 5 patients out of 32 (15·6 per cent) is low by previous standards, but the 5 deaths require special consideration in the effort to reduce mortality in the future.

We have considered the possibility that the patient's conscious level on admission influences the mortality. All the patients in category A (alert) and in category C (comatose) survived, the 5 fatalities being in category B (drowsy) on admission.

Of the 5 fatalities, 4 patients had a sizeable extension of the abscess along the falx cerebri. The subdural pus may represent rupture of an intracerebral abscess. When there is no improvement on appropriate treatment the presence of further undrained pus must be considered and a carotid angiogram should be taken.

Raised Intracranial Pressure.—Once pus has been localized and drained, enough time must be gained for the antibiotics to control the infection. The inflammatory process itself is associated with cerebral oedema. A subdural abscess is often complicated by thrombophlebitis of the cortical veins or even of the venous sinuses which causes further oedema of the brain. The use of intravenous mannitol with dexamethazone will often decrease cerebral oedema. In spite of treatment with antibiotics and medical measures to combat cerebral oedema the patient's level of consciousness may fail to improve. Surgical decompression should be considered if a comatose patient is not improving in 24 hours. This principle is illustrated by the following case.

CASE REPORT

A boy of 16 was admitted drowsy but answering simple questions. A month previously he had been hit on the left eye by a tennis ball and had developed an intra-orbital abscess, which had been drained and treated with systemic penicillin and streptomycin. Three weeks later he had become feverish with headache and vomiting. The lumbar cerebrospinal fluid pressure at that time was 230 mm.; protein 200 mg. per ml., sugar 75 mg. per ml., white cells 49 per c.mm. The fluid was sterile.

When transferred to the neurosurgical unit there was neck rigidity, photophobia, tenderness over the right side of the forehead, left hemiparesis, and left hemianopia. Gamma scan of the brain showed increased uptake over the edge of the right cerebral hemisphere, and carotid angiography demonstrated a subdural abscess. On the day of admission the abscess was evacuated through bur-holes. The patient was given chloramphenicol, 10 per cent mannitol intravenously 8-hourly, and dexamethasone 10 mg. on admission and 4 mg. 6-hourly.

In spite of treatment the patient responded only to painful stimuli the next morning. The pupils were fixed and dilated. Fourteen hours after the bur-hole drainage a large right frontal flap was turned and the dura was opened. There was a small amount of residual subdural pus. Two large cortical veins were thrombosed. The frontal lobe was so swollen that the wound could not be closed. The frontal pole was amputated 10 cm. behind its tip, the dura was left open, and the scalp was closed in layers. During the next week the patient became alert but had a left hemiparesis. One year after operation he was walking unaided and was seeking employment.

Acknowledgements.—We should like to thank Messrs R. H. Shephard, Julian J. Taylor, B. Fairburn, and J. Andrew for permission to include patients who have been under their care.

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RENAL FUNCTION AND HYPERTENSION IN PRIMARY HYPERPARATHYROIDISM

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SUMMARY

Fifteen patients with histologically proven primary hyperparathyroidism have been investigated with special reference to renal function and the occurrence of hypertension. The patients have been followed up clinically, biochemically, and radiographically for a period of 8 months to 5 years after surgery. In all cases the serum-calcium levels returned to normal immediately after parathyroid adenectomy.

Satisfactory renal function was maintained in all but 1 of the cases who had had normal preoperative renal function tests. However, renal damage once established persisted and even progressed after parathyroid adenectomy. Renal function, therefore, did not improve after operation.

At follow-up examination a decrease in the number of renal calculi was found in only 2 cases. None of the patients showed formation of new renal calculi or increase in size of those present preoperatively.

Hypertension was present in 6 patients preoperatively. Six months after operation 2 more patients became hypertensive. Both of these patients had shown evidence of renal damage preoperatively. In another case the patient became normotensive 3 months after operation. The severity of renal functional impairment did not bear any relationship to the degree of hypertension although it is possible that the hypertension is secondary to the renal lesion.

RENAL complications are well recognized in patients with hyperparathyroidism; it is not surprising, therefore, that renal damage with subsequent alterations in renal function may ensue. A survey of 15 patients with primary hyperparathyroidism, operated on by one of us (J. G. G.) at the North Staffordshire Hospital Centre between 1966 and 1970, has been carried out, with particular reference to renal function and hypertension and the relationship of these two factors. Five of the 15 cases presented initially with urological symptoms, and the remainder with neurological or bone and joint or abdominal symptoms (*Table I*). On radiological examination, however, 10 cases were found to have nephrolithiasis or nephrocalcinosis; 2 of the remaining cases had passed renal calculi previously.

MATERIALS

This series comprised 15 patients with primary hyperparathyroidism; 8 were male and 7 were female. Their ages ranged from 20 to 60 years, with 10 cases over 40 years of age. The lesion in each case proved to be a simple adenoma of the chief-cell or clear-cell variety, arising in the inferior glands in 11 cases (*Table II*).

Two patients required a second operation because their serum-calcium levels, which fell initially following the first operation, rose again above normal levels. In 1 case a further tumour was found embedded in the lower pole of the thyroid gland following thyroidectomy. This was thought to be a second tumour, although the possibility of it being an extension of the original tumour could not be ruled out. In the second case a tumour was found situated at the lower pole of the thyroid gland at the initial operation and confirmed on frozen section to be parathyroid tissue. The second exploration revealed another tumour lying behind the manubrium sterni. In both cases the serum calcium returned to normal levels following the second operation.

Table I.—PRESENTING SYMPTOMS OF PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

Symptoms	*No. of Patients*
Urinary	
Ureteric colic	4
Dysuria and frequency	1*
Neurological	
Migraine	1
Hemiparesis	1
Abdominal	
Acute pancreatitis	1
Splenic infarct	1
Subacute intestinal obstruction	1
Bone and joint	
Vague joint pains	3
Fractured neck of femur	1
Asymptomatic	1†

* This patient did not have a urinary infection. A stone was present in the lower end of the left ureter which passed spontaneously

† Hypertension found on routine insurance examination.

Table II.—POSITION OF THE LESION AND SEX OF PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

SEX	NO OF PATIENTS	POSITION OF LESION			
		Right		*Left*	
		Superior	Inferior	Superior	Inferior
Male	8	2	2	2	2
Female	7	—	4	—	3
Total	15	2	6	2	5

METHODS AND DIAGNOSIS

Serum Calcium.—All the patients underwent a full blood and urine examination pre- and postoperatively. The diagnosis of primary hyperparathyroidism was made essentially on the classic biochemical triad of hypercalcaemia, hypophosphataemia, and hypercalciuria. The biochemistry was carried out in the Metabolic Unit Laboratory

(*Table III*). Two patients (Nos. 9 and 11; *Table III*) exhibited fluctuations in the serum-calcium levels which were between raised and normal on random blood-samples taken during the preoperative period. The diagnosis of primary hyperparathyroidism was confirmed by failure of parathyroid suppression with both calcium infusion and steroids.

Table III.—Serum Calcium and Phosphate Levels in Patients with Primary Hyperparathyroidism

Case No.	Serum Calcium (mg. per cent)		Serum Phosphate (mg. per cent)	
	Pre-operative	Post-operative	Pre-operative	Post-operative
1 H. B.	14·4	9·2	2·4	2·5
2. L. D.	14·0	9·4	2·5	3·2
3. E. E.	14·0	10·0	2·5	2·6
4. J. H.	15·2	6–10·2	1·9	3·0
5. J W.	12·9	9·9	1·6	3·2
6. L G.	11·7	10·7	2·0	2·9
7. A G.	13·5	9·7	2·2	2·4
8. E B.	11·9	10·0	1·9	3·0
9. M. W.	12·2	10·3	2·2	2·5
10. D J.	16·0	9·5	2·0	2·7
11. J. L.	12·5	9·9	2·2	2·8
12. E. L.	11·0	10·5	1·9	2·7
13. A. S.	14·1	10·2	1·8	2·2
14 W D.	12·0	8·8	2·3	3·5
15. R. H.	13·1	8·1	2·3	3·1

Bone Disease.—Skeletal radiographic surveys and bone biopsies were carried out to establish the presence or absence of bone changes.

Renal Function.—Renal function was estimated by assessment of the blood-urea, plasma creatinine, and creatinine clearance, and by intravenous pyelographic studies.

Hypertension.—The presence and degree of hypertension were studied. Blood-pressure readings were taken in the recumbent position after a period of rest. The 'normal' blood-pressure was taken as 140/90 mm. Hg. The diastolic pressure, being a measure of arteriolar pressure, was considered more important than the systolic pressure in assessing the degree of hypertension. All the patients with hypertension were screened to exclude other causes.

RESULTS

The patients have been followed up for a period of 8 months to 5 years after surgery.

Serum Calcium.—In all cases the serum-calcium levels fell to normal immediately after parathyroid adenectomy. However, in 2 cases (Nos. 4 and 11; *Table III*) the calcium levels were found to have risen above normal about a year after the first operation. The calcium levels remained raised until a second exploration. In 1 case (No. 4) a further tumour was found embedded in the lower pole of the thyroid gland. In the other case (No. 11) a second tumour was found behind the manubrium sterni. The calcium levels returned to normal after the second operation.

In all except 2 cases (Nos. 7 and 13; *Table III*) the serum-phosphate level rose above 2·5 mg. per cent. Prior to operation only 2 cases (Nos. 2 and 3) had persistent serum-phosphate levels of 2·5 mg. per cent. All the other cases had serum-phosphate levels below this figure.

Bone Disease.—Five of the cases (Nos. 1, 3, 4, 11, and 15; *Table IV*) showed the presence of osteitis fibrosa on skeletal survey and these results were confirmed by bone biopsy. Patients with bone changes all had renal function impairment.

Renal Function.—None of the patients had a urinary infection either pre- or postoperatively. This was confirmed on several midstream specimens of urine taken at intervals.

Table IV.—Findings of Intravenous Pyelography and Bone Biopsy in Patients with Primary Hyperparathyroidism

Case No.	Intravenous Pyelography			Skeletal Survey and Bone Biopsy
	Function	Nephro-lithiasis	Nephro-calcinosis	
1. H. B.	Adequate	Unilateral	—	Osteitis fibrosa
2. L. D.	Adequate	Nil	—	Normal
3. E. E.	Poor	Bilateral	—	Osteitis fibrosa
4. J. H.	Adequate	Nil	Bilateral	Osteitis fibrosa
5. J. W.	Adequate	Nil	—	Normal
6 L. G.	Adequate	Unilateral	—	Normal
7. A. G.	Adequate	Nil	—	Normal
8. E. B.	Adequate	Unilateral	—	Normal
9 M. W.	Adequate	Nil	—	Normal
10. D. J.	Adequate	Bilateral	Bilateral	Normal
11. J L.	Poor	Bilateral	—	Osteitis fibrosa
12. E L.	Adequate	Nil	—	Normal
13. A. S.	Adequate	Unilateral	—	Normal
14. W. D.	Adequate	Unilateral	—	Normal
15 R. H	Adequate	Nil	Bilateral	Osteitis fibrosa

Blood-urea.—The blood-urea was elevated in 4 cases preoperatively (Nos. 4, 7, 11, and 15; *Table V*). In 1 of these cases (No. 7) the blood-urea returned to normal levels 3 months after parathyroid adenectomy and it has subsequently remained normal. In 1 other case (No. 1), although the blood-urea was normal preoperatively, it became elevated 3 months after operation and has remained elevated since.

Plasma Creatinine.—Four patients (Nos. 1, 4, 11, and 13; *Table V*) had a raised plasma-creatinine level preoperatively. Two of these patients (Nos. 4 and 11) also had a raised blood-urea. Another case (No. 1) developed a raised blood-urea 3 months postoperatively. The fourth case (No. 13) with a raised plasma-creatinine level had no other evidence of renal functional impairment. A further patient (No. 14) developed a raised plasma-creatinine level 6 months after parathyroid surgery.

Creatinine Clearance.—In 14 cases the creatinine clearance was determined. Four of these (Nos. 1, 4, 11, and 15; *Table V*) were low preoperatively and these results were mirrored in the preoperative blood-urea and plasma-creatinine results. A further 4 cases (Nos. 3, 7, 9 and 14) showed low creatinine-clearance levels 6 months after operation. One of these (No. 9), however, was a laboratory error. The other 3 cases have shown a persistently low creatinine clearance. They also had other signs of renal impairment, namely, a raised blood-urea and plasma creatinine or poor function on radiographic examination.

Intravenous Pyelographic Studies.—Three patients (Nos. 6, 10, and 15; *Table IV*) presented with ureteric colic and required removal of their urinary-tract stones as they were causing obstruction. One was impacted in the pelvi-ureteric junction and required a pyelolithotomy (No. 6; *Table V*). The other 2 patients had stones removed from the lower end of the ureter by Dormia extraction (Nos. 10 and 13). Their renal function, as assessed by intravenous pyelographic studies, blood-urea, plasma creatinine, and creatinine clearance, was satisfactory both before and after removal of the stones (*Table III*).

Table V.—RESULTS OF RENAL FUNCTION TESTS IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

CASE NO.	BLOOD-UREA (mg. per cent)		PLASMA CREATININE (mg. per cent)		CREATININE CLEARANCE (ml. per min.)	
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative
1. H. B.	38	82	1·7	2·8	43	15
2. L. D.	22	29	0·8	0·8	100	102
3. E. E.	28	31	—	1·4	—	55
4. J. H.	40	50	1·6	—	46	—
5. J. W.	24	38	0·9	0·9	83	174
6. L. G.	38	28	0·8	0·8	108	101
7. A. G.	45	32	1·3	1·1	81	51
8. E. B.	36	24	0·7	0·8	105	136
9. M. W.	25	32	1·0	1·0	129	135
10. D. J.	36	30	1·3	1·2	107	91
11. J. L.	48	72	2·3	2·7	39	32
12. E. L.	32	34	1·1	1·1	99	99
13. A. S.	21	26	1·9	1·7	90	97
14. W. D.	30	28	1·3	1·6	84	67
15. R. H.	58	64	1·4	1·2	45	51

Two cases (Nos. 3 and 11; *Table IV*) showed poor function on radiographic examination. One of these (No. 3) had a non-functioning left kidney. As this patient is also hypertensive she is at present under consideration for a nephrectomy. The remaining 13 patients showed adequate function as assessed by radiology.

Five cases (Nos. 1, 6, 8, 13, and 14) had unilateral renal calculi and 3 cases (Nos. 7, 10, and 11) had bilateral stones. None of these was causing obstruction as they were small and situated in the renal parenchyma. Three patients (Nos. 4, 10, and 15) had bilateral nephrocalcinosis. One of these patients (No. 10) also had bilateral renal calculi. Two patients (Nos. 5 and 12) had passed calculi following attacks of ureteric colic previously but their radiographs on the present occasion were clear.

It is evident from a comparison of the renal function studies and the radiographic findings that the disturbance in renal function was not associated with urinary-tract obstruction in this series.

After parathyroid surgery subsequent intravenous pyelography did not show any change in the size of the renal calculi, although 2 patients did pass several stones spontaneously. None of the patients showed formation of new renal calculi or growth of those present preoperatively after operation.

Blood-pressure.—Nine of the patients were normotensive preoperatively whilst 6 were hypertensive (*Table VI*). Three of the latter cases (Nos. 4, 7, and 9) had severe hypertension (diastolic pressure over 120 mm. Hg) and 3 (Nos. 1, 14, and 15) had moderate hypertension. Two patients (Nos. 3 and 11) who were previously normotensive developed moderate hypertension 6 months after operation. One patient (No. 15) who was hypertensive preoperatively became normotensive 3 months after operation. The hypertensive patients are moderately well controlled on drug therapy.

Relationship between Impaired Renal Function and Hypertension.—Six of the 15 patients (Nos. 1, 3, 4, 7, 11, and 15; *Table V*) had impairment of renal function preoperatively. Four of these (Nos. 1, 4, 7, and 15) also had hypertension. Six months postoperatively the other 2 patients with renal insufficiency (Nos. 3 and 11) also became hypertensive. Renal function did not improve after parathyroid adenectomy. In 3 cases (Nos. 1, 7, and 11; *Table I*) renal function continued to deteriorate, as shown by a rising blood-urea and creatinine or a lowering of the creatinine clearance. In 1 case (No. 14) impairment of renal function became apparent 6 months after operation. This patient was hypertensive preoperatively. The severity of renal functional impairment did not bear any relationship to the degree of hypertension.

Table VI.—ASSESSMENT OF BLOOD-PRESSURE IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

CASE NO.	BLOOD-PRESSURE				COMMENT
	Normotensive		*Hypertensive*		
	Pre-operative	Post-operative	Pre-operative	Post-operative	
1. H. B.	—	—	170/115	140/100	On therapy
2. L. D.	140/90	140/90	—	—	—
3. E. E.	130/90	—	—	160/100	—
4. J. H.	—	—	180/120	190/110	On therapy
5. J. W.	120/70	120/80	—	—	—
6. L. G.	140/80	140/80	—	—	—
7. A. G.	—	—	170/130	140/100	On therapy
8. E. B.	130/70	120/80	—	—	—
9. M. W.	—	—	220/150	200/120	On therapy
10. D. J.	120/85	140/90	—	—	—
11. J. L.	160/90	—	—	170/100	—
12. E. L.	130/80	120/80	—	—	—
13. A. S.	140/80	130/80	—	—	—
14. W. D.	—	—	200/110	150/95	On therapy
15. R. H.	—	120/80	150/110	—	—

DISCUSSION

Renal damage in hyperparathyroidism is probably caused by hypercalciuria and hypercalcaemia (Epstein, 1968), although a direct action of parathormone on the renal tubule cannot be excluded (Edvall, 1958). The incidence of hypertension is increased, as compared with a similar series for the same age and sex in the rest of the population, and is thought to be secondary to the renal lesion (Hellstrom, Birke, and Edvall, 1958).

Hellstrom and others (1958), in a series of 105 cases, showed that almost all their patients had renal insufficiency. They found that renal damage and hypertension persisted and in some cases progressed after parathyroid adenectomy. Hellstrom and Ivemark (1962) confirmed these results and showed that a raised preoperative blood-urea carried a poor prognosis. Out of 20 cases with a raised preoperative blood-urea, 16 had died prior to the follow-up examination, 12 from uraemia. Unfortunately, the authors do not state the time interval between operation and death. Mathiesen, Murj, and Sanders (1967) showed that one-third of their patients developed renal insufficiency and hypertension in spite of the fact that no evidence of renal damage had been found preoperatively. Pyrah, Hodgkinson, and Anderson (1966) found that 28 per cent of their patients developed hypertension in the postoperative period. Frank, Nathan, Lazebrik, and De Vrigs (1968) described an improvement after parathyroid surgery in over 75 per cent of their patients who had had renal insufficiency preoperatively. Three patients showed an improvement in both urea and creatinine clearance postoperatively. Despite the improvement in renal function all of their cases showed persistence of hypertension. Ohlsson (1970) found that renal function was preserved following parathyroid adenectomy. However, hypertension was still a problem, being present in 40 per cent of his patients.

Our results indicate that satisfactory renal function may be maintained in those cases with normal preoperative renal function tests. However, renal damage, once established, persists and may even progress after parathyroid adenectomy. Urinary infection was not present in any of our cases. Several midstream urine specimens were cultured from every patient, both pre- and postoperatively. None of them grew organisms at any time. This would suggest that infection is not a factor in producing the renal damage of primary hyperparathyroidism. In only 1 case did hypertension improve after surgery. Two other patients developed hypertension postoperatively and both of these had renal damage, suggesting that the hypertension may have been secondary to the renal lesion. Urinary-tract obstruction was not a causative factor in producing renal damage.

Acknowledgements.—We have pleasure in acknowledging the help of Dr. W. van't Hoff, who is in charge of the Metabolic Unit, North Staffordshire Royal Infirmary, and Dr. G. M. Aber, who gave advice on the renal function studies. We also thank our colleagues who referred the cases.

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SPLENOSIS

A CASE REPORT AND SOME CONSIDERATIONS ON THE FUNCTION OF SPLENOTIC TISSUE

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SUMMARY

A further case of intra-abdominal autotransplantation of splenic tissue is presented. The main importance of the condition probably lies in its recognition at laparotomy.

In the present case although the autotransplanted tissue was histologically similar to normal splenic tissue no normal splenic function could be ascribed to it.

The term 'splenosis' refers to the condition of autotransplantation of multiple small splenic nodules following traumatic rupture of the spleen. The condition is an uncommon one, only 51 cases being recorded in the world literature, including 3 in the British literature. A further case is described, together with some investigation of the condition.

CASE REPORT

A. C., born on 4 April, 1950. This boy of Italian extraction was admitted to hospital on 18 Aug., 1967, following a road-traffic accident. He had collided with the rear of a stationary vehicle while cycling and on admission was noted to be suffering from a laceration of the left thigh and bruising of the left upper abdomen and lower chest wall. He was observed for some 12 hours but at the end of this period laparotomy was thought advisable. At operation a stellate tear in the diaphragmatic surface of the spleen was noted and there was blood in the peritoneal cavity. Splenectomy was performed and the patient's recovery was rapid and uneventful.

On 10 Oct., 1969, the patient was readmitted complaining of severe colicky lower abdominal pain and vomiting of 24 hours' duration. He had just returned from 6 weeks' holiday in Europe. His abdominal pain was initially central but later became more marked in the right iliac fossa.

On examination he was mildly pyrexial (temperature 36·5° C.) and slightly dehydrated, with a dry, coated tongue and noticeable foetor. Examination of the abdomen revealed generalized lower abdominal guarding and rigidity, more pronounced on the right side.

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Bowel-sounds were hyperactive but not obstructive in character. The white-blood count was 6400 per c.mm. It was felt that the patient was suffering from acute appendicitis and the abdomen was explored through a right grid-iron incision.

Operative Findings and Procedure.—On visualizing the peritoneal cavity free fluid was immediately noted, but this was not purulent, and the appendix was macroscopically normal. Further exploration revealed a small-bowel obstruction due to a loop of terminal ileum about 60 cm. from the ileocaecal valve having become adherent to the peritoneal aspect of the previous left paramedian scar.

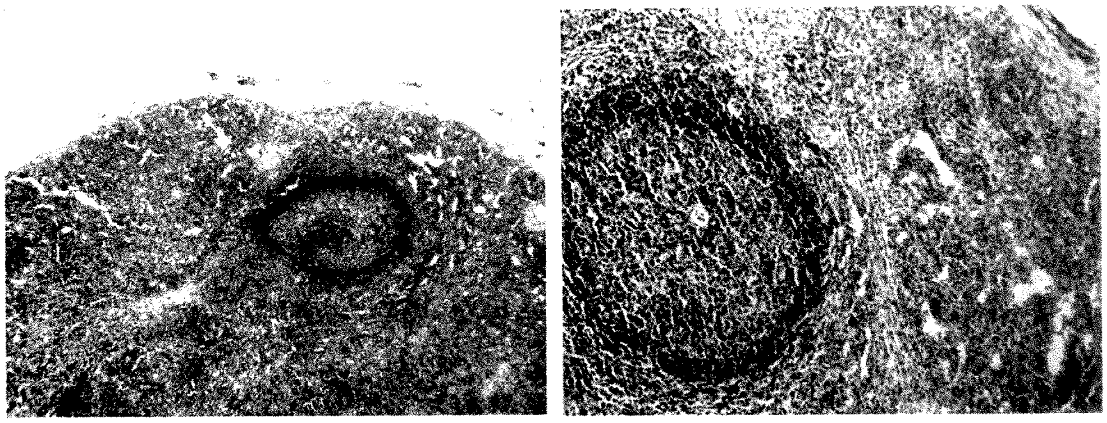

Fig. 1.—Photomicrographs of the splenotic tissue. A, Low-power view, showing splenotic tissue with a well-defined capsule, a lymphoid follicle, and pulp containing many small sinusoids. (× 30.) B, Detail, showing a lymphoid follicle on the left with a central arteriole, pulp and sinusoids on the right, and a boundary capsule on the top right. (× 84.)

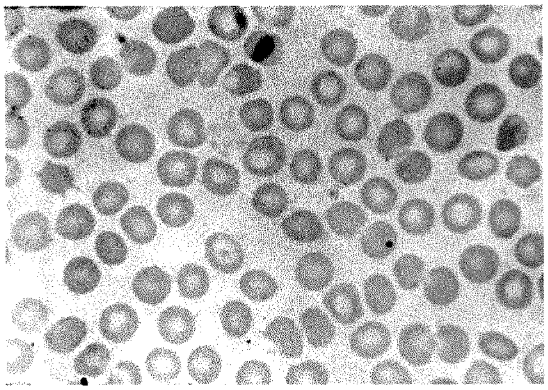

Fig. 2.—Photomicrograph of the peripheral blood-film of 2 March, 1970. Leishman's stain. (× 332.)

It was also noted that the small intestine, small intestinal mesentery, greater omentum, parietal peritoneum, and caecum were studded with small nodules (2 mm.–1 cm.) of purplish-violet tissue. This tissue was not unlike splenic tissue in appearance and one of the larger nodules was removed from the serosal surface of the caecum and sent for histological examination. There were about 20–30 nodules of this tissue in the peritoneal cavity.

The obstructed loop of ileum was freed from its attachment to the splenectomy scar, no nodules of splenic-like tissue being noted at this point. The abdomen was closed in a routine manner. Postoperative recovery was uneventful, apart from a brief period of paralytic ileus during which time intravenous fluids were administered. The wound healed normally and the patient was discharged on the tenth postoperative day.

Histology.—The specimen submitted for examination was a small nodule of very vascular tissue, measuring 10 × 5 × 4 mm. It had the structure of a normal spleen with sinusoids filled with blood and well-defined lymphoid corpuscles which, however, did not contain ellipsoids. There was a capsule which was thick and intact. Photomicrographs of the splenotic tissue are shown in *Fig. 1*.

Investigations.—Since the peripheral blood-film in splenectomized individuals contains an abnormally high number of red blood-cells containing Howell-Jolly bodies and an increased number of target cells it was decided to investigate the peripheral blood-film of this patient in the late postoperative period. A venepuncture was performed on 2 March, 1970. The usual haematological estimations were carried out, and several blood-films were made with special stains. The full haematological picture is given in *Table I*, and a photomicrograph of the blood-film illustrating Howell-Jolly bodies and target cells is shown in *Fig. 2*.

Table I.—Results of the Haematological Investigations

Haemoglobin	14·4 g.
Packed-cell volume	44 per cent
Mean corpuscular haemoglobin	33 per cent
Red-blood count	$5{\cdot}14 \times 10^6$ c.mm.
Mean corpuscular volume	87 c.μ
Reticulocytes	1 per cent
Platelets	320,000 c.mm.
Differential white-blood count:—	
Neutrophils	43 per cent
Eosinophils	3 per cent
Basophils	1 per cent
Lymphocytes	46 per cent
Monocytes	7 per cent
Blood-film:—	
A moderate number of target cells were present and some red-blood cells contained single Howell-Jolly bodies (approximately 1 per cent of red-blood cells). Siderocytes were present, as were occasional giant platelets. The picture was compatible with hyposplenism.	

DISCUSSION

The patient presented here has been shown to have the condition 'splenosis', that is, multiple intra-abdominal autotransplants of splenic tissue following traumatic rupture of the spleen. The condition was originally described by Albrecht in 1896, and the term 'splenosis' was coined by Buchbinder and

Lipkoff in 1939. The condition is a rare one, only 3 cases appearing in the British literature, in spite of the fact that traumatic rupture of the spleen is a not uncommon result of severe trauma. Nodules of splenotic tissue have been reported in sites other than the abdominal cavity, notably the thoracic cavity, and in the layers of the abdominal wall in relation to an abdominal wound. That the condition is almost certainly a true autotransplantation and not a metaplasia has been demonstrated by the experimental reproduction of the condition in animals.

The surgical importance of the condition lies mainly in its recognition and differentiation from haemangiomata or endometriomata. Nodules of normal autotransplanted splenic tissue (splenotic tissue) do not normally give rise to any pathological effects, except perhaps as in the cases of Cotlar and Cerise (1959) and Zachary and Emery (1959). In the former, splenotic tissue adhering to the serosal surface of the small bowel gave rise to intestinal colic which was relieved by resecting the affected bowel. In the latter case, which was similar to the one described here, the terminal ileum was adherent to the peritoneal wall and was obstructed and, at this point, splenotic tissue was present. Postoperative adhesions with associated splenotic nodules were also the cause of intestinal obstruction in the cases of Davis, Alexander, and De Young (1963) and Prasad and Beck (1968).

Where autotransplantation has occurred in a patient with a previously abnormal spleen pathological effects have been described owing to continuing splenic function (Gill, 1944; Stobie, 1947). This evidence that splenotic tissue is capable of function is supported by Rogers (1963). Zachary and Emery (1959) quote a personal communication suggesting that the resultant mass of splenotic tissue collectively assumes the size of a normal spleen. With these thoughts in mind, we investigated the present case for evidence of functioning splenotic tissue.

The histology of the transplanted tissue was found to be similar to, if not identical with, normal splenic tissue. This was also the finding in most other reported cases of splenosis, except in the cases of Shaw and Shafi (1937), Bunch and Spivey (1946), and Storsteen and ReMine (1953).

In contrast, examination of the peripheral blood-film demonstrated that it was consistent with that of a splenectomized or hyposplenic person. This raises the question of how much splenotic tissue is necessary to revert the splenectomized person's blood-film to normal, if it is indeed capable of function at all. We can find no definite answer to this. As further investigation in our case would have entailed the use of radioactive material it was not thought to be justifiable. We must, therefore, assume from our findings that either the splenotic tissue had no function or insufficient autotransplanted tissue was present to change the peripheral blood-film.

Acknowledgements.—We are grateful to Mr. H. C. Reid for permission to report this case, to Dr. R. W. Payne for advice and interpretation of the blood-films, and to Dr. J. E. Craik for the histological reports.

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ISOTOPE VENOGRAPHY

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SUMMARY

An isotope method of venography using ^{99m}Tc as pertechnetate (or MAA technetium) and a gamma camera is described. Initial results are encouraging. Good visualization of the major venous channels in the lower limbs and pelvis can easily be obtained. Venous occlusion and the formation of collaterals, particularly in the pelvis, are well shown. It appears to be possible to infer the presence of deep venous occlusion in the calf when delayed filling is seen through normal popliteal and femoral veins. The procedure is entirely painless and can easily be performed in the out-patients' department. It avoids the pain consequent on injection of the usual radiographic contrast media and the phlebitis which may also follow their injection. It does not afford the same degree of anatomical detail but this is of minor importance if operative intervention is unlikely.

The combination of the Anger gamma camera and modern artificially produced short-lived isotopes has meant that pictures of gamma activity can be obtained in short periods of time and thus even rapidly changing distributions of isotopes can be recorded. The gamma camera has been used to perform investigations analogous to those carried out by conventional radiography such as angiocardiography (Matin and Kriss, 1970) and aortography (Rosenthal, 1966a, b; Freeman and Mindelzun, 1968; Tori, Marabini, and Fattovitch, 1970). Venography has also been described by Rosenthal (1966c). With growing interest in venous occlusion and pulmonary infarction it was decided to investigate the potential value of isotope venography by using the gamma camera, adapting the method specifically for assessment of the veins of the lower limbs and pelvis. This paper presents the details of the method as it is currently used and also gives some preliminary results.

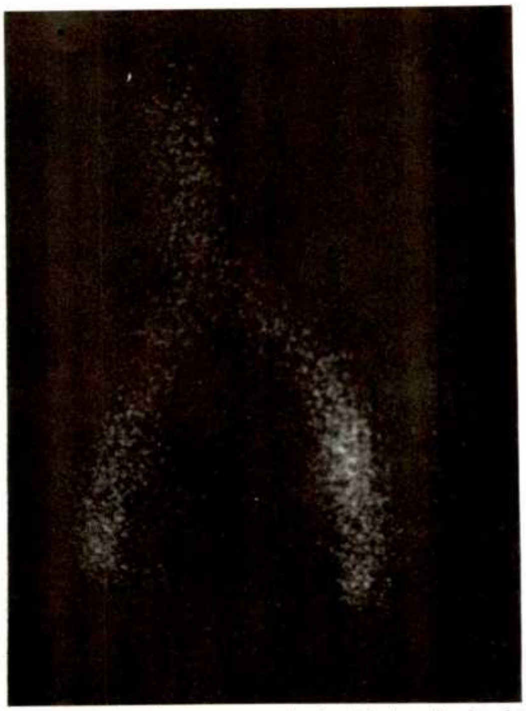

FIG. 1.—Film taken 10–20 seconds after injection, showing the external and common iliac veins uniting to form the inferior vena cava.

MATERIALS AND METHODS

The patient lies supine on the examination table under the gamma camera. A small butterfly cannula is inserted into a vein on the dorsum of each foot and patency is maintained by slow intermittent injections of normal saline. The patient is then carefully positioned under the camera head so that the region of the upper femoral veins, the iliac veins, and their union into the inferior vena cava is shown. The position is checked by taking a single polaroid picture with isotope markers placed on the symphysis pubis and the umbilicus. The camera head is lowered so that it is as close to the patient as possible; slight angulation towards the patient's head is helpful. Isotope is injected bilaterally, a bolus effect being obtained by inflating cuffs above each ankle prior to injection and following the isotope with a small 'chaser' injection of 2–3 ml. saline. Each injection contains 1 m.c. of ^{99m}Tc pertechnetate in about 0·3 ml. of saline. The camera timer should be started simultaneously with the injection to check the first

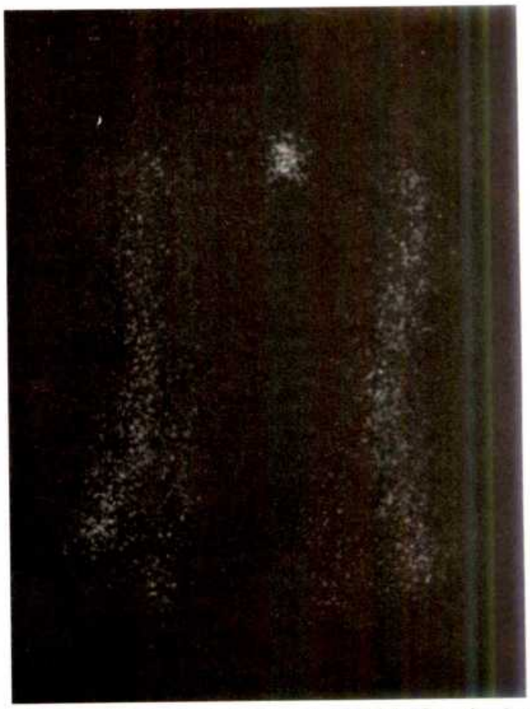

FIG. 2.—Film taken 50–60 seconds after injection, showing the common femoral veins and the lower part of the external iliac veins. The saphenous veins can be seen on each side uniting with the femoral veins. The central marker is above the symphysis.

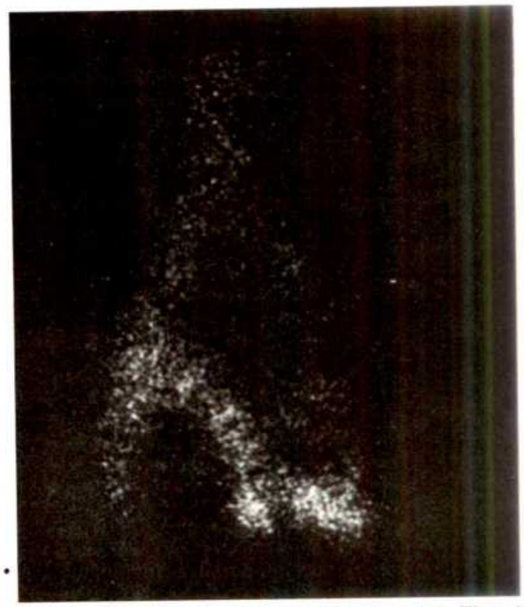

FIG. 3.—Film taken 25–35 seconds after injection. There is occlusion of the left common iliac vein. A large collateral system is seen transferring isotope from the left to the right side.

appearance of isotope under the crystal, and 10-second polaroid exposures are taken. Each series consists of 4–5 films. In some cases of venous occlusion films taken at longer intervals (up to 3 minutes) may be necessary to show lingering isotope. A second series can be taken of a different region if indicated, e.g., to show the femoral and popliteal veins when the positioning markers may be placed on the symphysis and between the knees. In order to overcome background activity from the first injections 2 m.c. should now be injected on each side. A third series is not practicable as the level of background activity greatly interferes with visualization.

Bilateral simultaneous injections seem to be essential as interpretation depends in part on the comparative rate at which isotope appears and fades from each side.

Equally satisfactory results have been obtained using ^{99m}Tc MAA when the injection procedure can produce both venograms and lung scans. This is particularly convenient when looking for venous occlusion and associated pulmonary infarction.

RESULTS

The normal appearances of isotope venograms are illustrated in *Figs.* 1 and 2. *Fig.* 1, which was taken 10–20 seconds after injection and centred on the pelvis, shows the wishbone configuration of the external and common iliac veins uniting to form the inferior vena cava. The arrival and fading of isotope were simultaneous on both sides and isotope density on the two sides was similar. *Fig.* 2, which was taken 50–60 seconds after injection and centred over the thighs (marker on symphysis pubis), shows the femoral veins and the lower part of the external iliac veins. The saphenous vein on each side can be seen medially and uniting with each femoral vein. Again, appearance, clearing, and density are equal on both sides although considerable individual variation in flow is shown in these 2 cases.

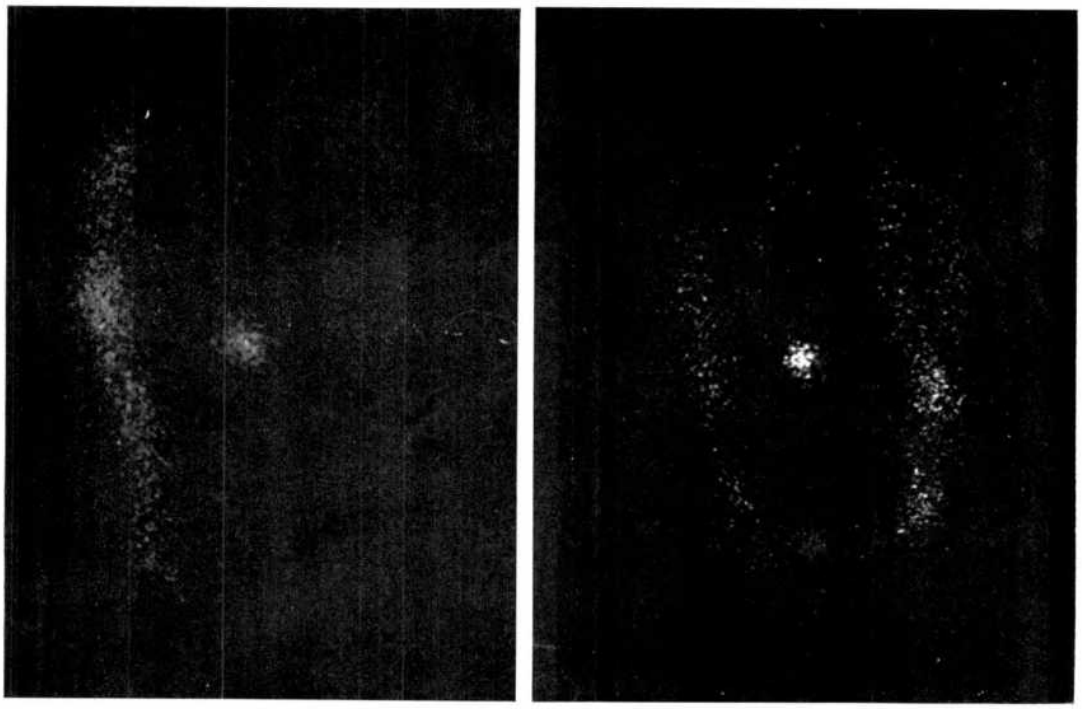

FIG. 4.—A, Film taken 5–15 seconds after injection, showing normal appearances on the right side. B, Film taken 25–35 seconds after injection. The isotope on the right side is fading, and isotope has appeared on the left side, being delayed relative to the right side. Deep-vein thrombosis was inferred and confirmed by routine venography.

Two pathological situations are illustrated in *Figs.* 3 and 4. *Fig.* 3 shows a left iliac vein occlusion with formation of a collateral from left to right. *Fig.* 4 A shows normal venous drainage through the right femoral vein taken 5–15 seconds after injection, but a later film (*Fig.* 4 B) taken at 25–35 seconds shows residual activity on this side and the appearance of a faint, delayed isotope pattern on the left. The combination of unilateral delayed flow through normal venous channels (the popliteal vein also appeared normal but is not illustrated) implied deep venous occlusion in the calf which was confirmed by conventional venography.

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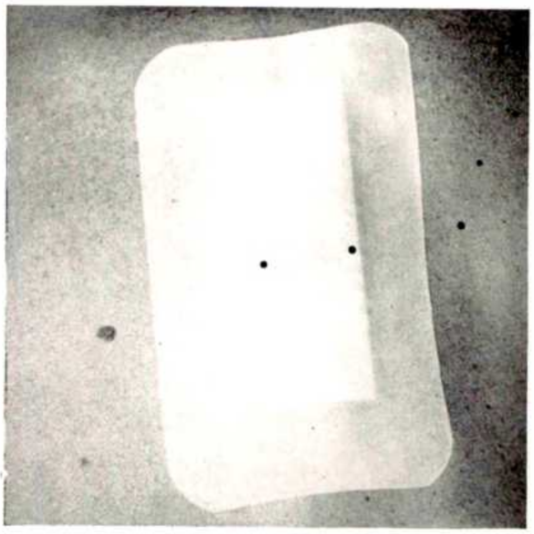

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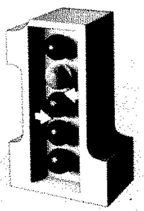

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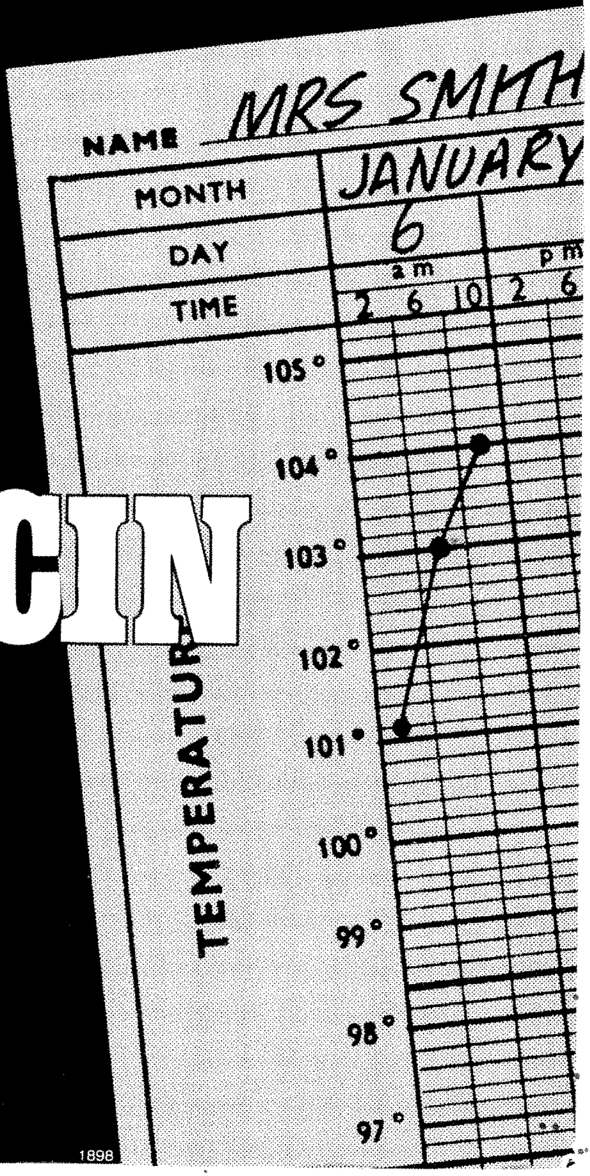

1898

STERCORAL PERFORATION OF THE SIGMOID COLON

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SUMMARY

Stercoral perforation of the sigmoid colon is probably more common than is generally appreciated. The condition should be considered in patients who present with peritonitis, localizing signs in the left iliac fossa, and a history of chronic constipation. Operation after a period of resuscitation offers the only hope of survival and resection of the affected sigmoid colon with exteriorization appears to be indicated.

Two additional examples of this condition are described and the salient features are reviewed.

THE presence of faecaliths in the rectum is a relatively common finding in surgical practice, particularly in patients with organic disease, the elderly, the debilitated, and the bedridden. Although often associated with troublesome constipation and spurious diarrhoea, and on occasions with rectal bleeding, the condition is generally amenable to prompt diagnosis and treatment. While faecaliths are observed less frequently in the sigmoid colon, it is now recognized that their presence in this situation may carry a higher risk of serious morbidity and even mortality.

Berry (1894) was probably the first to describe a case of stercoral perforation of the sigmoid colon, his patient being an elderly male who had suffered from chronic constipation for many years. Since that time similar cases have been reported sporadically, but Liedberg (1969) could collect only 17 cases from the literature. In view of the apparent rarity of the condition 2 further cases are reported and the salient features reviewed.

CASE REPORTS

Case 1.—A 67-year-old female was admitted as a surgical emergency with a 24-hour history of generalized abdominal colic, progressive pain in the left iliac fossa, and vomiting.

The patient gave a history of similar attacks of colic and vomiting extending over 20 years but on only one occasion, 5 years previously, had the pain approached its present magnitude. On that occasion a subsequent outpatient barium-enema examination had been performed in her local hospital and she was advised that her symptoms were due to faecal overloading of the colon and that constipation should be avoided. After colonic lavage her own doctor considered that the colon had been evacuated satisfactorily but volunteered the information that 'something could possibly have been left behind'. Despite occasional mild attacks of colic and vomiting the patient had remained reasonably well up to the time of her present admission. Regular bowel movements had been achieved by a wide variety of laxatives, the daily administration of cascara being her ultimate choice. On the day of admission the bowels had apparently opened normally, with the passage of a formed stool.

On examination the patient was obese, flushed, but not obviously shocked. (Temperature, 37·6° C.; pulse 100 per minute, sinus rhythm; blood-pressure 150/80 mm. Hg; white blood-count 16,800 cells per c.mm.; blood-urea 43 mg. per cent; serum electrolytes normal.) The abdomen was generally tender with maximal tenderness and guarding localized to the left iliac fossa. Bowel-sounds were present but infrequent. Rectal examination revealed no abnormality except a positive faecal occult-blood test. A chest radiograph was normal. Abdominal plain films showed faeces in the large bowel and suggested a rounded opacity in the left iliac fossa.

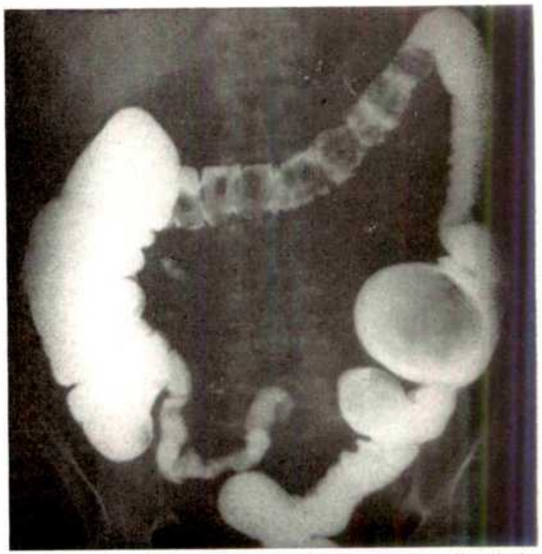

FIG. 1.—*Case* 1. Barium-enema film, showing two diverticula in the lower descending and sigmoid colon; both appear to contain a rounded faecalith.

Laparotomy was undertaken shortly after admission on the clinical diagnosis of perforated diverticular disease of the sigmoid colon with paracolic abscess formation. At operation a paracolic collection of pus was encountered around a grossly distended sigmoid and descending colon. The cause of these findings was revealed as a necrotic area, 2 cm. in diameter, on the antimesenteric aspect of the midsigmoid colon overlying a solid immovable mass within the bowel. In view of the uncertain nature of the mass and the doubtful viability of the bowel around the necrotic area, a 16-cm. length of sigmoid colon was resected with exteriorization of both the proximal and distal colon. A large Portex drain was led down to the left iliac fossa through a separate stab incision and the patient was commenced on kanamycin (0·5 g. b.d.).

On opening the resected specimen the lumen was found to be almost completely occluded by a faecalith, measuring 10 × 8 cm., which had caused pressure necrosis of the overlying bowel wall. Microscopy revealed extensive mucosal ulceration around this necrotic area with marked inflammatory changes throughout the bowel wall. Distal to the main lesion a solitary diverticulum, measuring

3 × 2 cm., protruded from the bowel wall. The mucosa within the diverticulum showed superficial ulceration with focal replacement of the submucosa and muscle layers by granulation tissue. Marked melanosis coli was apparent throughout the resected specimen.

The patient's postoperative course was uneventful except for a wound infection, and colonic continuity was restored 4 weeks after the initial laparotomy. Her subsequent recovery was satisfactory and she was discharged home 8 days later with normal bowel function and has maintained excellent progress since. The original outpatient barium-enema films have since become available and reveal the presence of two faecaliths in the sigmoid region at that time (*Fig.* 1).

Case 2.—A 61-year-old female was admitted as a surgical emergency complaining of the gradual onset of colicky lower abdominal pain with vomiting.

The patient's past history included chronic osteomyelitis of the left femur since childhood which still gave rise to pain and a discharging sinus. She had suffered from sarcoidosis for 5 years for which she was receiving long-term corticosteroid therapy (prednisone 5 mg. b.d.). She occasionally required to take laxatives for constipation and the bowels had last opened with the painful passage of a hard stool 2 days prior to admission. She had lost 12 kg. in weight over the preceding 4 months and she had been anorexic with occasional vomiting—symptoms that she attributed to her osteomyelitis.

On examination she appeared ill, was noticeably dehydrated, and vomited intermittently. (Temperature 35·6° C.; pulse 120 per minute, sinus rhythm; blood-pressure 120/40 mm. Hg; haemoglobin 10·6 g. per cent; white-blood count 21,800 per c.mm.; blood-urea 41 mg. per cent; electrolytes normal.) Abdominal examination revealed lower abdominal tenderness, most marked on the left side, with guarding. Bowel-sounds were infrequent. Rectal examination revealed a mass of hard faeces and a positive faecal occult-blood test. A chest radiograph was consistent with pulmonary sarcoidosis while abdominal plain films showed the presence of free gas in the peritoneal cavity and faecal masses in the descending colon.

After an initial period of resuscitation, laparotomy was undertaken on the diagnosis of perforation of a hollow viscus (probably colonic diverticular disease) with peritonitis. Exploration revealed stercoral perforation of the sigmoid colon with faecal soiling of the peritoneum and gross paracolic infection. A large faecalith, 8 × 7 cm. in diameter, was partially protruding through a necrotic area of the antimesenteric border of the midsigmoid region. Resection of a 16-cm. segment of bowel was therefore performed with exteriorization of both the proximal and distal colon. A large Portex drain was led down to the left iliac fossa through a separate stab incision and the patient was commenced on parenteral kanamycin (0·5 g. b.d.) and ampicillin (500 mg. q.d.s.). Intravenous fluid requirements were monitored by regular assessment of the central venous pressure and her steroid régime was increased with parenteral hydrocortisone.

Pathological examination of the colon revealed a perforation, 4 cm. in diameter, overlying the faecalith. The proximal colon was thin-walled with flattening of the mucosa and was packed with hard faeces. Microscopy showed extensive ulceration of the mucosa with inflammation in all the layers and areas of necrosis, most marked around the perforation site. There was no evidence of neoplasia, diverticulum formation, or primary vascular disorders.

The patient made a satisfactory recovery with early function of the proximal colostomy although she remained pyrexial for 7 days with persistent elevation of the white-cell count. At the time of discharge to convalescence (13 days after laparotomy) the white-cell count was still 11,600 cells per c.mm., a finding interpreted as a feature of her discharging osteomyelitis sinus.

The patient was readmitted after a month's convalescence for the restoration of bowel continuity and she had no abdominal complaints at that time. At operation an abscess was encountered deep to the distal colostomy, but anastomosis was performed satisfactorily and her postoperative course was uneventful with rapid return to normal bowel function. She was discharged to convalescence 10 days after reoperation and has maintained satisfactory progress. It is anticipated that amputation may be required to deal with her residual orthopaedic problem.

DISCUSSION

It is difficult to determine the true incidence of stercoral perforation of the sigmoid colon. In a consecutive series of 175 routine autopsies Grinvalsky and Bowerman (1959) found 8 cases of stercoral ulceration of the large bowel, 4 of which were complicated by stercoral perforation of the sigmoid colon, an incidence of 2·3 per cent. It seems probable that the literature does not reflect accurately the true prevalence of the condition, particularly in the elderly, debilitated, and institutionalized patient.

Abnormal colonic function in the form of chronic constipation would appear to be the predisposing factor in stercoral perforation. However, it must be emphasized that, as in *Case* 1 of our report, faecaliths may persist for long periods in spite of an apparently regular and normal bowel function. It is probable that the larger of the faecaliths observed 5 years earlier on barium-enema films had remained in situ and had ultimately given rise to stercoral ulceration and perforation. In view of the virtually complete obturation of the colon revealed at operation it appears that only by the use of regular laxatives could earlier intestinal obstruction have been avoided. The precarious existence led by this patient is emphasized by her history of intermittent episodes of subacute intestinal obstruction.

In this context it is worth remembering the constipating nature of radiological examinations using barium and some forms of medical therapy. As Brearley (1954) and Berger and Shaw (1961) have pointed out, some of the medication employed in the treatment of duodenal ulceration, notably aluminium hydroxide and mixtures containing bismuth, may promote constipation. In the event of stercoral perforation the clinical diagnosis may readily be confused with that of perforated peptic ulcer in such patients. While these considerations were not apparent in our cases, the association between steroid therapy and perforated diverticular disease has recently been stressed (Canter and Shorb, 1971) and could confuse the preoperative diagnosis in patients on long-term steroid therapy. Diverticular disease has not been reported as a significant factor in stercoral perforation, but the pathologist's report in *Case* 1 raises the possibility that the original faecalith formation may have taken place in a large solitary diverticulum outwith the faecal stream. Whatever the cause of faecalith formation, the work of Grinvalsky and Bowerman (1959) now leaves little doubt that the ultimate perforation results from ischaemic necrosis due to pressure on the overlying colonic wall.

An accurate preoperative diagnosis was not achieved in either of our cases and was probably academic in that laparotomy was strongly indicated from the clinical picture of peritonitis. While the persistence of localizing signs in the left iliac fossa in a patient with a history of chronic constipation should raise the possibility of stercoral perforation, it is probable that the majority of cases will still be regarded as due to complicated diverticular disease or colonic neoplasia. In retrospect the correct diagnosis was readily available in *Case* 1 in view of the history, the clinical findings, and the presence of the faecalith on the abdominal radiograph. In *Case* 2 the responsible faecalith was not apparent radiologically.

There can be little doubt that surgical intervention after adequate resuscitation offers the only prospect of survival after stercoral perforation of the sigmoid colon. In the 19 patients now collected from the literature the 8 unoperated cases died whereas 9 of the 11 cases undergoing operation survived. There is no place for simple suture of the perforation with transverse colostomy as this does not remove the offending faecalith and perpetuates the risk of further complications. Resection of the affected segment of colon with its contained faecalith and exteriorization of both the proximal and distal colon offers the best approach. Subsequent restoration of continuity is unlikely to be difficult and can be undertaken as a planned procedure when conditions are favourable. A case could be argued for enlargement of the perforation to form a loop colostomy in the left iliac fossa with simultaneous removal of the faecalith. In our experience the extent of impaired colonic viability precluded this approach. Similarly, it may occasionally be justifiable to carry out an end-to-end anastomosis at the time of resection, but in this situation a protective transverse colostomy would seem mandatory and the patient will still require a second operation to restore normal function.

Acknowledgement.—The authors wish to thank Mr. I. B. Macleod for permission to publish details of *Case* 2.

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OBSERVATIONS ON ACUTE PANCREATITIS

A RETROSPECTIVE CLINICAL STUDY

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SUMMARY

1. Aetiological features were sought in a retrospective review of 93 cases of acute pancreatitis diagnosed and treated in Edinburgh hospitals between 1961 and 1970.

2. The incidence of alcoholism or precipitation by an excess of alcohol was 23 per cent, a figure which accords with reports from other parts of the world but which has no precedent in Great Britain. Possible reasons for this are discussed. There were no other unusual features.

3. The need for a prospective study to reassess our current experience in Great Britain is stressed.

THE wealth of literature on acute pancreatitis which has followed the first description of the disease in 1842 by Classen has been well reviewed in recent years (Richman, 1956; White, 1966). It is generally accepted that the disease is of multifactorial aetiology. Although Joske (1955) pleads to the contrary, most workers have accepted that gall-stone disease is an important aetiological factor. Certainly in a post-mortem study from Edinburgh (Gillespie, 1973) the incidence of gall-stone disease in a population dying of acute pancreatitis was much higher than one would expect in a random population sample, and it seems likely that the conditions are truly related. Trauma and a variety of metabolic disturbances are also apparently involved, and there has been a recent surge of interest in the role of viruses. In most countries of the world, although not, apparently, in Britain, alcoholism and over-indulgence in alcohol appear to play an important role in precipitating the clinical attack.

This paper presents a retrospective case-note search to quantify the incidence of known and presumed aetiological factors in clinical cases occurring in south-east Scotland in the decade 1961–70.

The limitations of retrospective study are well known and were accepted prior to the commencement of the search. As the search proceeded it became evident that only broad trends could be discerned as the quality of case recording and the nature and depth of case investigation varied greatly in different units. Therefore, no attempt was made to gather all the cases presenting in Edinburgh in the decade. This would have been a difficult exercise as certain hospitals had no adequate case-retrieval method during the major part of the decade. The cases reviewed, therefore, are the first 93 records offered by the record officers of the Royal Infirmary of Edinburgh and the Edinburgh Northern Hospital Group. They are broken down by source in *Table I*.

RESULTS

In patients under 60 years of age there is a preponderance of cases in males (male : female ratio, 2 : 1) but this ratio is reversed over the age of 60 (male : female ratio 1 : 3) (*Fig.* 1).

Amongst the men under 60 (*Fig.* 2) 19 out of 35 cases have a history of precipitation by a drinking bout or of alcoholism. In patients over 60 gall-stone disease accounts for around half of the cases while the other half has obscure aetiology. A summary of the aetiological features is given in *Table II*. Details of the patients in whom alcohol seemed to play a part are shown in *Table III.*

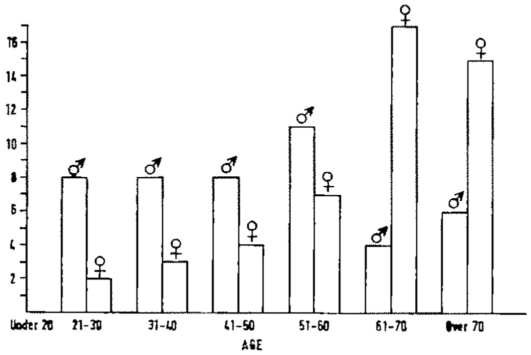

FIG. 1.—Age and sex of the cases under review

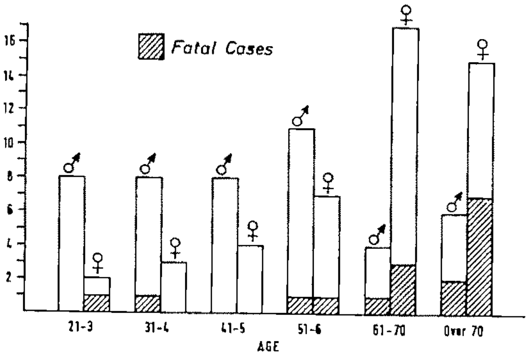

FIG. 3.—Mortality compared with age and sex.

Table I.—SOURCES OF THE CASES REVIEWED

YEARS	HOSPITAL	TYPE OF UNIT	NO OF CASES
1961–8	Eastern General, Edinburgh	General surgical General medical	26 2
1961–8	Western General, Edinburgh	General surgical General medical Gastro-intestinal unit	11 2 13
1968–70	Royal Infirmary, Edinburgh	General surgical General medical	30 9

DISCUSSION

Taylor (1949), in his Hunterian Lecture, stated that he had never seen a case of alcoholism in his series of patients. Pollock (1959) wrote: 'In not one single patient in the present series was there any association with alcohol excess.' In another Hunterian Lecture on the topic, Trapnell (1966) found 4 alcoholics among 403 patients with pancreatitis in the Bristol area, an incidence of 1 per cent. In contrast with this British experience, there is no doubt that in North America, South Africa, and

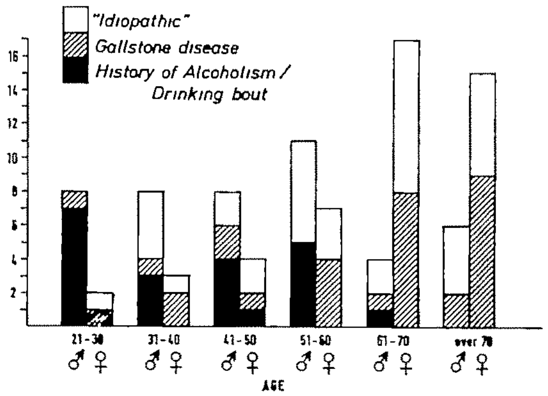

FIG. 2.—Principal supposed aetiological factors compared with age and sex.

Table II.—POSSIBLE AETIOLOGICAL FEATURES

AETIOLOGICAL FEATURE	NO. OF CASES		
	Male	Female	Total
Gall-stone disease	7	25	32
History of alcoholism/drinking bout	20	1	21
Postoperative	1	1	2
Postpartum	—	1	1
Possible viral aetiology, including viral hepatitis	1	1	2
Idiopathic	16	19	35

Table III.—THE INCIDENCE OF ALCOHOLISM AND ALCOHOLIC EXCESS

CASE NO.	AGE AND SEX	DETAILS
13	44 F.	Known alcoholic of many years' standing
14	20 M.	One of his episodes of the disease followed a drinking bout
51	27 M.	Onset followed heavy drinking bout
91	25 M.	Onset followed heavy drinking bout. Known heavy drinker
85	22 M.	Drinks 24 pints per week
53	29 M.	Alcoholic. Delirium tremens in ward
50	29 M.	Alcoholism confirmed at psychiatric interview
76	28 M.	Onset followed heavy drinking bout
4	36 M.	Onset followed heavy drinking bout
80	31 M.	Publican. Regular drinker
88	39 M.	Alcoholic; family evidence
79	43 M.	Onset followed drinking bout. Known heavy drinker
54	42 M.	Alcoholism confirmed at psychiatric interview
36	48 M.	Onset followed heavy spirit drinking bout
71	48 M.	Onset followed heavy drinking bout
83	59 M.	Onset followed ingestion of 10 whiskies
58	55 M.	Brewer's drayman. Onset followed heavy drinking bout
1	54 M.	Alcoholism confirmed at psychiatric interview
27	56 M.	Onset followed heavy drinking bouts (5–6 pints every night)
77	55 M.	Returns clerk in brewery. Stopped drinking after first attack
84	63 M.	Onset followed heavy drinking bout

Australia the proportion of cases which are associated with alcoholism and alcohol excess is between 20 and 65 per cent. The subject has been well reviewed by Richman (1956) and White (1966).

It has been the impression of many doctors in clinical practice in Edinburgh that alcohol might be incriminated from time to time in the genesis of the acute attack. In the present series 21 of 93 patients were either alcoholics or suffered their acute attack after excess of alcohol. Three of the 5 alcoholics were seen, it is true, in a specialist unit but the other cases presented randomly, mostly to general surgical units. It seems likely that some of those who are recorded simply as suffering an attack after an excess of alcohol may be alcoholics and, indeed, the incidence of alcoholic excess may be underestimated.

The incidence of alcoholism in Great Britain has been estimated by Williams (1965) to be 400 per 100,000. If this is so, we might expect 0·4 case per 100. In this series of 93 cases there are 6 certain alcoholics, an incidence of 6·5 cases per 100.

Two factors may be involved in determining the difference between this series and previous series in Great Britain. They are as follows:—

1. The incidence of alcoholism may have been underestimated in the past. Many alcoholics may have concealed the fact at the time of their attack, just as they are believed to have concealed it from their general practitioners (Bewley, 1970).

2. There may be differences in drinking and dietary habits between south-east Scotland and central and southern England.

There is a need for a prospective survey of the problem in different centres to reassess the importance of alcoholism.

The incidence of gall-stone disease in this series is 32 cases out of 93 (34 per cent), which accords with many other series but is lower than the 61 per cent recorded by Pollock (1959) and the 52 per cent cited by Trapnell (1966) in Great Britain. There were no overt cases of mumps and only 1 case which could be considered postpartum in origin. Seven per cent of Joske's patients (1955) had hyperlipaemia. In this series hyperlipaemia had been sought only on 13 occasions and was not found: there is, therefore, no evidence to offer of its significance in this region.

Acknowledgements.—My thanks are due to the various consultant surgeons and physicians for permission to carry out this search, to the records staff of the Royal Infirmary of Edinburgh and of the Edinburgh Northern Hospitals, and to Mr. T. J. McNair and Mr. J. W. W. Thomson for their help and encouragement.

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FUNDOPLICATION FOR HIATUS HERNIA

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SUMMARY

Eighty-eight patients who had symptomatic hiatus hernia were treated by fundoplication during 1967–70. Worth-while symptomatic benefit was achieved in 88 per cent of the patients who had reflux only and in 80 per cent of those who had radiologically demonstrable strictures as well as reflux.

Both as a primary and 'salvage' operation fundoplication gave equally good results, relieving 86 per cent of patients of their symptoms.

THE term 'reflux oesophagitis' was used first by Barrett (1950). This concept was a turning point in the understanding of the group of conditions which were known to affect the lower end of the oesophagus.

The commonest association with reflux has been found to be a sliding oesophageal hiatus hernia (Allison, 1951). Accurate reduction of the hernia and the restoration of normal anatomy do not always relieve the symptoms. In some cases the hernia is effectively repaired but reflux still occurs. Other patients may have reflux without a hiatus hernia, and in some the oesophagus is shortened by fibrosis and it is impossible to reduce the lower end into the abdominal cavity. These difficulties may be overcome by the operation of gastric fundoplication which was introduced by Rudolph Nissen in Switzerland in 1956. In this operation the fundus of the stomach is wrapped around the lower end of the oesophagus to form a cuff.

This paper presents the results of 88 symptomatic patients with hiatus hernia treated by fundoplication at the Kingston and Hammersmith Hospitals under the care of one consultant in the years 1967–70.

PATIENTS AND METHODS

All the patients in this series had one or more symptoms judged to be due to reflux oesophagitis, namely: regurgitation, reflux pain or heartburn, dysphagia, and vomiting.

A barium-swallow examination in all the cases confirmed the presence of gastro-oesophageal reflux or a hiatus hernia with or without reflux, spasm, ulceration, or stricture.

Oesophagoscopy and biopsy were not carried out in all the cases, but were not omitted in any case where the diagnosis was in doubt or the benign nature of a stricture or ulcer was uncertain.

Gastric acid secretion studies were carried out in all the cases where there was a suspicion of duodenal or gastric ulceration except in those cases of stricture in which a Ryle's tube could not be introduced.

Selection for Operation.—Operation was performed for one or more of the following reasons:—

1. Severe dysphagia.
2. Failure to control symptoms by adequate medical treatment, consisting of postural control, weight reduction, and the use of drugs such as antacids and antispasmodics.
3. Patients in whom previous operations had failed to control symptoms.
4. Persistent blood-loss.

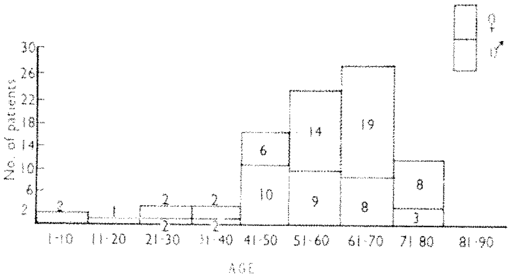

FIG. 1.—Age distribution in 88 patients undergoing fundoplication for hiatus hernia.

Operative Technique.—Fundoplication was performed via an abdominal incision in all except 1 case. In this case perforation of the oesophagus occurred during mobilization of a short oesophagus and to protect the repaired oesophagus fundoplication was carried out through a left thoracotomy. The operative technique employed was as follows.

A size 16F Ryle's tube is passed into the stomach transnasally. Inability to pass this size tube indicates the necessity for resection of the stricture.

The abdomen is explored through a midline upper abdominal incision and any associated pathology noted, particularly of the gall-bladder, stomach, and duodenum.

Access to the hiatus is achieved by mobilization and retraction of the left lobe of the liver and incision of the peritoneum in front of the distal oesophagus and cardia.

The hernia is reduced and the lower end of the oesophagus drawn down into the abdomen. The margins of the right crus of the diaphragm are clearly defined.

The fundus of the stomach is freed by division and ligation of the short gastric vessels and, in most cases, the left gastric vessels also. An effort is made to avoid injury to the spleen, but where the surgeon considers that access would be made easier and safer thereby, the spleen is removed. The hiatus is narrowed with interrupted thread sutures which approximate the margins of the right crus behind the oesophagus. The terminal oesophagus is then surrounded by a cuff of stomach obtained by wrapping the freed fundus around the back of the oesophagus, passing it through the divided lesser omentum, and securing it to the anterior wall of the stomach with interrupted thread sutures. This procedure constitutes the Nissen fundoplication.

Our modification of the Nissen procedure consists of rolling the plicated fundus of the stomach circumferentially up on the oesophagus with interrupted thread sutures in such a way as to produce an 'unspillable' inkwell effect and adding pyloroplasty. Vagotomy is carried out when a duodenal ulcer and/or high gastric acid secretion is present.

Postoperative Assessment.—All the patients have been interviewed at follow-up clinics both at the Hammersmith and Kingston Hospitals. Eighteen patients had fundoplication in 1967, 21 in 1968, 26 in 1969, and 23 in 1970; the results were assessed in December, 1970.

Radiological studies were not performed routinely for the purpose of this review but were carried out where persistence of significant symptoms made it necessary to do so.

The results of surgery were graded as 'symptomless', 'improved', 'failed', and 'died'.

There were 88 patients in this series (46 at Hammersmith Hospital and 42 at Kingston Hospital).

The ages varied from 10 to 80 years, more than half of the patients falling in the fifth to seventh decades (*Fig.* 1). There were 53 females and 35 males. There were 84 sliding herniae and 4 para-oesophageal herniae.

RESULTS

Six out of the 88 patients died in the immediate postoperative period. This gives an operative mortality of 6·8 per cent.

Three of the patients aged 68, 75, and 77 years died of bronchopneumonia on the second, eighth, and fifth postoperative days respectively.

One patient, a hypertensive man aged 65, died on the fourth postoperative day following splenectomy, fundoplication, and cholecystectomy. On the third postoperative day he suddenly developed acute chest pain and pulmonary oedema, thought to be due to a pulmonary embolus or myocardial infarct, and died in spite of attempts at resuscitation.

One patient developed a subphrenic abscess and died of peritonitis and bronchopneumonia following drainage of this abscess. He was aged 71 and died on the tenth postoperative day.

One patient, aged 63, died on the fourth postoperative day of acute dilatation of the stomach, the Ryle's tube having become inadvertently displaced.

Failures.—There were 6 failures in the series, i.e., an incidence of 6·8 per cent.

Case 1.—M. E., a man of 30 years, was admitted with a 7-year history of reflux, retrosternal pain radiating to the jaw, and inability to swallow solids, although he could swallow warm liquids. A barium-meal examination preoperatively was reported as showing a sliding hiatus hernia with two pouches thought to be ulcers at the lower end of the oesophagus. A fundoplication did not relieve his symptoms. Subsequent manometric studies revealed that he also had achalasia of the cardia. Since review in December, 1970, he has become symptom-free.

Case 2.—S. C., a man of 71 years, had total dysphagia, and a barium-swallow examination showed a high impassable stricture at the level of the clavicles thought at first to be a malignant stricture. Two biopsies of the stricture showed gastric epithelium and the diagnosis of Barrett's oesophagus (Barrett, 1950) was made. Bouginage did not relieve his symptoms and a fundoplication did not relieve his dysphagia. He could hardly swallow his own saliva and had a permanent gastrostomy. One year later he was proved to have an inoperable carcinoma.

Table I.—OVERALL RESULTS OF FUNDOPLICATION FOR HIATUS HERNIA

HOSPITAL	DIED	ALIVE	NO SYMPTOMS	IMPROVED	NO RELIEF
Hammersmith Kingston	4 2	42 40	32 33	6 5	4 2
Total	6	82	65	11	6
Percentage	6·8		73·9	12·5	6·8
			86·4		

Case 3.—L. C., a 53-year-old woman, had no relief whatsoever from a fundoplication operation. Since a thyroid operation 13 years previously she had had a most impressive and bizarre type of generalized twitching and nervousness for which extensive neurological investigations led to a diagnosis of 'hysteria'. However, a barium-meal examination showed persistent herniation of the stomach into the chest, and we consider her symptoms to be genuine.

Case 4.—N. A., a woman of 68 years, has had no relief of any of her symptoms of dysphagia, reflux, and heartburn following fundoplication in 1967. Barium-meal examination shows the persistence of a small sliding hernia with reflux in spite of good evidence of fundoplication below the diaphragm.

Case 5.—I. C., a woman of 68 years, had an exploration of the common bile-duct in 1963, transabdominal repair of hiatus hernia and splenectomy in March, 1966, transthoracic repair of hiatus hernia in September, 1966, and was not relieved by fundoplication in 1968.

Case 6.—L. B., a woman of 66 years, had a sliding hiatus hernia with stricture treated by bouginage and pylorectomy in 1962 and was not relieved by fundoplication in 1967. She subsequently had a gastrostomy, followed by resection of the stricture and a colon graft. This failed to relieve her symptoms. She then had a further resection and a Roux-en-Y jejunal graft and following this procedure is able to swallow normally.

Cases improved by Fundoplication.—Sixty-five of the 88 patients, i.e., 73·9 per cent, were completely relieved of all their symptoms, and 11 others (12·5 per cent) were improved; i.e., 86·4 per cent were symptomatically improved by the operation. Of the patients who were improved after operation, only 2 still have fairly severe symptoms. Overall, therefore, it can be said that of the 82 patients who survived the operation, 76 have improved sufficiently to have thought the operation worthwhile and have been glad to have had the operation. These results are shown in *Table I.*

Patients who had Stricture (*Table II*).—This is a very important group of patients for whom resection is often advocated. In fact some of these patients were admitted with a view to resection.

Table II.—RESULTS OF FUNDOPLICATION FOR HIATUS HERNIA IN PATIENTS WHO ALSO HAD OESOPHAGEAL STRICTURE

TYPE OF STRICTURE	HOSPITAL	DIED	ALIVE	NO SYMPTOMS	IMPROVED	NO RELIEF
Barium-swallow strictures confirmed at operation or oesophagoscopy	Hammersmith Kingston	1 0	15 7	8 5	4 1	3 1
	Total	1	22	13	5	4
	Percentage	4·4		56·5	21·7	17·4
				78·2		
'Spasmodic strictures', i.e., barium-swallow strictures not confirmed at operation or oesophagoscopy	Hammersmith Kingston	0 0	4 0	4 0	0 0	0 0
	Total	0	4	4	0	0
	Percentage			100		
All 'strictures' shown on barium-swallow film	Total	1	26	17	5	4
	Percentage	3·7		63	18·5	14·8
				81·5		

All 4 patients who had spasmodic strictures, i.e., patients in whom strictures were shown on the barium-swallow film but which were not confirmed at operation or oesophagoscopy, were completely cured of their symptoms.

Of the group that had established strictures, no less than 13 of the 22 patients who survived operation were completely cured of their symptoms and 5 others improved following fundoplication.

Thus, of 27 patients in whom a barium-swallow examination showed the presence of a stricture associated with a hiatus hernia, 81·5 per cent have obtained worth-while relief following fundoplication, and this result is worthy of emphasis, considering the alternative method of treatment advocated.

Patients who had Hiatus Hernia with Reflux only but No Stricture (*Table III*).—Forty-nine of the surviving 56 patients in this group were completely symptom-free and 5 others improved, i.e., 54 out of the surviving 56 patients benefited from the operation. One of the 2 failures was the patient who was subsequently shown to have achalasia.

Patients in whom Previous Operations had failed to control Symptoms (*Table IV*).—There were 23 patients in whom a variety of previous operations had either failed to control symptoms or provided only temporary relief. One of them died, and of the remaining 22, 17 were completely symptom-free and 3 others improved following fundoplication.

The nature of the previous operations is shown in *Table V*. We consider that the relief and improvement of symptoms in 86·7 per cent of these patients are again worthy of comment, considering that these are failures from other standard operations for hiatus hernia.

Table III.—RESULTS OF FUNDOPLICATION FOR HIATUS HERNIA IN PATIENTS WITH REFLUX BUT NO OESOPHAGEAL STRICTURE

HOSPITAL	DIED	ALIVE	NO SYMPTOMS	IMPROVED	NO RELIEF
Hammersmith	3	23	20	2	1
Kingston	2	33	29	3	1
Total	5	56	49	5	2
Percentage	8·2		80·3	8·2	3·3
			88·5		

Table IV.—RESULTS OF FUNDOPLICATION FOR HIATUS HERNIA IN PATIENTS WHO HAD HAD PREVIOUS OPERATIONS TO CONTROL SYMPTOMS

HOSPITAL	DIED	ALIVE	NO SYMPTOMS	IMPROVED	NO RELIEF
Hammersmith	1	15	14	1	0
Kingston	0	7	3	2	2
Total	1	22	17	3	2
Percentage	4·3	95·7	73·8	12·9	9
			86·7		

Table V.—NATURE OF PREVIOUS OPERATIONS IN 23 PATIENTS

TYPE OF OPERATION	KINGSTON HOSPITAL	HAMMERSMITH HOSPITAL	TOTAL NO. OF PATIENTS
Transthoracic repair	3	6	9
Transabdominal repair	0	5	5
Transthoracic and trans-abdominal repair	1	1	2
Pylorectomy, pyloroplasty, and gastro-enterostomy	3	2	5
Others	—	2	2
Total	7	16	23

Patients who had Fundoplication as a Primary Operation (*Table VI*).—Five of the 65 patients in this group died and 56 out of the surviving 60 patients were helped by the operation. The surviving failures included *Case* 1, who also has achalasia, and *Case* 2, who had an impassable stricture at the level of the clavicles associated with Barrett's oesophagus which later proved to be a carcinoma.

Complications.—The complications encountered in this series are shown in *Table VII*. The last two complications merit special mention.

Gastric Distension.—In 1 case gastric distension led to death and in another to a burst abdomen. Provision of adequate gastric decompression either via a transnasal tube or, if this fails, gastrostomy in the immediate postoperative period is emphasized.

Diarrhoea.—Two cases of diarrhoea postoperatively were encountered in patients who had not had vagotomy as a deliberate procedure. In 1 patient fundoplication was carried out at the primary operation. She developed diarrhoea; barium-meal and follow-through and barium-enema examinations were normal apart from rapid transit time. An insulin test, however, suggested complete vagotomy, but the patient has not accepted to come into hospital for further investigations to exclude other possible causes of her diarrhoea. The other patient had a splenectomy, abdominal repair of hiatus hernia, and pyloroplasty in 1967 but had persistent symptoms. A fundoplication was carried out subsequently. Vagotomy was not done deliberately. Postoperatively she developed diarrhoea which was extensively investigated. Eventually an insulin test suggested a complete vagotomy and she is believed to have post-vagotomy diarrhoea.

Table VI.—RESULTS OF FUNDOPLICATION FOR HIATUS HERNIA IN PATIENTS WHO HAD NOT HAD A PREVIOUS OPERATION

HOSPITAL	DIED	ALIVE	NO SYMPTOMS	IMPROVED	NO RELIEF
Hammersmith	3	27	18	5	4
Kingston	2	33	30	3	0
Total	5	60	48	8	4
Percentage	7·7		73·8	12·3	6·2
			86·1		

Table VII.—COMPLICATIONS IN THE SERIES OF 88 PATIENTS UNDERGOING FUNDOPLICATION FOR HIATUS HERNIA

COMPLICATION	TOTAL NO. OF CASES	NO OF DEATHS
Intestinal obstruction	4	—
Subphrenic abscess	5	1
Deep-vein thrombosis	5	—
Burst abdomen	2	—
Wound abscess	5	—
Chest infection	8	3
Intercostal neuralgia	1	—
? Pulmonary embolus	1	1
Gastric distension	4	1
Diarrhoea	2	—

Splenectomy.—Splenectomy was performed in 52 out of 88 patients (61 per cent). Twenty-four of these patients (46 per cent) had some complication after operation. By contrast, 36 of 88 patients did not have splenectomy (39 per cent) and 7 of these (20 per cent) had complications. Therefore the incidence of complications in the group that had splenectomy was significantly higher than in the group that did not have this procedure ($\chi^2 = 9{\cdot}63$, $P < 0{\cdot}01$).

Vagotomy and Pyloroplasty.—Vagotomy and pyloroplasty were carried out in 23 out of 88 patients

(26 per cent). In none of these patients was there any complication that could be attributed to that operation *per se*.

Relief of Individual Symptoms.—Reflux pain was relieved in about 90 per cent of patients, regurgitation in 83 per cent, and vomiting in 87·5 per cent.

DISCUSSION

The Nissen fundoplication creates a cuff of stomach around an intra-abdominal length of oesophagus. Any rise in pressure in the stomach tending to cause reflux is immediately blocked by the equivalent rise in pressure in the cuff around the oesophagus. Affolter and Rosetti (1970), Moran (1971), and Morgan (1971) have all demonstrated that fundoplication augments the pressure normally exerted by contraction of the distal oesophageal sphincter mechanism without altering the resting pressure. Another advantage of fundoplication is that if the oesophagogastric junction cannot be reduced below the diaphragm then it may be left in the chest. The procedure will still cure reflux (Nissen, 1960). Nissen and Rosetti (1962), Smiddy and Ross (1964), Krupp and Rosetti (1966), Naef, Savary, and Jacques (1970), Polk and Zeppa (1971), and Morgan (1971) have all reported favourably on the Nissen fundoplication. Other surgical procedures have been devised to produce a similar effect in reducing reflux (Baue and Belsey, 1967; Collis, 1968).

We have presented our experience with the use of fundoplication as a means of surgical treatment of symptomatic hiatus hernia in a consecutive series of 88 patients treated from 1967 to 1970 and reviewed in December, 1970. Fundoplication has achieved good results when used both as a primary operation and as a 'salvage' operation in patients whose previous operations have failed to relieve their symptoms. Good results were achieved in patients who had hiatus hernia with reflux and in whom radiological strictures were demonstrated, and this group we think merits special mention.

A further follow-up of these cases is desirable to be sure that the good results are maintained. It is on record, however, that Tanner and Hardy (1970) noted an 80 per cent improvement in patients whom they had treated by some other technique of repair, and that this figure remained the same in two groups of patients assessed by independent observers at 3 years and 15 years, thus suggesting that the majority of the failures of operation occur early. This has been the experience of Collis (1961) and has also been our impression from the present series.

In the absence of any controlled trial of the many operative procedures (Earlam and Ellis, 1967) that have been used for hiatus hernia, it is not possible to make any statistically valid comparison.

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TORSION OF THE ISOLATED FALLOPIAN TUBE

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SUMMARY

Torsion of the isolated Fallopian tube is a relatively rare condition which has been known for over 65 years. The number of cases reported probably exceeds 300. The cases reported here illustrate different presenting signs and causative pathology.

TORSION of the isolated Fallopian tube was first described by R. Hamilton-Bell in a paper entitled 'Torsion of the pedicle in hydrosalpinx and other morbid conditions of the fallopian tube' given to the Obstetrical Society of London in April, 1904.

The actual number of cases reported in the literature is uncertain but would seem to be a little in excess of 300 (Blair, 1961).

This paper reports 2 cases occurring with slightly different presenting signs and causative pathology.

CASE REPORTS

Case 1.—A 19-year-old, nulliparous, unmarried nurse presented with right iliac fossa pain. The pain had come on gradually over the past 2 days and had then remained constant in the right iliac fossa and had not radiated. The pain had not been associated with defaecation or micturition. The patient had been anorexic for 24 hours but there had been no vomiting, diarrhoea, or pyrexia. The patient's last menstrual period had been 12 days prior to admission and her menses were quite regular every month, lasting for 5 days. There was no possibility of pregnancy. There was no previous history of any illness although there was a strong family history of tuberculosis, both parents having been treated in the past. She had had no previous similar episode of pain.

On examination the patient was a pale girl with flushed cheeks; she was lucid and co-operative. She was apyrexial and had no lymphadenopathy, oedema, or jaundice. Her abdomen was slightly obese. There was no obvious organomegaly, but there was marked tenderness and guarding in the right iliac fossa with rebound tenderness present in the right iliac fossa and a positive Rovsing's sign. Rectal examination revealed a rectum loaded with faeces and marked tenderness in the right iliac fossa but no pain or tenderness on movement of the cervix. A provisional diagnosis of acute appendicitis was made and the patient was taken to the operating theatre for laparotomy. The abdomen was opened by a right grid-iron incision and it was immediately noted that the peritoneal cavity contained a considerable quantity of straw-coloured fluid. This was removed by suction, a bacteriology swab taken, and inspection carried out. The appendix, caecum, rectum, and fundus of the uterus appeared to be covered with a large number of small vesicular blebs with a slight haemorrhagic reaction surrounding each bleb. A diagnosis was not made at this time and the appendix which appeared to be quite normal was removed in the usual manner. Further exploration of the abdomen through the incision showed the right Fallopian tube to be turgid and black, oozing dark blood from the fimbrial ostia. As access was very poor through the grid-iron incision this was closed and a lower midline incision performed. The pelvis was then more adequately inspected and the uterus, ovaries, and the left Fallopian tube were noted to be normal. However, the right Fallopian tube seemed to be twisted around itself in a clockwise direction approximately 1½ turns (540°). As the tube appeared to be non-viable it was removed in the usual manner. The abdomen was closed without drainage.

The pathologist's report revealed that the appendix contained threadworms in the lumen with some congestion of the serosa and a little inflammatory exudate on the serosal surface. Sections at three deeper levels through the block were made and revealed definite foci of epithelioid cells in the serosa and showed tubercles in two places with small focal areas of caseation. The Fallopian tube was reported as being deeply congested. On sectioning the empty Fallopian tube thickening of the tube with marked vascular congestion was noted. Numerous follicles of epithelioid cells were present. In some of these there were small areas of caseation and in many there were large multinucleated giant cells associated with a moderate polymorphonuclear leucocyte infiltration of the mucosa. Ziel-Nielsen staining showed occasional acid- and alcohol-fast bacilli. The general appearances were that of a tuberculous salpingitis.

The diagnosis of pelvic tuberculosis was later confirmed by inoculation of curettings obtained at dilatation and curettage of the uterus into a guinea-pig which at autopsy showed progressing tuberculosis. The patient was treated with antituberculous chemotherapy and after a short spell in hospital was allowed home to continue on her chemotherapy.

Case 2.—A nulliparous, married woman, aged 22 years, attended the Casualty Department of the Western General Hospital, Edinburgh, complaining of severe lower abdominal and right iliac fossa pain; she had vomited between nine and twelve times since the previous evening. The patient's bowels had moved normally and 2 weeks prior to this she had had a suspected urinary-tract infection for which no causative organism had been found. The patient's last menstrual period had been 2 weeks prior to her admission and had been quite normal. She reported that during intercourse the previous evening she had experienced marked dyspareunia. The patient had no past medical history of note and her family history was not significant.

The patient was apyrexial and her pulse and blood-pressure was quite normal. She did, however, look ill and was in obvious pain. The pain was reported as beginning the previous evening, coming on quite suddenly, and had lasted almost continuously until admission. The pain was in the right iliac fossa and although being appreciated over the whole lower abdomen did not radiate.

Examination revealed a thin woman holding herself very still. The abdomen was markedly guarded and she had extreme tenderness in the right iliac fossa. Rebound tenderness was elicited. Pelvic examination demonstrated a tender, firm mass in the pouch of Douglas, approximately 5 cm. in diameter, and the mass was quite fixed. Rectal examination revealed an empty rectum and it was possible to delineate a circumscribed tender mass in the pouch of Douglas. The uterus was felt quite separately from this mass. The diagnosis of torsion of a right ovarian cyst was made and arrangements were made for laparotomy. The abdomen was entered by a lower right paramedian incision and the peritoneal cavity was seen to contain a serosanguineous fluid with a few small clots. The right Fallopian tube was noted to be enlarged to approximately 5 cm. in diameter and extremely engorged with blood. The tube was twisted through approximately 1½ turns (540°) on a long mesosalpinx. The right ovary was healthy and distinct from this torsion. The left ovary and tube appeared to be normal as was the uterus. A right salpingectomy was performed in the routine manner and the abdomen was closed with drainage. The patient made a rapid recovery from this procedure and was discharged home after 8 days.

The pathologist's report noted a large haemorrhagic cyst measuring 5 cm. in diameter arising from the Fallopian tube. The floor of the cyst was stained with blood and showed several plaque-like areas of firm, warty growth. Microscopic examination showed that this specimen was derived from the Fallopian tube and associated tissues. The epithelial lining of the tube was normal, with the wall and surrounding tissues very congested and oedematous. Arising in the connective tissues surrounding the Fallopian tube was a cyst lined by a flattened, cuboidal epithelium. In some places the wall of the cyst was thickened and comprised sclerotic fibrous tissue and muscle mixed with areas of recent haemorrhage. The cyst was thought to be parovarian in origin.

The appearances were those of extreme vascular congestion and oedema in the Fallopian tube and parovarian cyst.

DISCUSSION

It would seem that there are no clear pathognomonic features related to the presentation of the condition of torsion of the isolated Fallopian tube. Pain and tenderness in either or both iliac fossae are relatively common and therefore the commonest preoperative diagnosis is that of acute appendicitis. It is not surprising that most of the reports are of involvement of the right side of the pelvis and Blair (1961) stated that 3 out of 4 cases were diagnosed as acute appendicitis. Peritonism or peritonitis was observed, associated with the presence of blood in the peritoneal cavity or close to the gangrenous tube. Nausea and vomiting may occur although these symptoms are more usually associated with ovarian torsion or gastro-intestinal upset.

No completely satisfactory theories of aetiology have been put forward. Torsion of the absolutely normal tube is extremely rare (Blair, 1961). It would appear that torsion is more likely to occur in the presence of an unusually long mesosalpinx or a hydatid, Morgagni, or parovarian cyst, as in *Case* 2. The twisting of the tube in the foetus may persist to some degree in adult life and thus initiate the torting process.

It is possible that torsion may be caused by abnormal motility of the tube and that intra-uterine devices may be instrumental in altering the normal activity and motility of the tube; thus their presence may well be related to the occurrence of torsion. It would seem feasible that torsion should be associated with marked congestion of the tube which may occur in a disease process or at certain stages in the menstrual cycle. Torsion would probably occur as the veins of the mesosalpinx are longer than the arteries and more distensible. Thus venous congestion would tend to cause the veins to rotate around the arteries which are more rigid. Artery blood-flow would continue because of the higher pressure, increasing the torsion and thus further causing gross venous congestion. Various theories have been put forward related to acceleration or deceleration of the body; notably the Sellheim theory proposed by Hugo Sellheim (1870–1936) and quoted by Blair (1961). Abnormalities of the pelvic organs related to previous surgery may also be an aetiological factor. A case of torsion following Pomeroy sterilization (Kendrick, 1965) and 1 following hysterectomy (Bowers, 1940) have been reported. It would seem likely that torsion following surgery is related to abnormal positioning or the presence of adhesions or adhesive bands around which the tubes can twist (Jeffcoate, 1969).

Tubal disease is a very important factor, and Bland-Sutton in 1904 commented: 'It is a fact that the Fallopian tube, when distended with simple fluid and blood, pus or even when gravid, does twist its pedicle.'

Temple in 1950, reporting 2 cases of torsion occurring in association with a pyosalpinx, commented that the occurrence of torsion is even more rare in the pyosalpinx as it is usually bound down by adhesions. Other authorities as far back as Targett in 1904 considered that almost all cases of twisted pyosalpinx were tuberculous. In the present *Case* 1 there was indeed a tuberculous salpingitis and it is possible that congestion associated with this process was instrumental in causing the torsion.

It seems that the major predisposing factor in the aetiology of torsion is an increase in the size of the tube, whether this is due to disease, associated anatomical abnormalities, or even physiological states such as pregnancy or menstruation.

A direct relationship with menstruation has not been established by any writer on this subject. However, it is interesting that there have been few cases of torsion of the isolated tube in premenarchical patients (Blum and Sayre, 1937). On the other hand, Jeffcoate (1969) states that in his experience torsion occurs usually in the child or adolescent.

The diagnosis has never been made preoperatively. It is therefore important that the operator diagnosing appendicectomy in the menstruating female should bear in mind the possibility of gynaecological pathology. I feel that there is a very good case for utilizing a lower right paramedian incision in this type of case which would obviate the necessity to perform two incisions which does occur from time to time. The advantages are obvious. Some attempts have been made to conserve the torted tube and it is imperative that the contralateral tube and ovary should be inspected before a firm decision is made to remove the diseased tube. If the causative pathology is an abnormally long mesosalpinx then plication of the mesosalpinx may be performed.

Good results have been reported using conservative measures and Rogers (1925) saved one tube from bilateral torsion and Blair (1961) in his series of 4 cases not only saved one tube but the patient went on to have a normal successful pregnancy. It is important, however, that if conservation is envisaged a further diagnosis as to aetiology should be made. If conservation had been attempted in *Case* 1 the diagnosis of tuberculosis could possibly have been missed.

PROGNOSIS

These patients will have a very similar prognosis to the patient who has had a salpingectomy for ectopic pregnancy.

Following salpingectomy the chances of conception are reduced and the risks of a tubal pregnancy are increased to 10–15 per cent of all pregnancies, i.e., forty times greater than the overall risk of 0·3 per cent (Jeffcoate, 1969).

In *Case* 1 the patient will run a very high risk of tubal pregnancy if she conceives at all as it is almost certain that the contralateral tube has some involvement in the tuberculous process.

Thus, isolated torsion of the Fallopian tube is an uncommon condition which is rarely if ever diagnosed prior to operation. This is a diagnosis which should be considered and such cases exemplify the advantages of using a right lower paramedian incision to open the abdomen in a female of fertile years where a diagnosis is in doubt.

Acknowledgements.—I would like to thank Mr. A. T. R. Hamilton, Raigmore Hospital, Inverness, for permission to report *Case* 1, and Dr. F. R. Clark, Western General Hospital, Edinburgh, for permission to report *Case* 2.

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SHORT NOTES OF RARE OR OBSCURE CASES

ATHEROSCLEROSIS AND ANEURYSM FORMATION IN A SAPHENOUS VEIN-GRAFT

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Summary

A case in which a saphenous vein by-pass graft inserted 5 years previously developed atherosclerosis and aneurysm formation 3–4 years later is described.

The autogenous saphenous vein is the preferred conduit for repair of occluded arteries in the leg and is also used with increasing frequency for coronary-artery repair. It is easy to suture, remains patent in low-flow situations, and has a very low incidence of long-term complications.

Atheromatous deterioration and aneurysmal formation in a saphenous vein-graft are extremely rare. In a 10-year review of 295 saphenous vein-grafts in 1967 Darling, Linton, and Razzuk did not find evidence of these complications.

The present report is a case of atheromatous deterioration and aneurysmal dilatation in a saphenous vein-graft which had been inserted 5 years previously.

CASE REPORT

The patient, a 63-year-old male, was admitted in 1970 for treatment of intermittent claudication. Five years before, in January, 1965, he had been operated upon in another hospital and a saphenous vein by-pass graft had been inserted from the left common femoral artery to the popliteal artery. On examination in 1970, he had a large abdominal aneurysm and diminished femoral pulses bilaterally. The proximal portion of the vein-graft was enlarged to approximately 2·5 cm. in diameter and the patient stated that he had been aware of increased pulsation in this area for about 1 year.

An aortogram revealed aneurysms in the aorta and both iliac arteries. Both external iliac arteries were narrow. The vein by-pass was patent and the proximal 5 cm. were dilated and aneurysmal.

At operation in October, 1970, the aortic and iliac aneurysms were excised and an aortofemoral by-pass graft was inserted. Dissection in the left groin revealed a fusiform aneurysm of the proximal 5 cm. of the vein-graft. One portion of the wall of the fusiform aneurysm was the site of a small false aneurysm and a yellow, atheromatous-appearing content was exuding from it (*Fig.* 1).

Since the patient had no usable segment of saphenous vein in either leg and since there was the possibility

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of other areas of deterioration in the by-pass graft the aneurysm was resected, the vein by-pass was ligated, and a femoropopliteal prosthetic by-pass was inserted.

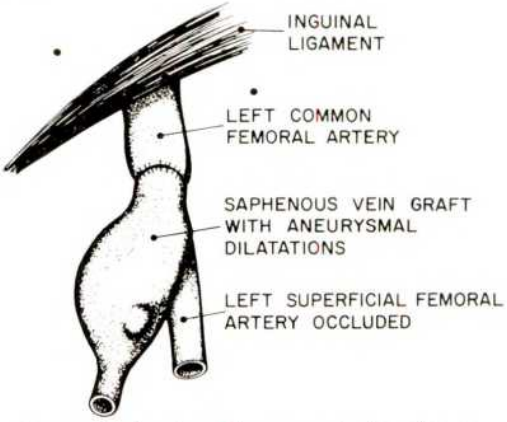
INGUINAL LIGAMENT
LEFT COMMON FEMORAL ARTERY
SAPHENOUS VEIN GRAFT WITH ANEURYSMAL DILATATIONS
LEFT SUPERFICIAL FEMORAL ARTERY OCCLUDED

FIG. 1.—The location of the aneurysm in the saphenous vein-graft.

On gross examination the wall of the venous aneurysm was thickened and yellow. Histological examination revealed extensive atherosclerosis with subintimal fibrosis and cholesterol deposition (*Fig.* 2).

DISCUSSION

Both atheromatous deterioration and aneurysm formation in saphenous vein-grafts in the arterial system are very rare. Beebe, Clark, and DeWeese (1970) described atheromatous changes in a man with hypercholesterolaemia and hyperlipidaemia. We have been unable to find a report of an aneurysm in a saphenous vein-graft. Pillet and Roux (1969) reported a fusiform aneurysm in a superficial femoral vein-graft which had been used as a replacement for a section of superficial femoral artery.

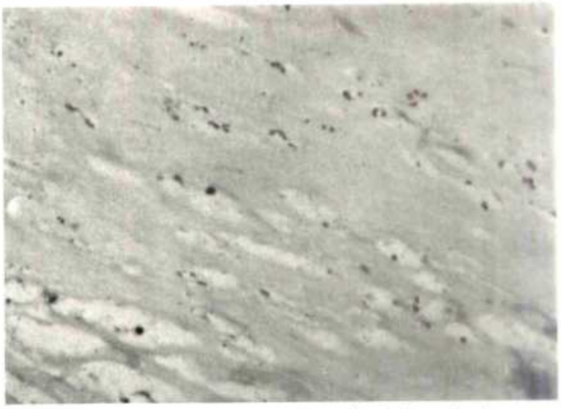

FIG. 2.—Histological section of the wall of the vein showing cholesterol deposits and giant-cell formation.

The present report shows that although atheromatous deterioration and aneurysm formation in a saphenous vein-graft are extremely rare they may occur.

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ADULT HYPERTROPHIC PYLORIC STENOSIS

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SUMMARY

Adult hypertrophic pyloric stenosis is an uncommon condition which when encountered is usually mistakenly diagnosed as carcinoma of the antrum. It is a benign disease resulting from hypertrophy of the circular fibres of the pyloric canal and is recognizable radiologically by narrowing and elongation of the pyloric canal. The aetiology is in doubt but the condition is probably congenital. The treatment of choice is partial gastrectomy.

SINCE the disease was first described by Jean Cruveilhier in 1835 adult hypertrophic pyloric stenosis has remained something of a surgical curiosity and, to date, fewer than 200 cases have been described in the world literature. In the majority of the cases the diagnosis has been made at operation, the preoperative diagnosis usually being carcinoma of the antrum or peptic stricture.

The following case report illustrates a further example of this unusual condition.

CASE REPORT

HISTORY.—A 42-year-old male presented with a 7-week history of epigastric pain, anorexia, and rapid weight-loss of about 6·3 kg. Vomiting occurred copiously every second or third day, the vomitus containing semi-digested food particles recognizable as having been eaten some time previously. Prior to this he had suffered from mild dyspepsia for a number of years without vomiting.

EXAMINATION.—No abnormality was found other than slight epigastric tenderness. A succussion splash was not elicited at the initial examination but was subsequently found to be present.

BARIUM STUDIES.—A barium-meal examination showed excess fasting juice. The pyloric canal was narrowed and elongated and bulged into the duodenal cap (*Fig.* 1). The mucosal pattern looked abnormal and peristalsis was restricted. A crater was present on the lesser curvature and had the appearance of a benign ulcer (*Fig.* 2). The possibility of benign adult hypertrophic pyloric stenosis was considered, but carcinoma of the antrum could not be excluded.

OPERATION.—The musculature of the pyloric canal was found to be smoothly and uniformly hypertrophied with a maximum thickness of 1·2 cm. The duodenum was normal with no evidence of peptic ulceration. Situated on the lesser curvature was a large ulcer which was obviously benign. A Polya gastrectomy was performed.

The postoperative course was complicated by a pulmonary infarct on the tenth postoperative day. The patient, however, subsequently recovered and enjoyed complete relief of his gastric symptoms.

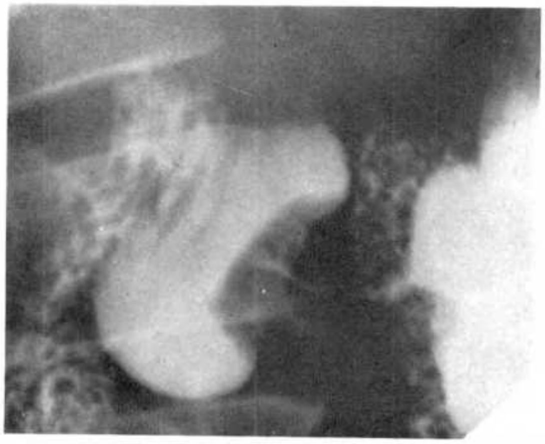

FIG. 1.—Barium-meal radiograph, showing narrowing and elongation of the pyloric canal and bulging into the duodenal cap.

HISTOLOGY.—Examination of the pyloric canal showed diffuse hypertrophy of the circular muscle coat of the pylorus, confirming the diagnosis of hypertrophic pyloric stenosis (*Fig.* 3).

DISCUSSION

Pathology.—The thickness of the muscle of the normal adult pyloric canal ranges from 4 to 7 mm. with an average of 5·1 mm. In adult hypertrophic pyloric stenosis this measurement is increased to 1–1·5 cm. on average, but measurements of up to 3 cm. have been recorded (Knight, 1961). This increase is mainly due to hypertrophy of the circular muscle component, involving either the whole circumference of the pylorus or a focal segment of it. Focal hypertrophy frequently occurs at the 'torus'— the point at which the two oblique loops of circular fibres meet at the lesser curvature (Keet, 1956).

Radiology.—Although a number of diagnostic features have been postulated, these are by no means consistent and the condition commonly eludes radiodiagnosis. The first important paper on the radiological aspects of the condition stressed the importance of bulging of the pyloric muscle into the duodenal cap (Kirklin and Harris, 1933) and this point was reiterated by subsequent authors (Sherman, Yen, Bowden, and Selby, 1959). This feature, however, may be produced in normal subjects by manual pressure on the stomach.

The presence of a cleft between the hypertrophied muscle and the fibres of the pylorus itself has been demonstrated not infrequently, and has been considered by many to be of diagnostic importance (Twinning, 1933; McNaught, 1957; Sherman and others, 1959). Again this is not a constant finding.

The most consistent sign is elongation of the narrowed pyloric canal, often with 'funnelling' of the proximal end (Keynes, 1965).

Aetiology.—This remains in doubt. Prolonged pylorospasm has been suggested as a possible cause, but it is difficult to see how such a common finding could be a significant factor in such an uncommon condition.

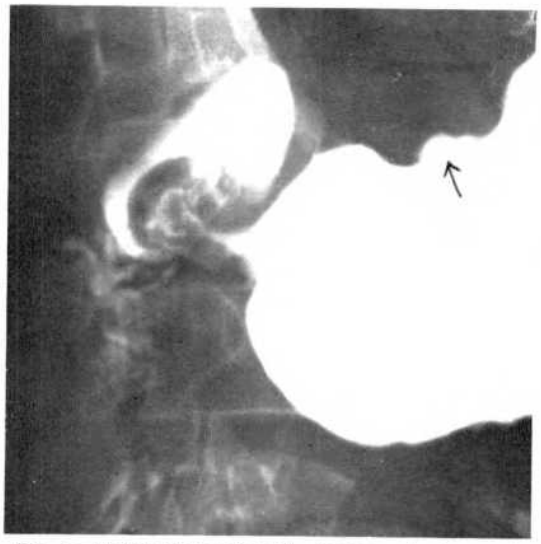

FIG. 2.—Barium-meal radiograph, showing a benign gastric ulcer on the lesser curvature.

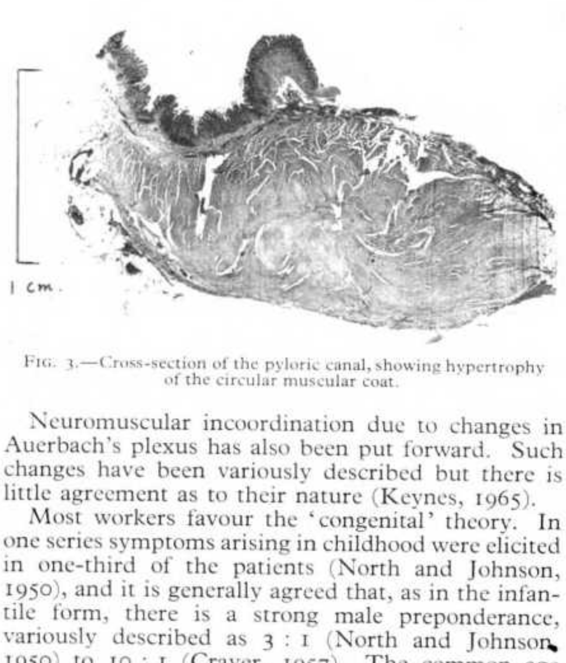

FIG. 3.—Cross-section of the pyloric canal, showing hypertrophy of the circular muscular coat.

Neuromuscular incoordination due to changes in Auerbach's plexus has also been put forward. Such changes have been variously described but there is little agreement as to their nature (Keynes, 1965).

Most workers favour the 'congenital' theory. In one series symptoms arising in childhood were elicited in one-third of the patients (North and Johnson, 1950), and it is generally agreed that, as in the infantile form, there is a strong male preponderance, variously described as 3 : 1 (North and Johnson, 1950) to 10 : 1 (Craver, 1957). The common age of onset of symptoms, however, is 31–60 years (North and Johnson, 1950), and why the majority of patients remain asymptomatic until middle age is not clear. It may be that the condition is aggravated or merely brought to light incidentally by concomitant gastric pathology; although sometimes occurring alone the condition is much more commonly associated with some other abnormality such as gastric ulcer, hypertrophic gastritis, or gastric polyposis (Keynes, 1965). It has been suggested that in these circumstances the hypertrophy may be a secondary phenomenon but in fact the converse is probably true (McCann and Dean, 1950), as it has been shown experimentally in dogs that occlusion of the pylorus produces gastric ulceration (Dragstedt, 1954).

Treatment.—As regards treatment it is generally agreed that the procedure of choice is a Billroth-I gastrectomy (North and Johnson, 1950; Craver, 1957; Knight, 1961).

A Ramstedt pyloromyotomy, indicated in the infantile form, is not recommended as it predisposes to diverticulum formation through the large defect in the pyloric musculature (McCann and Dean, 1950).

In the debilitated patient in whom a partial gastrectomy might be considered excessively hazardous either a Heineke pyloroplasty (Knight, 1961) or a gastro-enterostomy (Craver, 1957) is acceptable, although the former may prove technically difficult if the pylorus is grossly thickened, while the latter has the serious disadvantage of precluding visualization of a lesion which it may be difficult to distinguish from carcinoma.

Acknowledgement.—My thanks are due to Mr. K. Fraser for permission to publish the case report and for advice in the preparation of this paper.

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INTRAPULMONARY LIPOMA ASSOCIATED WITH MULTIPLE PULMONARY HAMARTOMAS

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SUMMARY

A pulmonary lipoma is described in a 64-year-old male, involving the right middle lobe, associated with a separate area of intrapulmonary ossification and a central intrabronchial hamartoma.

It is postulated that the lipoma most probably arose from one of the multiple pulmonary hamartomas.

PULMONARY lipomas are rare tumours, and to date 39 cases have been reported in the English literature. Lipomas of the lungs may be divided into (*a*) bronchial and (*b*) subpleural, depending on their site of origin. The majority of examples reported are endobronchial lipomas arising from the submucosa of a large bronchus. In this report we describe a peripheral intrapulmonary lipoma associated with pulmonary ossification and a polypoid intrabronchial hamartoma.

CASE REPORT

A man of 64 years was investigated for an episode of haemoptysis, which had been small in amount, 2 weeks earlier. He had few other symptoms but had been a pipe smoker. Twelve years previously he had had a radiograph of the chest which was reported as showing old tuberculosis. At the present time a chest radiograph showed a patch of calcification with a little fibrosis at the right apex. There was also a little indefinite nodular shadowing in the region of the right middle lobe.

Bronchoscopy revealed a small 'warty tumour' arising from the lower wall of the right upper-lobe bronchus and causing partial obstruction of the lumen. A biopsy was taken and showed a mildly chronic inflammatory-cell infiltrate in dense fibrous stroma, the surface being lined by respiratory-type epithelium.

Bronchography showed severe stenosis within the origin of the right upper lobe bronchus and also complete non-filling of the middle lobe. There was compensatory emphysema in the lower lobe.

Thoracotomy was performed by Mr. D. B. Clarke and the right upper and middle lobes were resected with sleeve resection of the main bronchus at the origin of the upper lobe to include the whole of the tumour there. The middle lobe contained a mass surrounded by bullous emphysema.

Postoperative recovery was complicated by sputum retention but expansion of the lower lobe was obtained and the patient recovered and was discharged on the twelfth day. Five weeks later there was slight further haemoptysis, but bronchoscopy and biopsy showed only granulation tissue at the site of resection.

PATHOLOGY.—The resected specimen consisted of the upper and middle lobes of the right lung. Dense fibrous adhesions were present in the transverse fissure and over the pleural surface of the upper lobe. Collapsed, thin-walled, emphysematous bullae were located at the periphery of the middle lobe. A large ill-defined mass (*Fig.* 1), measuring 7 × 4 × 4 cm., expanded the middle lobe. The lobulated fatty mass extended up to the pleural surface of the lobe. No intrabronchial fatty tumour was found. A firm sessile polyp (1 cm. in diameter) was situated at the origin of the upper-lobe bronchus, partially obliterating the lumen and resulting in collapse and induration in the distal lung. An ill-defined calcified focus (2 cm. in diameter) was located at the periphery of the upper lobe.

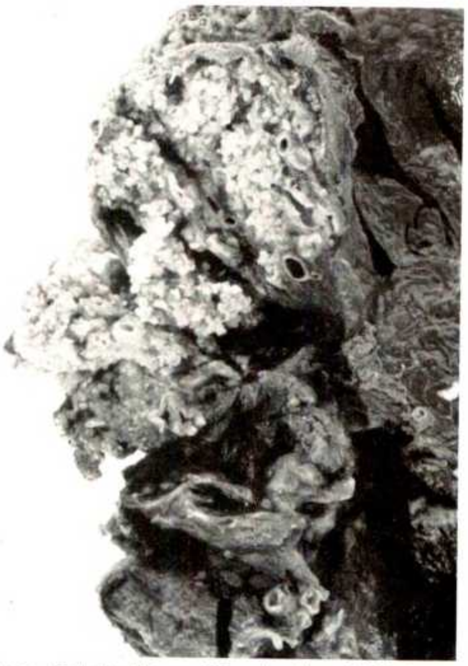

FIG. 1.—Lobulated lipoma filling the right middle lobe.

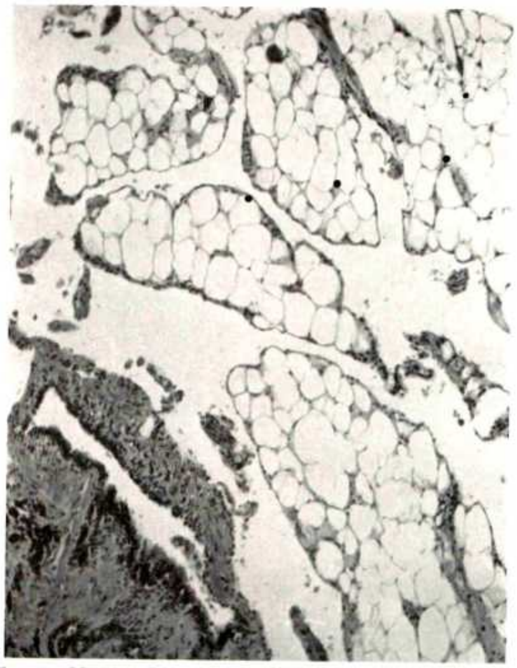

FIG. 2.—Mature adipose tissue separated by thin fibrous septae. H. and E. (× 162.)

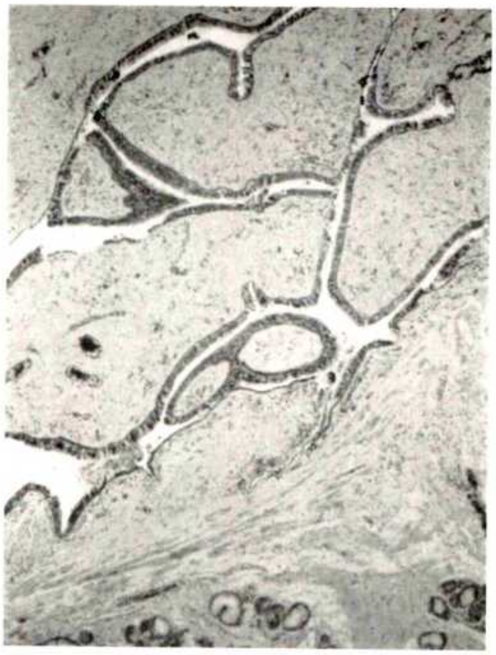

FIG. 3.—Cleft-like spaces lined by non-ciliated columnar epithelium in intrabronchial hamartoma. H. and E. (× 162.)

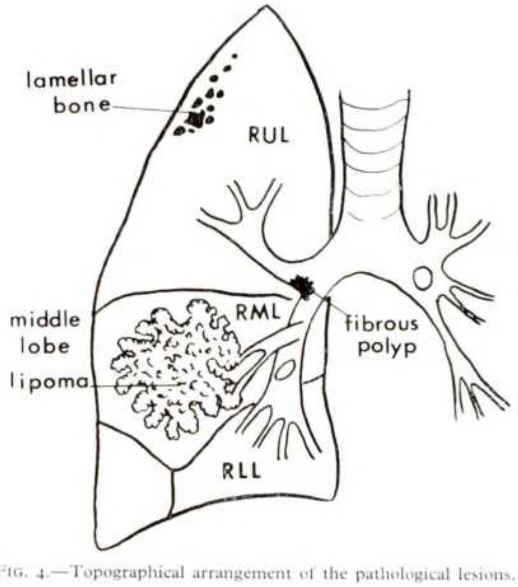

FIG. 4.—Topographical arrangement of the pathological lesions.

Histologically the mass in the middle lobe was a simple lipoma consisting of mature vascular adipose tissue (*Fig.* 2) forming delicate lobules encircling the bronchi and accompanying vessels.

The orifice of the upper-lobe bronchus was partially occluded by a hamartomatous polyp consisting of a fibrovascular stroma traversed by slit-like clefts covered by non-ciliated, columnar-celled epithelium (*Fig.* 3).

A further hamartoma consisting of foci of metaplastic bone was located at the apex of the upper lobe (*Fig.* 4). There was no evidence of pre-existing fibrosis. The bone consisted of mature lamellar trabeculae enclosing fatty haemopoietic marrow (*Fig.* 5).

DISCUSSION

Fat is a normal constituent of the bronchial wall and is located in the submucosa of the bronchi down to 1 mm. in diameter (Watts, Claggett, and McDonald, 1946); it may also be found beneath the pleura.

Lipomas may arise from the fatty tissue within the lung and are divided into (*a*) those in the bronchi and (*b*) those beneath the pleura.

Pulmonary lipomas are rare tumours—only 39 cases are recorded in the English literature—although they are probably commoner than appears from the published cases.

Table I.—REPORTED CASES OF INTRAPULMONARY LIPOMAS

AUTHOR	AGE AND SEX		SIZE (cm.)	LOCATION
Kernan (1927)	50	M.	2·0 × 1·0	R. main bronchus
Myerson (1928)	47	M.	2·3 × 1·6 × 0·6	L. main bronchus
Jackson and Jackson (1932)	64	F.	—	L. main bronchus
Wessler and Rabin (1932)	48	M.	—	L. lower bronchus
McGlade (1939)	48	M.	5·0 × 1·7	L. main bronchus
Vinson and Pembleton (1942)	29	F.	—	L. main bronchus
Watts and others (1946)	51	M.	2·0	L. upper bronchus
Whalen (1947)	61	M.	—	L. main bronchus
Lell (1949)	40	M.	—	R. main bronchus
Carlisle and others (1951)	52	M.	1·4 × 1·1	L. upper bronchus
Som and Feuerstein (1951)	55	M.	2·0 × 1·5	R. lower bronchus
Som and Feuerstein (1951)	59	M.	2·3 × 1·8 × 1·0	R. upper bronchus
Touroff and Seley (1951)	48	F.	1·5 × 1·0	L. lower bronchus
Beaton and Heatly (1952)	36	M.	1·5	L. main bronchus
Brewin (1952)	63	M.	—	L. main bronchus
Smart (1953)	60	M.	—	L. main bronchus
Shapiro and Carter (1954)	46	M.	1·5	L. upper bronchus
Edwards (1954)	78	M.	4·0 × 2·0 × 2·0	R. main bronchus
McCall and Harrison (1955)	60	M.	2·5	L. main bronchus
Ochsner and others (1957)	35	M.	3·0 × 0·5	R. main bronchus
Hutcheson and others (1958)	56	M.	1·3 × 1·0 × 1·0	R. lower bronchus
Hutcheson and others (1958)	32	M.	2·0 × 1·0	R. upper bronchus
Taheri and others (1960)	63	M.	—	R. main bronchus
Plachta and Hershey (1962)	71	M.	7·8 × 4·2 × 2·3	R. lower bronchus
Caldarota and others (1964), 6 cases	49*	M.	—	—
Staub and others (1965)	55	M.	—	R. middle bronchus
Jablakow and Rubnitz (1966)	50	M.	2·0 × 2·0 × 1·0	L. upper bronchus
Crutcher and others (1968)	52	M.	2·0 × 1·5 × 1·5	L. upper bronchus
Ramsey and others (1969)	46	M.	1·5 × 0·6	R. middle bronchus
Jensen and Petersen (1970)	54	M.	Pea	R. upper bronchus
Jensen and Petersen (1970)	60	M.	1·5 × 1·0	R. upper bronchus
Jensen and Petersen (1970)	59	M.	Pea	R. upper bronchus
Bellin and others (1971)	58	F.	2·0 × 1·0 × 0·5	L. main bronchus
Bellin and others (1971)	66	M.	3·0 × 0·5	L. upper bronchus
Jones and others (1972)	64	M.	7·0 × 4·0 × 4·0	R. middle bronchus

* Average.

Bronchial lipomas account for the majority of the cases, and present as dumb-bell-shaped tumours projecting into the lumen of large bronchi.

Subpleural lipomas are very rare; such tumours were reported by Shapiro and Carter (1954) and Spencer (1968). The occurrence of a mainly peripheral intrapulmonary lipoma has been described by Touroff and Seley (1951), Shapiro and Carter (1954), and Plachta and Hershey (1962). Only 2 other reports concern middle-lobe lipomas (Staub, Barker, and Langston, 1965; Ramsey, Oster, and Foreman, 1969).

Intrapulmonary lipomas are much commoner in males (*Table I*), tending to occur around the fifth decade but with an age range from 29 to 78 years (average age, 52 years). Their size varies from 1·3 × 1 cm. to 7·8 × 4·2 × 2·3 cm. The tumour in the present case, measuring 7 × 4 × 4 cm., is the largest yet recorded. They appear to be slightly more common on the left than on the right side (*Table I*).

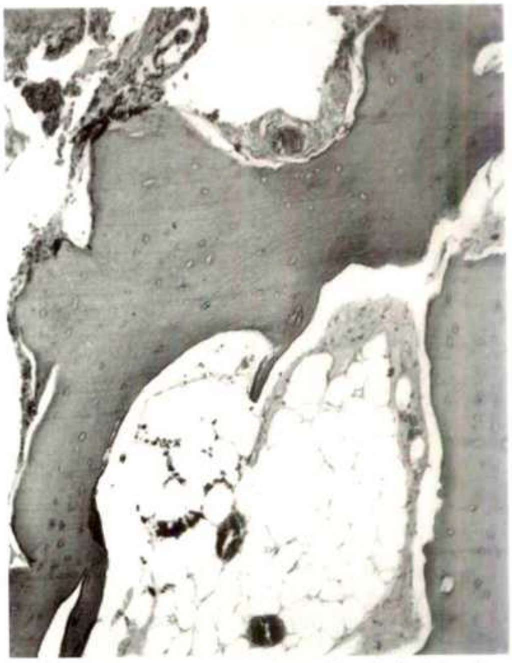

FIG. 5.—Cancellous bony trabeculae and enclosing fatty tissue containing foci of red marrow (bottom left). H. and E. (× 162.)

In the present case an unusual and interesting feature was the presence of osseous metaplasia (*Fig* 4) in the upper lobe. Nodular heterotopic ossification may occur within the lung alveoli in mitral stenosis, in organized inflammatory tissue, occasionally in the walls of a chronic cavity, and very rarely by a process of metaplasia within normal lung (Spencer, 1968). In our case there was no evidence of any pre-existing fibrous scarring in relation to the intra-alveolar bone. The bony trabeculae enclosed mature adipose tissue containing foci of metaplastic bone-marrow.

Metaplastic ossification and bone-marrow formation are also recognized in the centres of chondromatous hamartomas.

The 2 cases described by Bellin, Libshitz, and Patchefsky (1971) showed foci of metaplastic cartilage in association with myxomatous tissue within the lipoma. This cartilaginous metaplasia is very uncommon in bronchial lipomas, and Som and Feuerstein (1951) were the only other authors to note it in these tumours.

Metaplastic ossification and cartilagenous metaplasia have been described in lipomas in other sites

(Plaut, Salm, and Truscott, 1959). An alternative interpretation of the metaplastic osseous and adipose tissue in the upper lobe in the present case is that it was due to ossification occurring in a second intrapulmonary lipoma.

The polypoid tumour arising from the upper-lobe bronchus is a typical bronchial hamartoma consisting of non-ciliated, columnar-epithelial-lined, slit-like clefts between a fibrovascular stroma (*Fig*. 3).

Microscopically, bronchial hamartomas may also contain fat, although it is usually inconspicuous since it is distributed between bulky lobules of cartilage. They reproduce any of the components of bronchial tissue, including areas of fibrocartilage, bone, epithelial-lined clefts, glands, and smooth muscle (Spencer, 1968).

Bellin and others (1971) stated that the finding of cartilaginous metaplasia in pulmonary lipomas, as seen in their 2 cases and in that of Som and Feuerstein (1951), is very rare and should be differentiated from bronchial hamartomas.

In this report we suggest that the middle-lobe lipoma most probably developed from one of the multiple hamartomas present.

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INTRALUMINAL DIVERTICULUM OF THE DUODENUM

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IN contrast with primary and secondary diverticuli of the duodenum, which are fairly common, the intraluminal diverticulum of the duodenum is a very rare entity.

CASE REPORT

Mr. S. N., a theological student, aged 20 years, attended the Royal Salop Infirmary on 18 June, 1969, complaining of upper abdominal pain and vomiting soon after meals for 12 months. The pain was described as intermittent and localized in the epigastrium, and it never occurred at night. Intermittent discomfort and nausea followed almost immediately after meals and both the nausea and pain were relieved by vomiting. There was no history of melaena or haematemesis and no bowel irregularities were reported. Complete physical examination revealed nothing positive apart from slight epigastric tenderness. Routine investigations of the blood, urine, and stool did not reveal any abnormality.

A barium-meal examination (*Figs*. 1, 2) was done and the following was reported: 'In the descending part of the duodenum there is shown to be a blind-ended tubular duplication of the gut; this is lying within the lumen of the duodenum and when filled with barium it extended into the middle third of the transverse part of the duodenum. The opening within the main alimentary channel is in the second part of the duodenum near the ampulla. The duodenal cap was irritable and rather difficult to fill; there was slight tenderness to palpation and there does seem to be a deformity of the right fornix.' A tentative diagnosis of intraluminal diverticulum of the duodenum, though rare, was made and the patient was admitted on 14 Nov. for operative treatment.

The abdomen was opened through a right paramedian incision. The stomach was found to be slightly dilated. The duodenum looked normal externally and, on palpation, the second part of the duodenum felt thick, giving the impression of something slipping in between the fingers. The liver, pancreas, and biliary apparatus were found to be normal and there was no evidence of other abnormality in the alimentary tract. The duodenum was mobilized by Kocher's manœuvre and the second part was opened anteriorly by a longitudinal incision. The intraluminal diverticulum was immediately apparent as a blind pouch (*Figs.* 3, 4) arising close to the ampulla of Vater and extending up to the middle of the third part of the duodenum. The intraluminal diverticulum, measuring 5 × 2 cm., was partially obstructing the lumen of the duodenum. The opening of the diverticulum was closely related to the ampulla of Vater and the blind end was lying in the transverse part of the duodenum. The diverticulum was removed entirely and the defect in the mucous membrane was sutured with fine atraumatic catgut. Before the duodenum was closed a small incision was made in the pyloric antrum and the pylorus was examined under direct vision and digitally to exclude the possibility of duodenal ulceration.

The histological examination was described as follows: 'Microscopically the wall consists of a thin layer of fibrous tissue covered on each side by intestinal type mucosa. No inflammatory or malignant changes were seen.' (*Fig.* 5.)

The follow-up, 21 months after operation, has been satisfactory and the patient reports complete relief of symptoms.

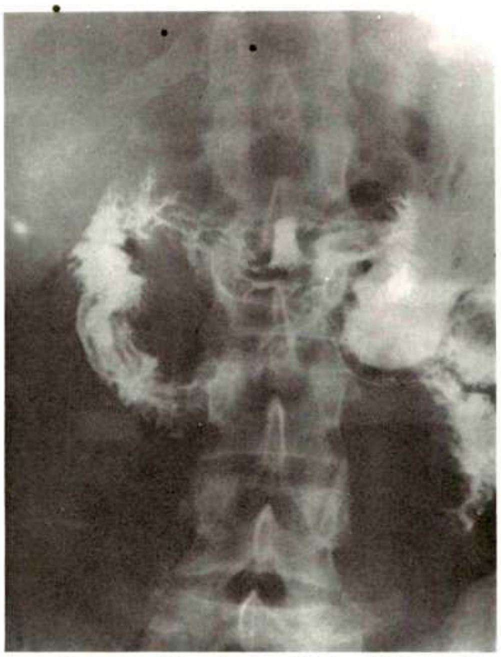

FIG. 1.—Barium-meal film, showing a blind-ended duplication of the gut lying in the descending part of the duodenum.

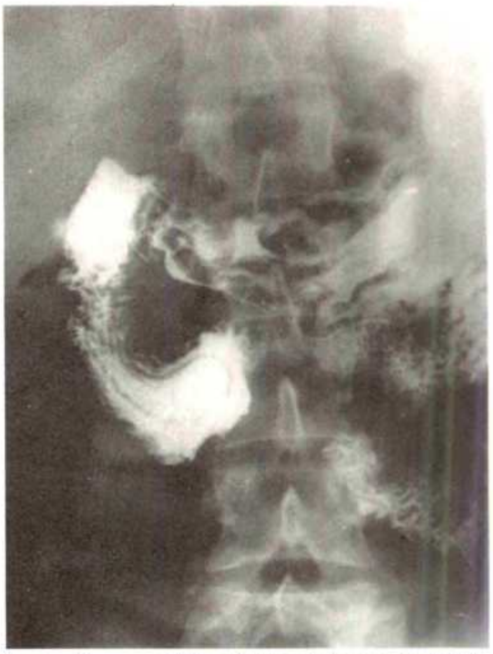

FIG. 2.—Barium-meal film, showing the barium-filled duplication extending into the middle third of the transverse part of the duodenum.

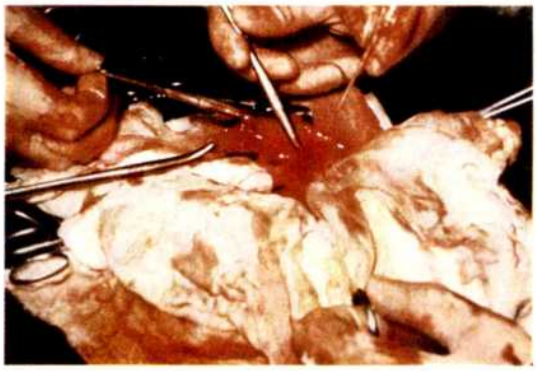

FIG. 3.—Operative appearances.

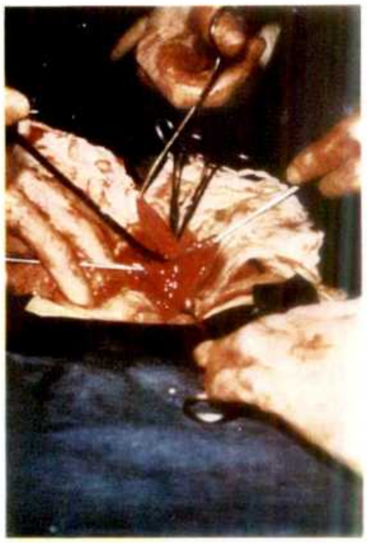

FIG. 4.—Operative appearances.

DISCUSSION

Very few similar cases have been reported in the world literature. In 1885 Silcock published the first pathological report of an intraluminal diverticulum of the duodenum. A very long period then elapsed in which no report of a similar anomaly can be found until 1949 when Kinzer published a radiological report of intraluminal diverticulum. Since then only 7 cases have been reported (Meyer and Edgren, 1956; Zatkin, Macy, and Kveton, 1959; Kohler, 1960; Coors and Mitchum, 1962; Kessler and Witmer, 1964; Petty and Mousley, 1966; Widmann, Schuman, and Poznanski, 1966).

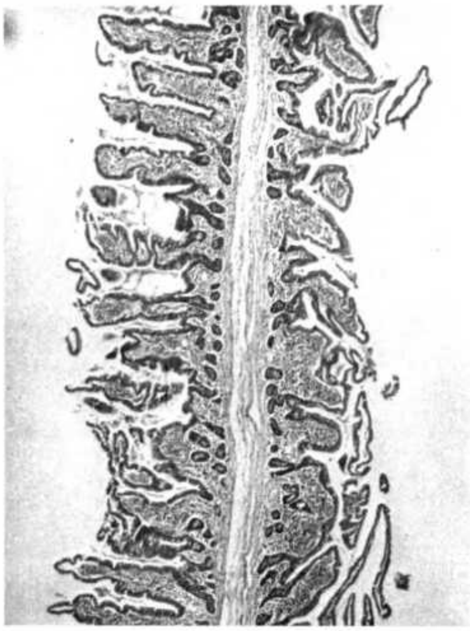

FIG. 5.—Section through the wall of the intraluminal diverticulum.

The aetiology of this lesion is unknown. It has been suggested that the anomaly represents true partial duodenal duplication. However, the facts that none of the reported cases was in babies or children and that a true duodenal duplication should contain all the layers of the duodenum while the intraluminal diverticulum has one layer of fibrous tissue which is covered on either side by intestinal epithelium do not support this theory.

Another theory is that the formation of the intraluminal diverticulum is caused by an incompletely developed duodenal diaphragm which sustains an almost continuous propulsive peristaltic force and forms an intraluminal sac which extends distally.

The third and most likely theory is that the folds of the mucosa in the second part of the duodenum which are transverse near to the ampulla of Vater are kept in almost continuous motion by peristaltic waves and gradually form an intraluminal sac.

All the previously reported cases have been found in adults aged from 22 to 71 years. The present case is in the youngest patient so far reported and has certain common features with other cases. The symptoms resemble those of peptic ulceration. Intermittent upper abdominal pain, discomfort, nausea, and vomiting were commonly found. Other symptoms included the invariable location of the intraluminal diverticulum in the second part of the duodenum with the opening lying proximally near to the ampulla of Vater and the blind end distally. The histological examination always shows epithelium on both sides of the diverticulum.

The diagnosis can be made only radiologically or at laparotomy. During screening peristaltic movements of the duodenum can be seen whilst the intraluminal diverticulum (translucent line) remains inert. Films should be taken in various positions in order to confirm that the diverticulum is intraluminal. The translucent line represents the thickness of the wall of the diverticulum.

Acknowledgement.—We should like to thank Dr. E. Rees, Department of Pathology, Royal Salop Infirmary, for the histological report and *Fig.* 5.

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REVIEWS AND NOTICES OF BOOKS

Clinical Neurosurgery. Proceedings of the Congress of Neurological Surgeons, St. Louis, Missouri, 1970. Edited by GEORGE T. TINDALL, M.D. 9 × 6 in. Pp. 557 + xxxviii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £8·25.

THIS volume is dedicated to Dr. Barnes Woodhall, guest and principal speaker at the Twentieth Annual Meeting of the Congress of Neurological Surgeons in October, 1970, at St. Louis, Missouri.

As one would expect, the majority of the contributors to this volume are from various surgical centres in America and Canada; there is one contributor from England, Mr. Walpole Lewin of Cambridge. He writes on 'Towards a Visual Prosthesis', and describes how an implant was inserted over the occipital cortex in a blind patient aged 47. Mr. Lewin has experimented on a series of baboons over the years and obtained some interesting results.

Dr. Barnes Woodhall contributes two interesting chapters on neurosurgical history. The first of these deals with 'Neurosurgery in the Past' and he concentrates mainly on the Dandy era, namely from 1926 to 1937. The second chapter is devoted to 'Neurosurgery of the Present', and Dr. Barnes Woodhall is of the opinion that neurosurgery came of age in the mid-trimester of this century.

The numerous contributors to this work cover every aspect of neurosurgical practice, such as neurogenic intermittent claudication, stenosis of the lumbar spinal canal, phantom limb pain, spontaneous intracerebral haemorrhage, cerebral ischaemia, brain scanning, stress ulceration, and the neurogenic bladder. The illustrations in this volume are very good.

At the end of each chapter there is a very complete list of references.

Every neurosurgeon will wish to possess this interesting book.

Year Book of Cardiovascular Medicine and Surgery. Edited by E. BRAUNWALD, M.D., San Diego; W. P. HARVEY, M.D., Georgetown; J. W. KIRKLIN, M.D., Alabama; A. S. NADAS, M.D., Boston; O. PAUL, M.D., Passavant; R. W. WILKINS, M.D., Boston; and I. S. WRIGHT, M.D., New York. 7½ × 5 in. Pp. 464. Illustrated. 1972. London: Lloyd-Luke. £6·80.

CARDIOVASCULAR medicine and surgery comprise a very active and progressive branch of medical science. *The Year Book of Cardiovascular Medicine and Surgery* helps to keep cardiologists and cardiac surgeons on their toes for it highlights all that is new during the year under review, namely 1971. The volume includes a considerable amount of research work on animals, such as the rat and the frog.

The normal and altered cardiovascular functions come under an extended review.

Cardiovascular disease in the infant and child is considered at some length and the result of surgical intervention assessed after some years.

Heart disease in adults, as one would expect, occupies a large section of this volume and articles on pacemakers are reviewed.

Angina pectoris and hypertension are considered at length.

Cardiovascular surgery, especially for ischaemic heart disease, is reviewed.

This is an excellent desk book for cardiologists and cardiac surgeons, and senior resident medical officers will find it of real value.

Les Tumeurs carcinoides du Tube digestif. By P. JOUANNEAU, Rouen, and M. MALAFOSSE, Paris. 9½ × 6½ in. Pp. 193. Illustrated. 1971. Paris: Masson et Cie, Editeurs. 45F.

OUR appreciation of carcinoid tumours of the digestive tract seems to have evolved from 'not very malignant, never giving metastases' to 'an affection that may have redoubtable endocrine and metabolic consequences'. The authors of the present book, setting out to provide an up-to-date and reasonably complete review of our knowledge, succeed to a very considerable extent. There is a general part dealing with important aspects, such as historical notes, pathology, diagnosis, applied physiology, and treatment. The fascinating biological features are amply discussed and explained. Armed with this knowledge, the reader can turn to the second half of the book, which deals with the various locations such as the small intestine, appendix, colon, etc. It is a pleasure to read this monograph, for in it we find a well-balanced blend of direct experience with the disease, based on 170 observations, and derived knowledge, obtained from the study of more than 500 papers. When treating a case of carcinoid tumour one will probably never turn in vain to this publication.

Curling's Ulcer. An Experiment of Nature. By STACEY B. DAY, BRUCE G. MACMILLAN, and WILLIAM A. ALTEMEIER, Cincinnati. 9 × 6 in. Pp. 286 + xxii. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $17.50.

ALTHOUGH some one hundred and thirty years have elapsed since Thomas Curling published his paper on the occurrence of duodenal ulcer after sustaining burns of the skin, little notice has been taken of this clinical observation, except for a passing notice in textbooks on surgery and pathology. With the establishment of burns centres at home and abroad following the Second World War a greater number of cases of Curling's ulcer has been collected.

The present monograph is published at an opportune time, for it gives a very comprehensive survey of the condition.

It is divided into three parts. Part 1 is concerned with the overall picture of post-burn gastro-intestinal ulceration as it has been explored by clinicians and research investigators over the years. The two World Wars presented a vast number of burn casualties and it was because of this that burn centres were introduced, especially in the Royal Air Force.

Part 2 is devoted to the clinical picture of Curling's ulcer and the accumulated clinical experience of the University of Cincinnati Medical Center General Hospital's Burns Unit and other burns units.

In Part 3 all the wide-ranging observations showing the multi-faceted nature of this condition are portrayed.

An excellent extensive bibliography can be found at the end of the book.

This is a worth-while guide for students and practitioners and as a reference book it could not be bettered.

In Appendix 1 there is a refreshing note on Thomas Blizard Curling, F.R.S., F.R.C.S., 1811–88.

Questions Colleagues Have Asked Me. By W. MELVILLE CAPPER, F.R.C.S., F.R.C.O.G., Bristol. Pp. 39. 1972. London: C.M.F. Publications. No price given.

THIS account is the substance of an address given at a meeting of the Christian Medical Fellowship on 15 March, 1961, in the hall of the Royal Commonwealth Society. Sir Clement Price Thomas, K.C.V.O., F.R.C.S., was in the chair.

This paper booklet has been published by the Christian Medical Fellowship in the belief that it will prove of inspiration and value to many surgeons both at home and abroad.

Sir Clement writes a foreword in which he speaks of Capper's influence and example.

A. S. Aldis of Cardiff contributes a tribute to a great Christian and a great surgeon. Melville Capper was a very active man and he examined in surgery at many universities and was on the Court of Examiners of the Royal College of Surgeons for several years.

Capper's experience as a devoted Christian is writ large in this excellent booklet, and surgeons far and wide will find much food for thought within its pages.

Die Inaktivitäts-Osteoporose. By J. MACH, Rostock. 8½ × 5¾ in. Pp. 207. Illustrated. 1971. Berlin: Verlag Volk und Gesundheit. 44.80 M.

DR. MACH has done a good job by writing a book about osteoporosis caused by inactivity, and it is probably the only complete survey of this subject. Osteoporosis is a symptom of diseases such as bone tuberculosis, Bechterew's disease, and rheumatic and neurological diseases.

Inactivity of the extremities because of bone lesions inevitably leads to osteoporosis, in the same way as muscle inactivity causes reduction of venous pumping, which can be demonstrated clearly in amputation stumps. Promoting muscular activity consequently is the logical method of preventing and healing osteoporosis; android steroids are perhaps the only other possibility. There are several methods of defining the degree of osteoporosis, for instance, by radiography, but a subtle technique is required to ensure that this is accurate.

Experiments have been performed on rabbits; on one leg the ischiatic nerve and the Achilles tendon were intersected, so that the breaking strength and elasticity of the legs could be measured. It was found that the breaking strength was significantly less on the artificially osteoporotic side.

Chemical tests showed that the calcium and phosphorus content did not decrease significantly in the artificially osteoporotic leg. The percentage of hydroxyproline, which is an important ingredient of collagen, appears to be lower than in healthy bone; this might prove to be one of the most reliable tests in determining osteoporosis.

Osteoporosis caused by weightlessness was discovered during the check-up of cosmonauts and this might be a warping for space flights in the future.

Advances in Surgery, Volume 5. Edited by CLAUDE E. WELCH, Boston, and JAMES D. HARDY, Jackson. 8¾ × 6 in. Pp. 354 + xiv. Illustrated. 1972. London: Lloyd-Luke. £8·65.

VOLUME 5 of *Advances in Surgery*, like the other volumes in this series, is devoted to a series of articles which covers certain aspects of surgery in which there has been significant progress within the past few years.

The best article in this book is that by Alan G. Parks dealing with all aspects of haemorrhoidectomy. The modern physiology of the rectum and anal canal is well set forth and the operative treatment of haemorrhoids is described in some detail. It is stimulating to see original line drawings which are easy to understand and which greatly enhance the written word.

Clinical diagnostic radiographs are described by Stuart S. Sagel and others, and they do demonstrate the great advances that have been made in current practices. New pharmacological agents have played their part in improving contrast media used in the chest, bile-ducts, and blood-vessels.

Insulinomas are considered in some detail by George L. Nardi, who records some 15 patients who were operated upon for hypoglycaemia. The pathology was found in the head of the pancreas in 5 cases, in the body in 4 cases, and in the tail in 6 cases.

The surgery of the parathyroid glands is dealt with by Chiu-an Wang, who considers that considerable progress has been made in the past decade in the diagnostic field of hyperparathyroidism.

The surgery of the adrenal glands is considered by John W. Raker, who advocates an arching, wide, transverse upper abdominal incision to explore the adrenal gland.

Diverticular disease of the colon is discussed in a lively and practical way by Richard and Robert Zollinger. Their article is illustrated by some very good line drawings.

Other subjects which come under critical review in this volume include the present status of tumour immunology, principles of tendon repair, and intra-abdominal sepsis.

This volume will be read with interest by all surgeons who wish to keep abreast of surgical advances.

A book for every surgeon's library because it is a useful reference volume.

Cancer do Pulmão. By JESSE P. TEISCEIRA, Rio de Janeiro. 8½ × 6 in. Pp. 197 + xiv. Illustrated. 1971. Rio de Janeiro: Editora Guanabara Koogan S.A. No price given.

THIS is a well-written, lucid textbook on carcinoma of the lung based largely on personal experience. The pathological, diagnostic, and therapeutic aspects are fully reviewed and are well illustrated. Although pre- and postoperative care and the techniques of thoracotomy and chest closure are well described, the resective procedures themselves are not discussed. Statistical data are presented based on 467 cases treated over 20 years, largely in one institution; the results conform with world-wide experience. A worth-while textbook for all doctors and particularly young general and thoracic surgeons.

Conduite thérapeutique d'Urgence chez les Polytraumatisés. By A. TRILLAT, Lyon, and A. PATEL, Garches. 9½ × 6¼ in. Pp. 118, with 16 illustrations. 1971. Paris: Masson et Cie, Editeurs. 28F.

THE paper which forms the major part of this book on the treatment of patients with multiple injuries was read at the annual meeting of the French Surgical College. To exclude minor problems the discussion was restricted to cases in which at least two serious injuries with repercussion on respiration or circulation were present. The treatment is discussed in relation to the first critical days and not to the late sequelae. The first part of the book analyses the different regions and tells us which conditions one should know and be aware of. The second part takes an integrated view and describes the types of patients one is likely to come across. The separate sections are very instructively summarized in small but most informative diagrams, and the whole subject-matter pertaining to the treatment is again condensed in one final 'master chart'. A very practical book that should find its way to all small hospitals and to the junior staff of the larger ones.

Cunningham's Textbook of Anatomy. Eleventh Edition. Edited by G. J. Romanes, C.B.E., B.A., Ph.D., M.B., Ch.B., F.R.C.S.Ed., F.R.S.E., Edinburgh. 10¾ × 8½ in. Pp. 996 + xv. Illustrated. 1972. London: Oxford University Press. £9.

Each of the systems in this, the fiftieth birthday or jubilee edition of a favourite, standard work has been revised by an expert anatomist or radiologist, and the length of the text has been kept down to the new, concise compass that so well fits the modified anatomical curricula found in many medical faculties today. Yet room has been found for good new material, especially in the sections on muscle action and on peripheral nerve injury. There is a new index which—so important in a work of this kind—gives the reader more than one chance of finding the fact he needs under headings of differing though equally familiar order. The diagrams and photographs are beautifully clear and the text is easy to read. The references have been brought up to date and include useful items on applied anatomy and radiology. It is a pity that space and other considerations have prevented the inclusion of more applied anatomy; those readers in the course of their surgical training would like to see this amended.

Gastroesophageal Reflux and Hiatal Hernia. Edited by David B. Skinner, M.D., Baltimore; Ronald H. R. Belsey, M.S., F.R.C.S., Bristol; Thomas R. Hendrix, M.D., Baltimore; and George D. Zuidema, M.D., Baltimore. 9 × 6 in. Pp. 208 + x. Illustrated. 1972. Edinburgh: Churchill Livingstone. £6.

This comprehensive review of the subject is a combined operation by members of the staffs of Johns Hopkins Hospital, Baltimore, and Frenchay Hospital, Bristol, in the proportion of 7 : 2, the majority dictating its transatlantic spelling and such inelegant neologisms as 'inapparent'.

After a short historical account the anatomy, physiology, and pathology of the lower oesophageal segment and of gastric reflux are described together with the symptoms of hiatus hernia. Then follows a description of modern investigations, the indications for medical and surgical treatment, the technical details of the surgical treatment, and finally two chapters on the management of recurrent hernia and of oesophageal strictures.

Oddly in so exhaustive a symposium nothing is said about aetiology, and the number of cooks involved leads to some disparity of view. For instance Dr. Hendrix in his chapter on the reflux barrier mechanism has little to say about the effect of the abdominothoracic pressure gradient which Mr. Belsey evidently (and this reviewer agrees) considers most important in preventing reflux; and the influence or very existence of that elusive lower oesophageal sphincter continues to be something of an embarrassment.

No distinction is made between para-oesophageal and 'rolling' hernias, although they are quite different, the former being congenital, the latter merely a radiological variant of an acquired sliding hernia. The diagrams illustrating them on p. 72 are misleading.

Mr. Belsey's account of the transthoracic technique of repair is excellent and is supported by an analysis of his own results. It is immediately followed by Dr. Zuidema's apologia for the abdominal approach, each of his arguments having been effectively demolished by Mr. Belsey. Dr. Zuidema reviews other authors' figures but gives none of his own.

The book is clear and readable and will be found useful by general surgeons and by Fellowship candidates who study it with a discriminating eye.

Coagulation Problems in Transplanted Organs. Edited by K. N. von Kaulla, M.D., Denver. 10 × 7 in. Pp. 190 + viii. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $16.50.

This book is the report of the proceedings of a symposium held in Germany in 1970. It has a number of contributions of high quality on the local coagulation occurring as a complication of rejection in transplanted organs. There are very adequate studies of the deposition of fibrin, fibrinolysis, and the production of fibrin-split products. With the exception of a contribution from Denver on hyper-acute rejection of renal allografts and xenografts there is very little on the nature of the initiating processes of coagulation. It is clear from this volume that studies on the ways in which an antibody combined with its antigen reacts to produce thrombosis and coagulation are needed. The role of platelets in the initiation of fibrin clot is not sufficiently discussed nor is the association between coagulation and complement activation. The conclusion that better anti-rejection drugs might be devised which interfere with coagulation as well as having an anti-complementary action is interesting, but, as in other situations of intravascular coagulation attacking the initiation processes, is more likely to be successful than trying to prevent the end-result of fibrin-stabilized intravascular thrombi. For those involved in the treatment of intravascular thrombosis there is much to stimulate in this book, as the changes in organ grafts provide such elegant experimental models for its study.

Innere Medizin, Parts 1 and 2. Third edition. Edited by Ludwig Heilmeyer, Freiburg, and Hans Adolf Kuhn, Wurzburg. 10½ × 7½ in. Pp. 1283 + xxxix. Illustrated. 1971. Berlin: Springer Verlag. DM.116.

This is the third and totally revised edition of a well-known textbook of general medicine aimed mainly at students. Increasing specialization in medicine has been dealt with by a large number of contributors, but the complete field of neurology has been omitted and paediatrics is excluded apart from infectious diseases. Illustrations are strictly limited but, on the other hand, the price of the two volumes is reasonable. The book is clearly written and contains an excellent subject index. It will certainly become popular with medical students in German-speaking countries.

Les Pièges de la Chirurgie vasculaire. By Jacques Dascotes, Lyon. 10 × 8 in. Pp. 168. Illustrated. 1972. Paris: L'Expansion Scientifique Française. 60F.

The title of this book—'Pitfalls in Vascular Surgery of the Limbs'—is certainly too modest. The authors mainly wished to point out the dangers that lie in wait in this field of surgery and how to avoid or to surmount them. They have, however, given much more; in fact a fairly complete handbook of operative surgery with an impressive amount of surgical pathology and some original alternatives to established methods. The first chapter describes the basic techniques in vascular operations and will provide anyone with a succinct introduction to this branch of surgery. The second chapter, rightly the longest one, discusses chronic obliterations with their topographical variations. The plea for using the extraperitoneal approach in aorto-iliac obliterations has a good case. The next chapter provides a fresh account of aneurysms and arteriovenous fistulae, while the fourth guides us through the dramatic world of the emergency cases. There are many clear line drawings, at which the French excel, and the reproduced roentgenograms are also amazingly informative. One has to admire the ease with which the authors find their way through this complicated field and can convey their acquisitions to others. The statement in the introduction that their experience is based on the treatment of 2600 patients certainly does not come as a surprise.

A Nurse's Guide to Anaesthetics, Resuscitation, and Intensive Care. By WALTER NORRIS, M.D., F.F.A.R.C.S., and DONALD CAMPBELL, M.B., Ch.B., F.F.A.R.C.S., D.A., Glasgow. 8½ × 5½ in. Pp. 181 + ix, with 112 illustrations. 1972. Edinburgh: Churchill Livingstone. £1·50.

THIS is a very interesting, easily understood, and well-written book. The photographs and diagrams are excellent and for the most part are self-explanatory. It is a book that should be purchased by consultants for the staff on their wards, as I am sure that it will be found useful for reference. My only criticism of the book is I feel that it should have a hard cover as reference books are handled so frequently.

Microbes in Action. Second edition. By HARRY W. SEELEY, jun., and PAUL J. VAN DEMARK, Cornell University. 11 × 8½ in. Pp. 361 + xii. Illustrated. 1972. San Francisco: W. H. Freeman and Company Ltd. £2·20.

THIS is a useful laboratory manual for students which aims at giving an appreciation of the basic characteristics of micro-organisms and their significance in disease, pollution, and other important factors affecting human life. The techniques of bacteriology are introduced by means of 90 experiments which include virus culture and serology. This up-to-date manual will be widely used in first-year university courses in microbiology.

Textbook of Surgery. Third edition. Edited by D. A. MACFARLANE B.Sc., M.Ch., F.R.C.S., London, and LEWIS P. THOMAS, B.Sc., M.Ch., F.R.C.S., Newport. 8½ × 5½ in. Pp. 796 + xi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £4.

THE style of this textbook, in size, clarity of print, and layout of its sections, makes it a leader in sources of information for the undergraduate. The first chapters introducing the general principles of injury, repair, and infection supported by a short description of the relevant anatomy and physiology provide the essential base upon which the student can erect a well-understood picture of each clinical problem as it is approached. The text is written with a uniform lucidity from which it is easy to draw information with each subject covered evenly and very adequately. Line drawings embellish the text and tables help the reader to gather information without confusion.

That this textbook has reached its third edition already is sure proof of its value. The editors and contributors are to be congratulated on producing such an excellent book for the undergraduate on which to lay the foundations of surgical knowledge.

Das Ultrakurznarkoticum Methohexital. Edited by PROFESSOR DR. R. FREY, Mainz, DR. F. KERN, St Gallen, and PROFESSOR DR. O. MAYRHOFER, Wien 9 × 6 in. Pp. 188 + x. Illustrated. 1972. Berlin Springer Verlag. DM.28.

THIS paperback reports a symposium which was held in Frankfurt in December, 1970, on the short-acting anaesthetic agent, methohexital. The first five papers are devoted to the pharmacology of this drug and its effect on the body. The majority of the papers review different series of patients in whom this drug was used as an induction agent for various types of surgery. It would appear that Brietal Sodium (methohexital) is a satisfactory and widely used anaesthetic agent. This volume should be of interest to anaesthetists.

Selected Exercises from Microbes in Action. Second edition. By HARRY W. SEELEY, jun., and PAUL J. VAN DEMARK, Cornell University. 11 × 8½ in. Pp. 227 + xii. Illustrated. 1972. San Francisco: W. H. Freeman and Company Ltd. £1·80.

THIS book is a shortened form of the author's manual *Microbes in Action.* It comprises 57 of the 90 exercises that make up the full text and is designed for short courses in introductory microbiology. New exercises for the second edition deal with antimetabolite action, biochemical oxygen demand, precipitin reaction, and other current topics of interest.

Early Diagnosis of Human Genetic Defects. Edited by MAUREEN HARRIS, Ph.D., Bethesda, Maryland. 9 × 6 in. Pp. 229 + ix. Illustrated. 1972. Bethesda: National Institutes of Health. $2.50.

THIS book contains details of a symposium held at the National Institute of Health, Bethesda, Maryland, in 1970. It deals with the problems of detecting metabolic errors and evaluates the techniques of examinations performed on amniotic fluid and considers the problems of screening in relation to large populations. The risks of the techniques and their likely value are well discussed as are the problems of genetic counselling and the ethics involved in the screening programmes.

The book can be recommended strongly to all those with an interest in this field and the cost is very reasonable.

Allgemeine und spezielle Chirurgie. Edited by MARTIN ALGOWER, Basel. 9½ × 6½ in. Pp. 620 + xxii. Illustrated. 1971. Berlin: Springer-Verlag. DM.48.

THE advantage of this surgical textbook, to which several outstanding Swiss surgeons contributed, is that it is entirely up to date.

Recent developments and techniques are recorded, while the inheritance of the past, when only of historical interest, is either briefly mentioned or omitted completely.

The chapters dealing with orthopaedics, urology, and paediatric surgery give a schematic survey, though no essential problems are left out.

The book is to be recommended for students and general practitioners in particular since much advice for surgery in general practice is included.

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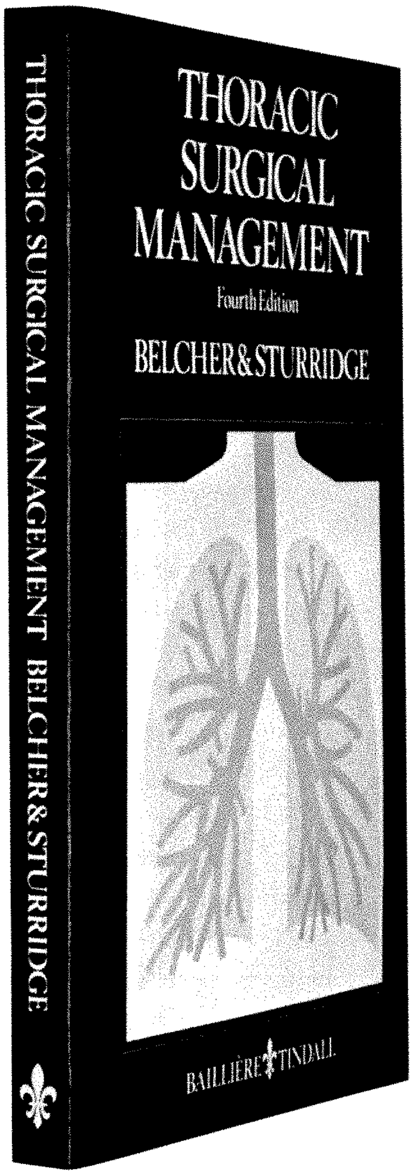
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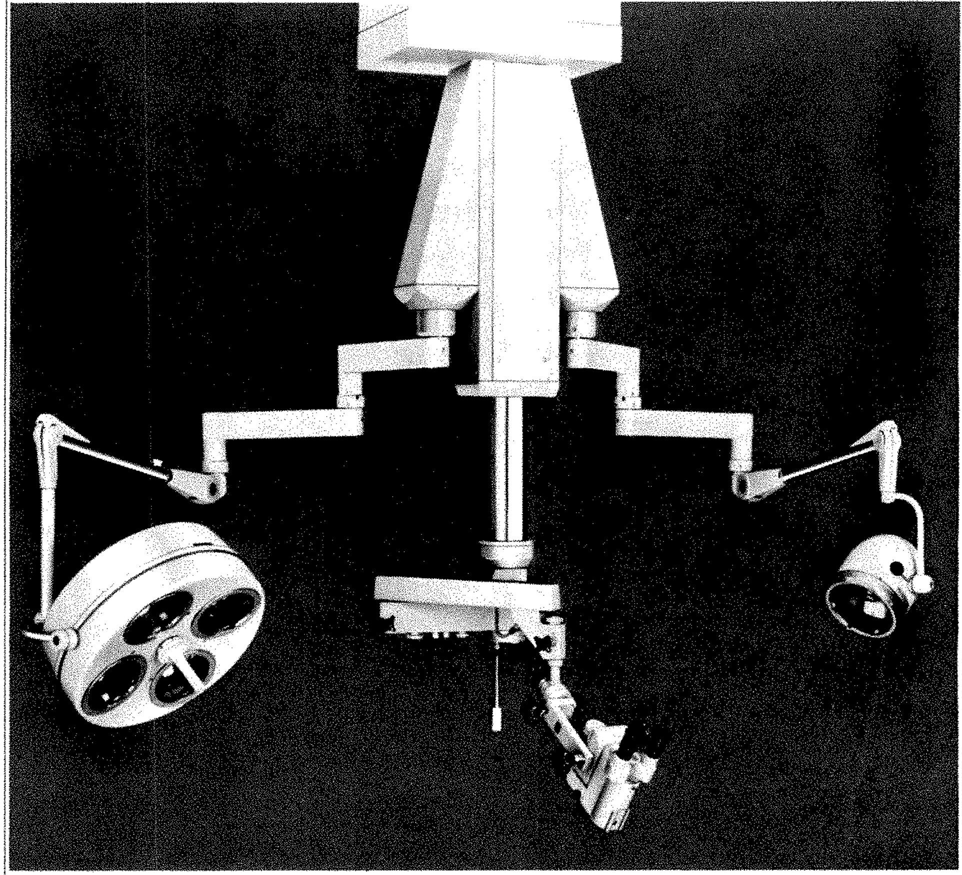

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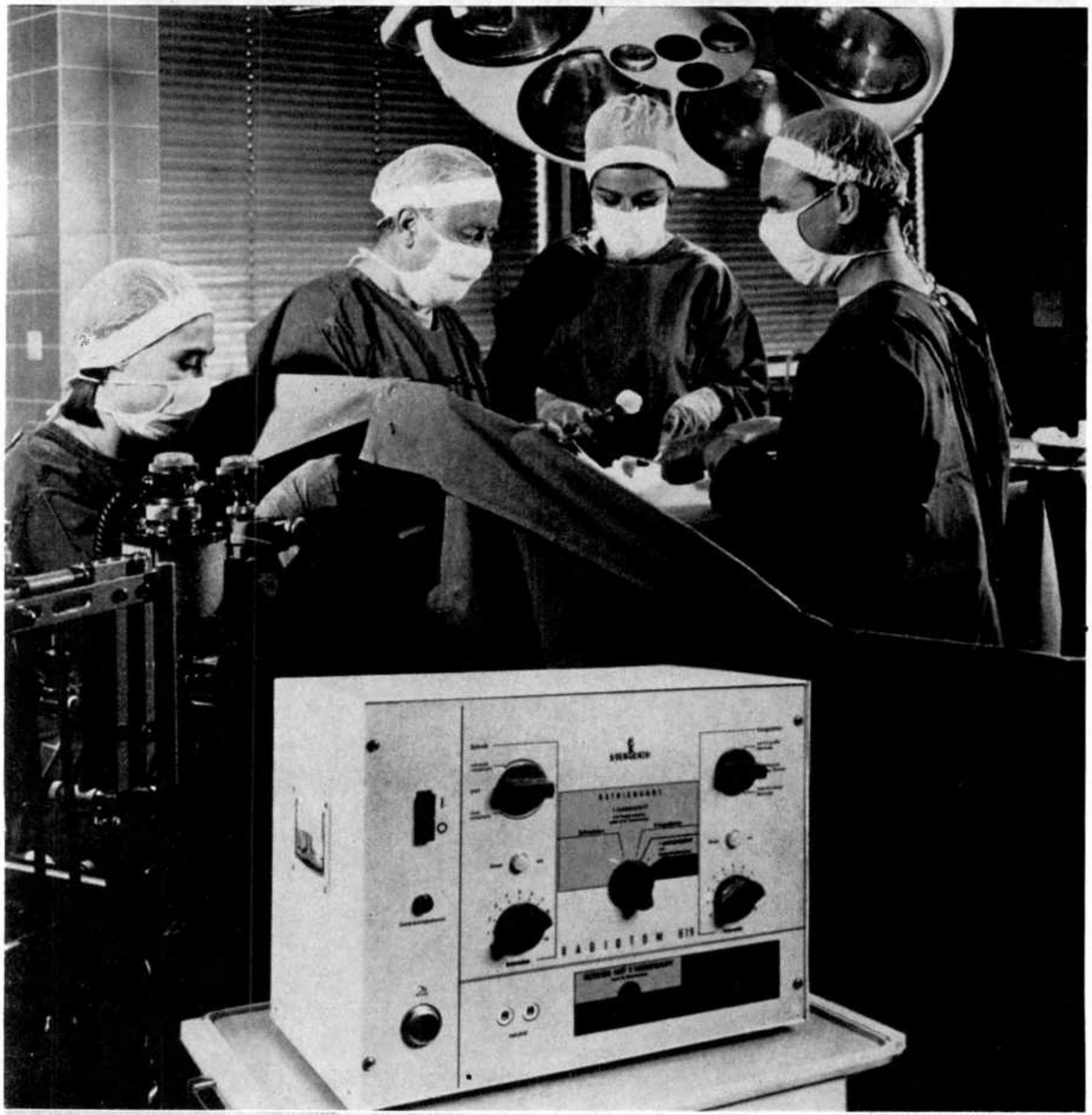

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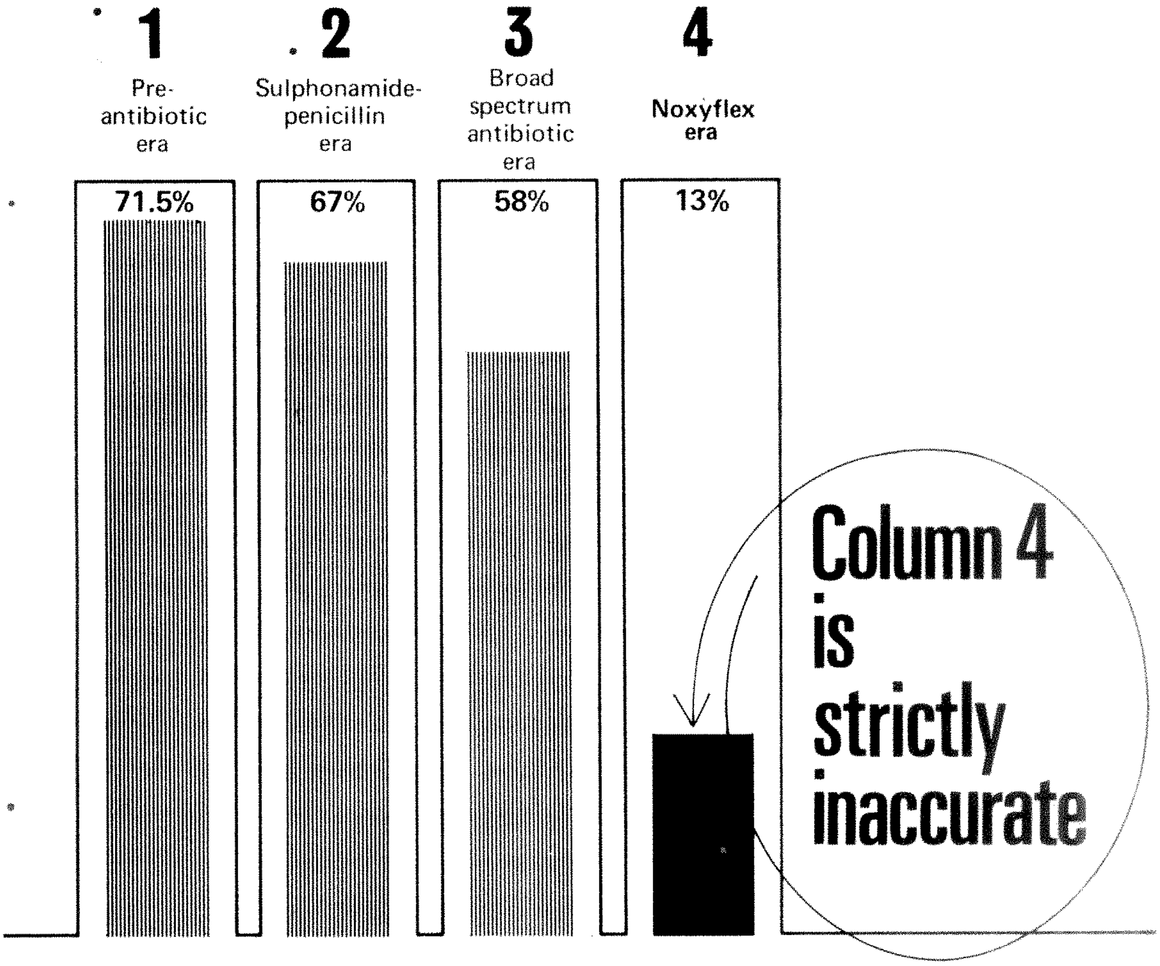

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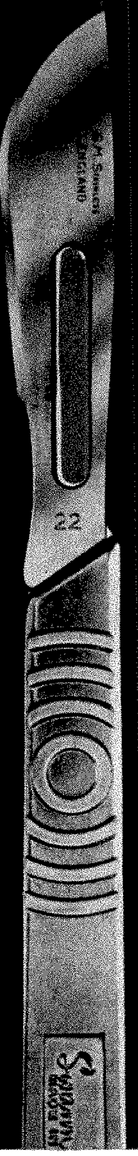

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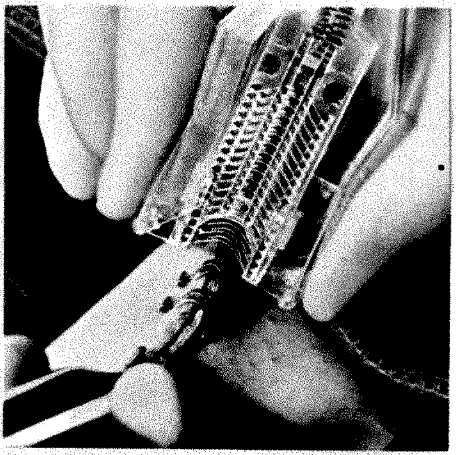

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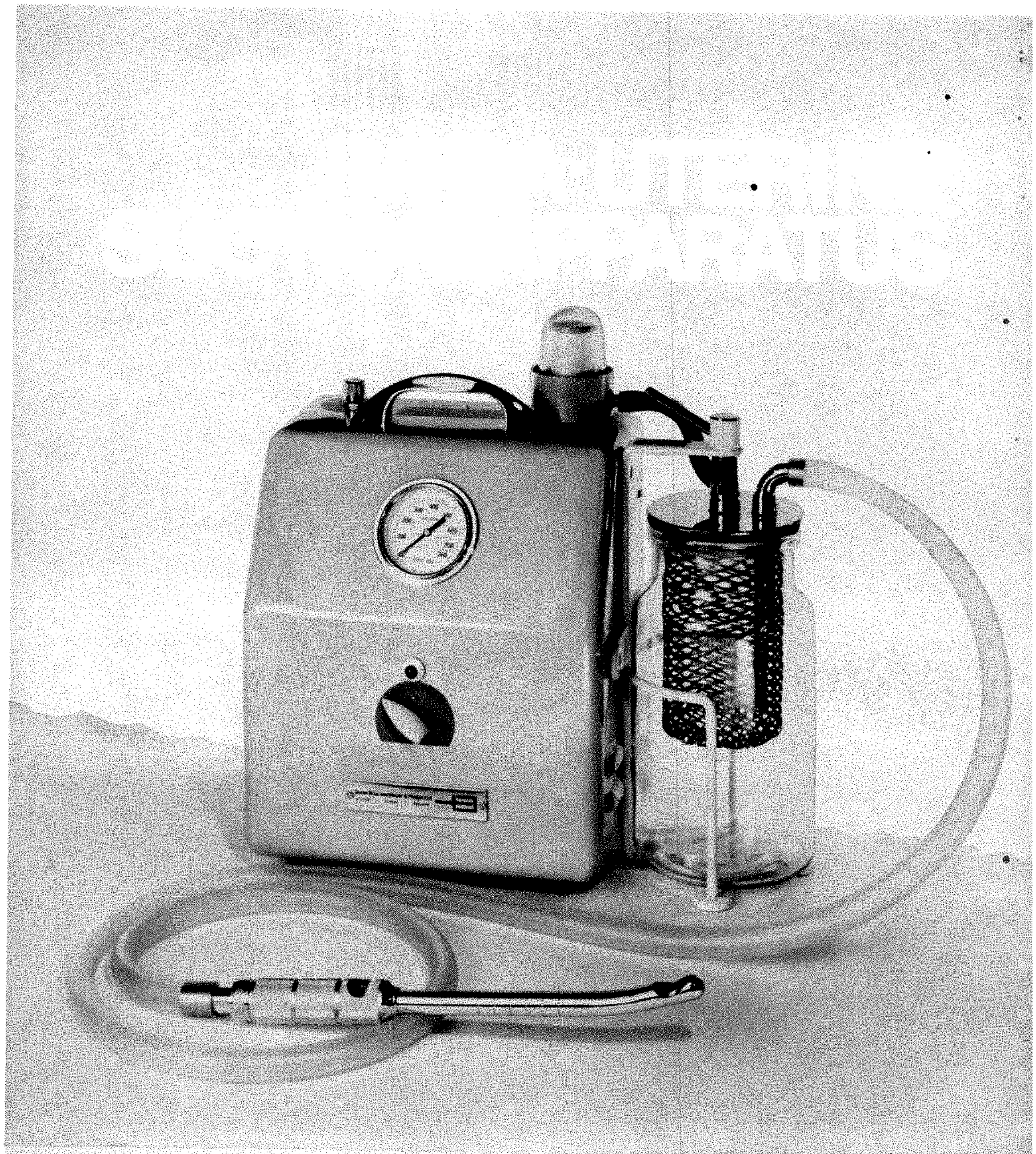

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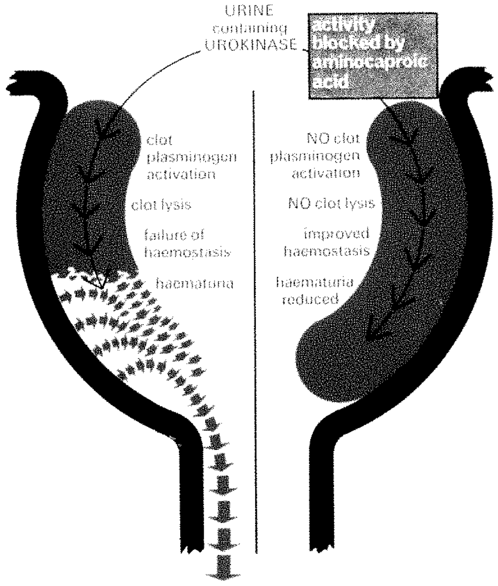

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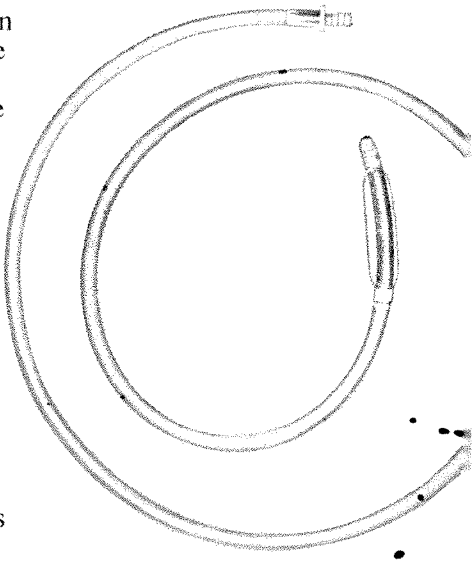

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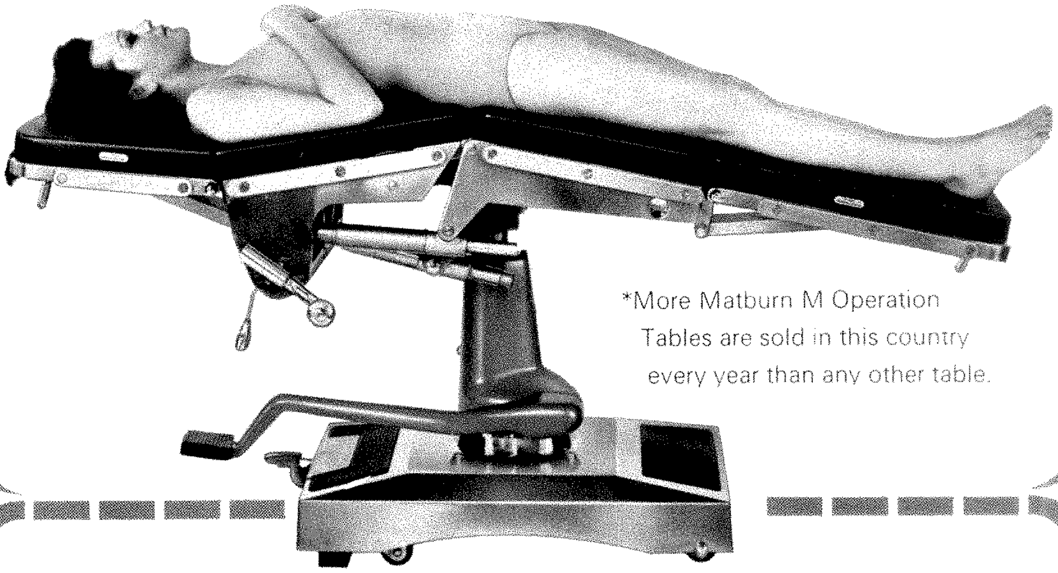

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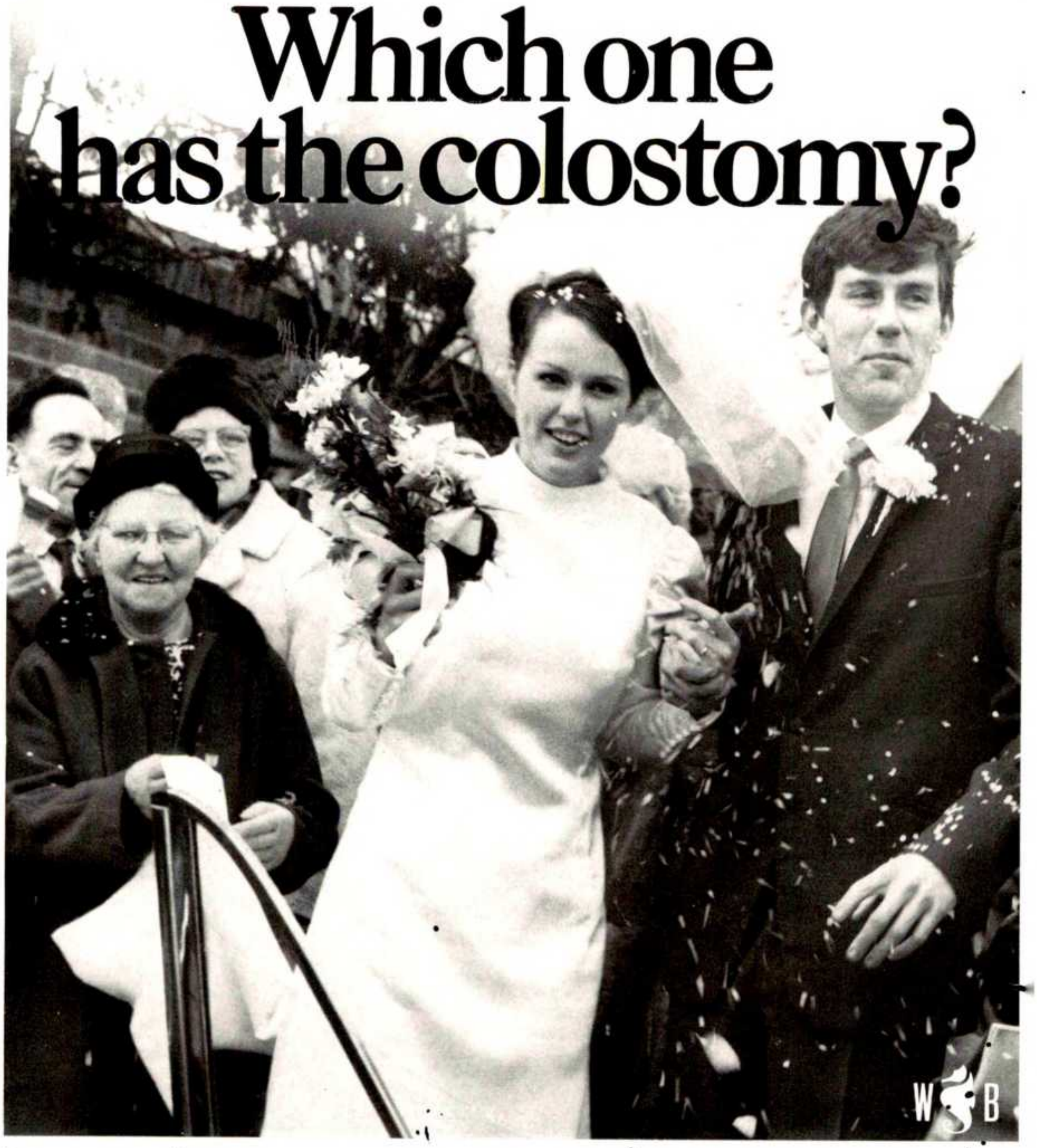
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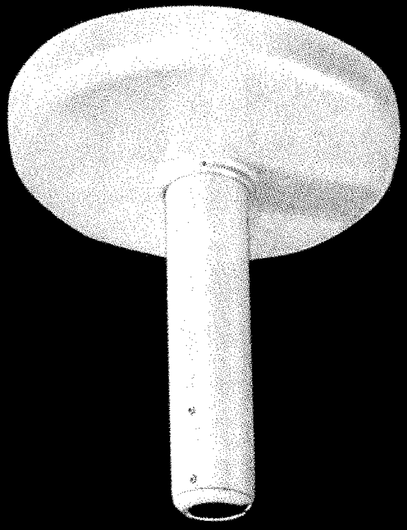

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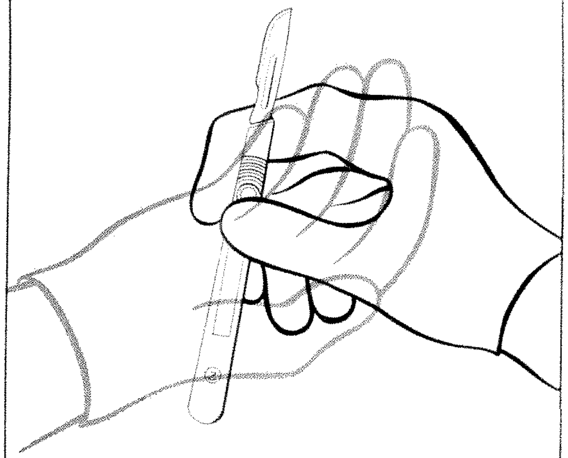

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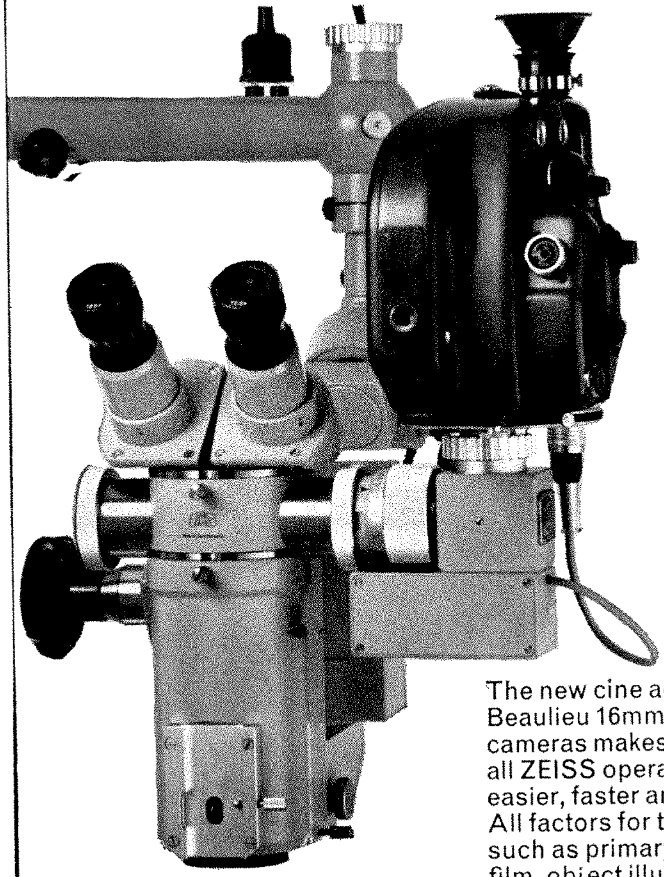

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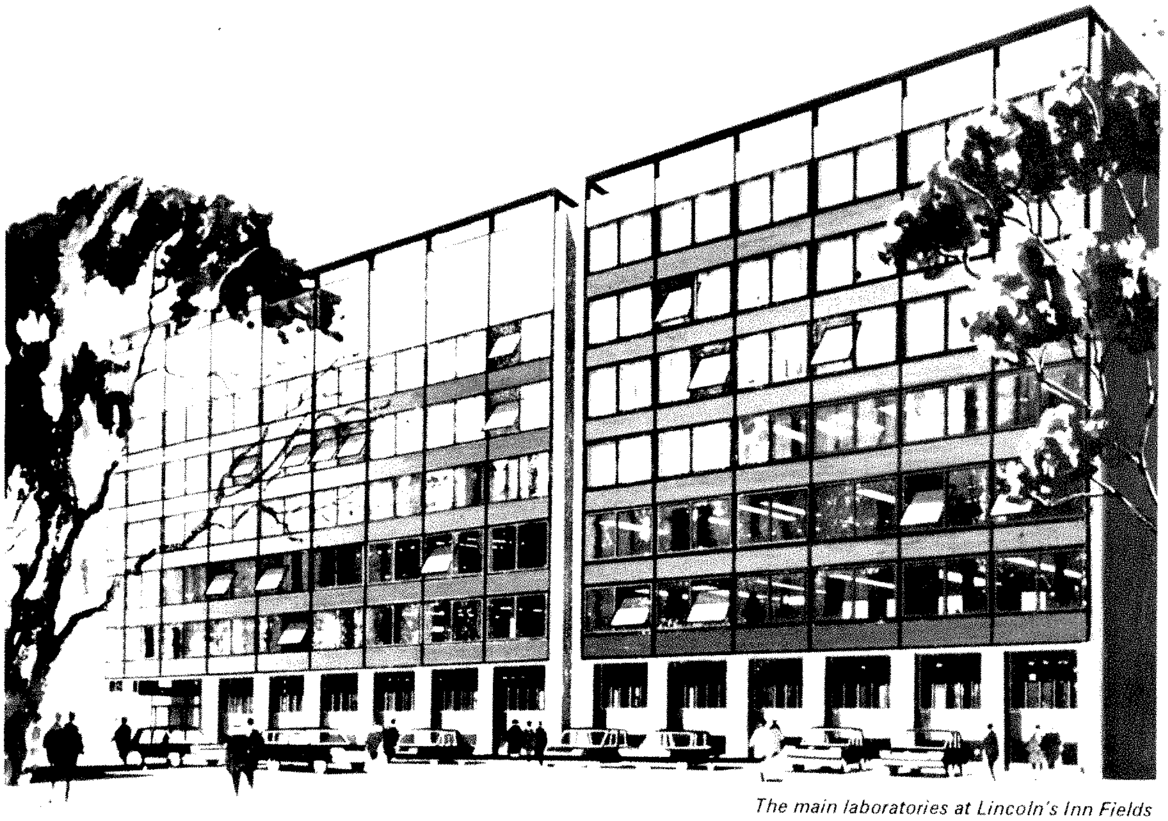

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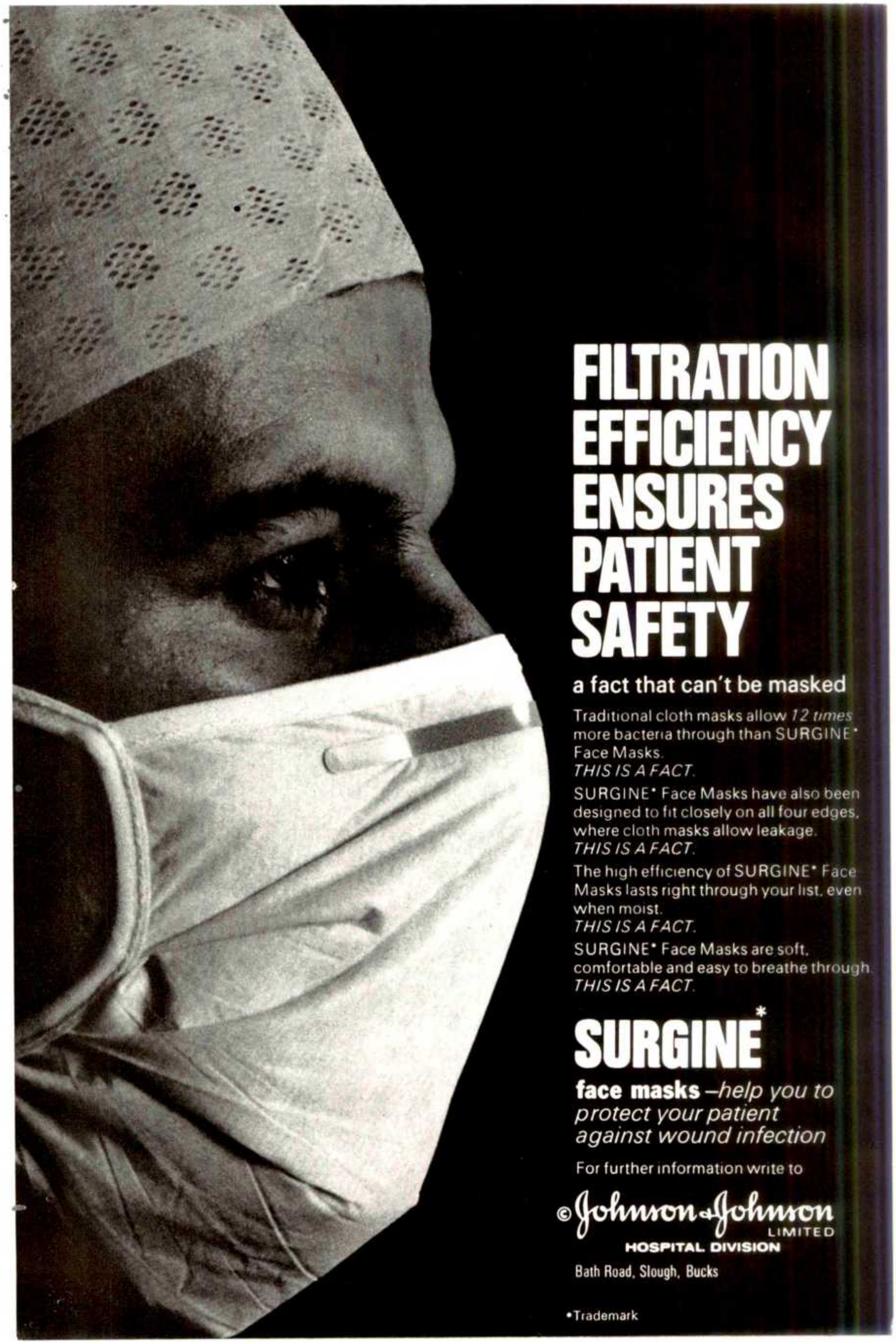

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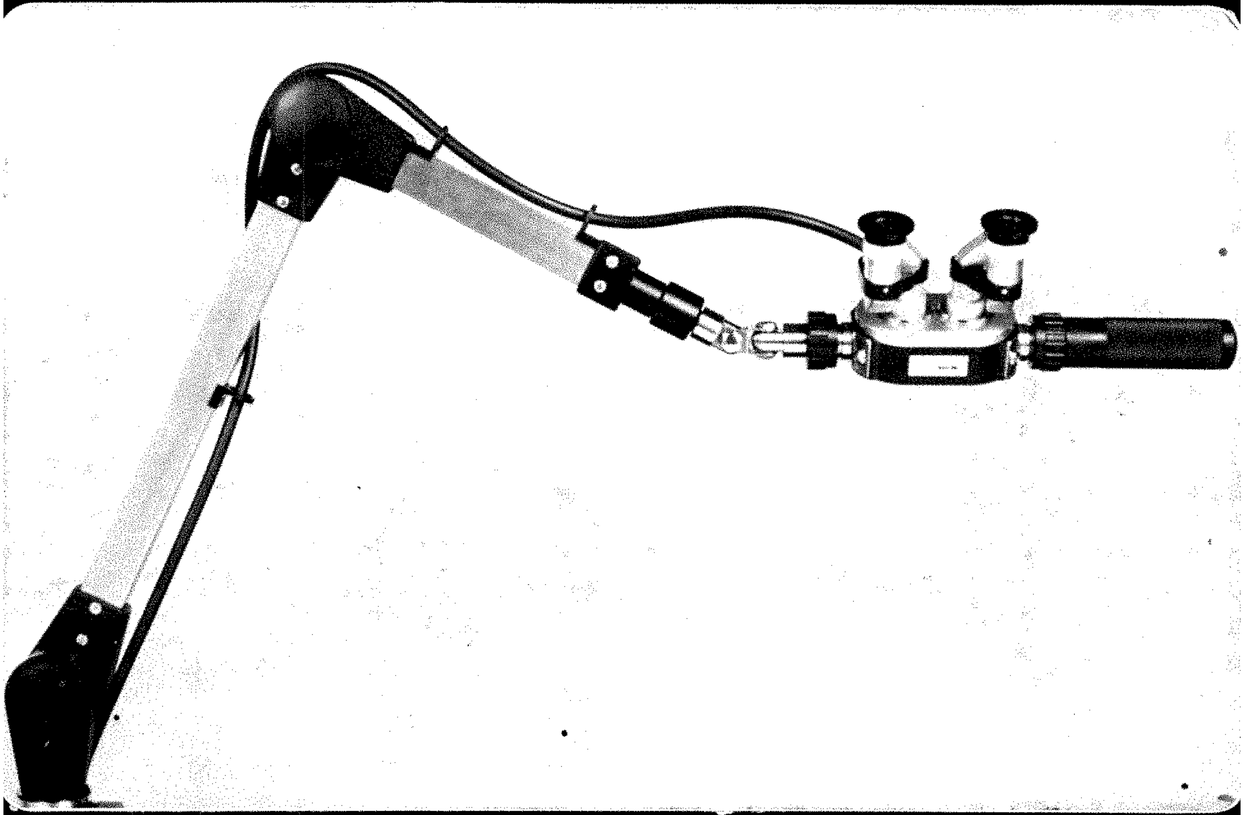

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THE

BRITISH JOURNAL OF SURGERY

Vol. 60 FEBRUARY 1973 No. 2

ORIGINAL PAPERS

CARCINOMA INVOLVING THE LOWER ALVEOLUS

AN APPRAISAL OF PAST RESULTS AND AN ACCOUNT OF CURRENT MANAGEMENT

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SUMMARY

Three hundred and fifty-six cases of carcinoma of the buccal mucosa, lower alveolus, and mouth floor treated under a policy of radiotherapy as the method of first choice are reviewed. Alveolar involvement, whether initial or by extension, greatly reduces the chance of radiotherapeutic success, and is more important in this respect than the exact site of origin of the tumour. A decision to switch to a trial of elective surgery in this group of cases with alveolar involvement was strengthened by major advances in surgical management, especially the evolution of satisfactory techniques of repair. A cardinal point is that tumour excision and closure of the mouth defect can now be accomplished reliably in one stage. The uses of the 'island' forehead flap and of Bakamjian's deltopectoral flap are discussed, as well as the methods of providing mandibular support when necessary. The authors' current techniques are described in detail on the basis of 82 consecutive radical procedures. A preliminary survey of the results suggests that surgery in this group may yield better results than radiotherapy.

In this paper based on the experience at Westminster Hospital the authors have endeavoured to set out a critical review of the treatment of mouth cancer, to focus attention on the mandible as an obstacle to successful radiotherapy, and to give an account of the current surgical procedures which now furnish an acceptable alternative.

THE HISTORICAL PERSPECTIVE

The history of the evolution of radical surgery for mouth cancer makes grim reading. Henry Butlin (1885, 1900), of St. Bartholomew's Hospital, traced it from the seventeenth century, noting such advances as the preliminary ligation of arteries, splitting of the cheek or division of the mandible to improve access, and the approach from the neck. In 1844 Sédillot had described midline splitting of the lip and mandible, and in 1858 Syme had used the method on two occasions, but both patients had died. A year later Fiddes (1859) reported a success, and Syme himself gave a dramatic account of a successful case in 1865. Kocher in 1880 recognized the implication of a metastatic node while removing a tumour of the tongue, and proceeded to excise the affected nodes through a Y-shaped neck incision. It was Kocher, too, who advocated tracheostomy for these operations. The first recorded in-continuity removal of a tumour of the central mandibular arch, mouth floor, and tongue was performed by Heath in 1875 (published in 1899). Gardham (1953) has described this successful case in some detail.

In a series of communications between 1894 and 1909 Butlin recorded his successes and failures in a series of over 200 excisions. In 5 patients with involvement of the mandible he established a technique for resecting the mouth floor, mandible, and nodes in continuity. Sound though the principles were, however, all 5 patients developed infection of the deep fascial planes of the neck, leading to fatal mediastinitis. Despite such setbacks surgeons continued to increase the scope of their operations. In 1906 Crile published a series of 132 radical neck dissections. Trotter (1913) stressed that a wide margin of macroscopically normal tissue around the growth was essential if surgical cure was to be hoped for. Modern concepts of *en bloc* resection of tumour, mandible, and nodes were evolved by Martin (1941, 1948), Sugarbaker and Gilford (1946), Conley and Pack (1949), Edgerton (1951), Ward and Robben (1951), Slaughter and Southwick (1952), and many others.

By this time, however, the ambitious scope of the excisions had outstripped the possibilities of repair.

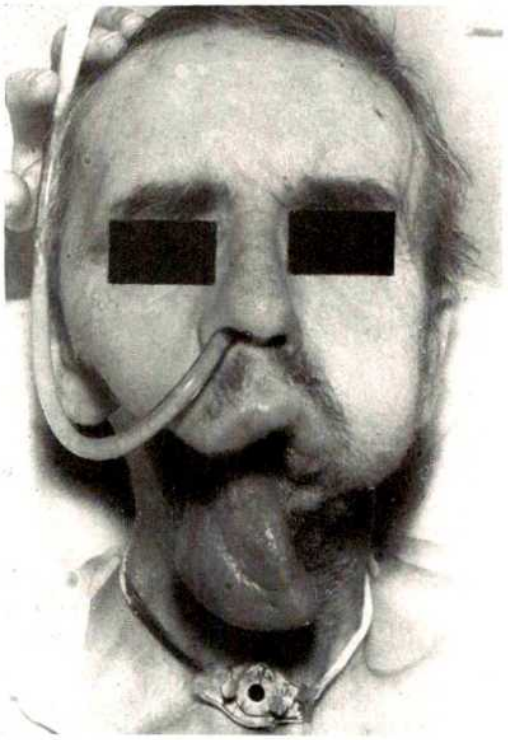


FIG. 1.—Failure of repair after excision of a carcinoma.

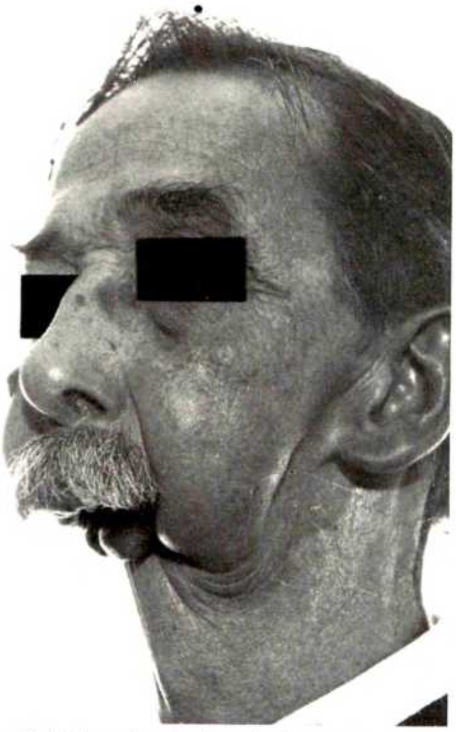


FIG. 2.—Unsightly end-result due to inadequate techniques of repair.

If the mortality was reduced by better anaesthesia and supportive methods, the morbidity and disablement were depressing. A main difficulty was the long interval which inevitably elapsed between the resection and the successful closure of the defect. During this time the often elderly and debilitated patients had to sustain all the miseries of a large oral fistula which were demoralizing to the patient, the nurses, and the rest of the ward (*Fig.* 1). All too frequently, eventual closure was obtained only at the cost of a tethered tongue and distorted facial soft tissues, leaving the patient after his long ordeal with a hideous and permanent deformity (*Fig.* 2).

Against this gloomy background, the possibilities of radium and radiotherapy had meanwhile gained increasing recognition as a welcome alternative. By the 1920's interstitial radium implantation was becoming standardized (Régaud, 1920, 1925; Lacassagne, 1921), giving good curative and palliative results with far less distress and mutilation to the patient. External irradiation (teletherapy), too, though at first crude and unsatisfactory, made phenomenal strides to become the sophisticated weapon that it is today, capable of excellent results and particularly useful in cases where radium implantation is impossible. At the Westminster Hospital radiotherapy was championed by Cade (1929), himself a surgeon, and for nearly 50 years it has been the agreed method of choice in treating primary mouth cancer. For the nodes, surgery has always been preferred.

Statistically satisfying comparison of the results of radiotherapy with those of surgery has always been difficult. Various large-scale reports have been published (Ledlie and Harmer, 1950; Ward, Edgerton, Chambers, and McKee, 1959; Ash, 1962; Frazell and Lucas, 1962), but the sources of the material and the degree of selection of the cases are often obscure and there is sometimes obvious disparity between surgical and radiotherapeutic series. Alford and Klopp (1958), writing of their surgical experience, admit: 'The present series included those patients in whom it was deemed possible to remove all visible and palpable cancer. Most of the lesions in these patients would have been classified as relatively early cancer . . .', yet later they claim: 'The results compare favourably with those obtained with radiation therapy.' The experience at the Memorial Center, New York, has been reviewed in an important series of papers (O'Brien and Catlin, 1965; Cady and Catlin, 1969; Harrold, 1971), but the comparisons are between modern radical surgery and obsolete radiotherapy. Binnie, Cawson, Hill, and Soaper (1972) have reviewed the *collected* nation-wide material from England and Wales made available by the National Cancer Registration Scheme begun in 1962, and they believe that the cases registered now include perhaps 90 per cent of the whole mouth cancer incidence. The figures demonstrate an apparent superiority of surgical over radiotherapeutic results, but the authors point out the invalidity of the comparison since the worst lesions and the poorest-risk patients were usually treated by radiotherapy.

We have always felt that the Westminster Hospital mouth cancer results in general (Cade, 1940) have compared favourably with those of radical surgery. In a study of 653 consecutive cases of tongue carcinoma (Cade and Lee, 1957) the over-all 5-year absolute cure rate for tumours of the anterior two-thirds of the tongue was found to be 35 per cent, and for lesions 2 cm. or less in diameter, 60 per cent. It must be stressed that the series included every case seen at a hospital which offers both irradiation and surgical treatment. Moreover, these results were obtained by the relatively minor procedures of radium implantation or teletherapy and minor diathermy, with neck dissection where necessary. The function of the healed tongue was in general far better than is usual after extensive glossectomy.

Table I.—Sex Distribution and Number of Cases treated from 1949 to 1965

Site of Lesion	No. of Males	No. of Females	Total No. of Cases
Buccal mucosa	74	47	121
Lower alveolus	63	30	93
Mouth floor	110	25	135
Total	247	102	349*

* There were also 2 patients with diffuse unclassifiable lesions, and 5 patients with multiple lesions not in same site.

Table II.—Age Distribution and Sex Ratios

Site of Lesion	Average Age (years)	Male Patients (per cent)
Buccal mucosa	64·5	61
Lower alveolus	65	68
Mouth floor	66	81

We have been increasingly aware, however, that radiotherapy has not been equally successful for all parts of the oral cavity and that failure is often seen in lesions close to bone. This feature tends to be concealed by the customary site classification so that for the present review we have grouped these three sites together as one continuous mucosal surface. In this way the effect of alveolar involvement on the results of treatment can be studied.

The appraisal has been made timely by the development of newer surgical techniques which are proving very successful in overcoming the former problems of resection and reconstruction, as described later in this paper.

I. REVIEW OF RESULTS 1950–65

Material.—From 1950 to 1965, 356 patients with carcinoma of the buccal mucosa, lower alveolus, and mouth floor were treated at the Westminster Hospital, London, and the Regional Radiotherapy Centre, Guildford, Surrey. Fifty of these cases had already received some treatment elsewhere and came with either persistent disease or major or minor recurrence of some kind. For the purpose of this review there seemed no point in separating these patients from the new cases. Nineteen patients had multiple lesions, and a total of 371 lesions was treated, including 13 adenocarcinomas. In *Tables I* and *II* the cases are analysed as to sex and age and location of the tumour. It should be noted that 133 patients (37 per cent) were between 70 and 79 years old, 38 (11 per cent) were between 80 and 89, and 6 patients were over 90 years old. Accurate T.N.M. staging (U.I.C.C. Geneva, 1968) has proved difficult in retrospect and the nearest approximation has been to divide the primary tumours into three groups according to whether the maximum diameter of the tumour was up to 2 cm., 2–5 cm., or more than 5 cm. (*Table III*). The tables comprise all the cases which were seen, including advanced lesions suitable for palliation only. Clinical node involvement as is shown in *Table IV* and those patients with no involved nodes at presentation have been subdivided into those who did and those who did not later develop malignant nodes. The clinical assessment of lymph-node involvement is notoriously inaccurate, and in the case of the mouth floor specially so because of the frequent enlargement and induration of the salivary gland owing to blockage of the duct.

Table III.—Staging of the Primary Lesion

Site of Lesion	Size of Lesion		
	2 cm. and less	2–5 cm.	5 cm. and more
Buccal mucosa	19	66	15
Lower alveolus	30	57	13
Mouth floor	25	68	7

All figures are percentages.

Table IV.—Degree of Lymph-node Involvement

Site of Lesion	No Involved Nodes at Presentation		Nodes Clinically Malignant at Presentation
	None at Any Time	Developed Later	
Buccal mucosa	42	28	30
Lower alveolus	40	14	46
Mouth floor	27*	26*	47*

* Salivary-gland enlargement due to duct involvement makes figures unreliable.

All figures are percentages.

Treatment.—The policy has remained remarkably constant for over 30 years.

Primary Tumour.—First preference, as already stated, was for interstitial radium therapy when possible, to a dose which was seldom less than 6000 rad and sometimes as high as 8000 or 9000 rad in about 7 days in small lesions (*Fig.* 3). If implantation was not possible teletherapy with cobalt or megavoltage X-rays was used, generally with multiple fields or a rotating source. In this way it was usually possible to achieve tumour doses of 6000 rad in 6 weeks without serious damage to the rest of the mouth.

The proximity of the mandible has always posed a problem because the bone, especially if it is exposed by ulceration or involved in the disease, is very vulnerable, and some risk of necrosis has to be accepted. When sequestration follows the insertion of radium needles very close to the bone, the resultant sequestrum is usually superficial and flake-like, separates cleanly if given time, and often heals soundly (*Fig.* 4), but in some advanced lesions with gross bone involvement treated by teletherapy more extensive necrosis is inevitable (*Fig.* 5). In suitable cases this has been dealt with by subsequent surgical ablation (*Fig.* 6); in a few others good palliation has been obtained by per-oral extraction of the dead bone with nibbling forceps.

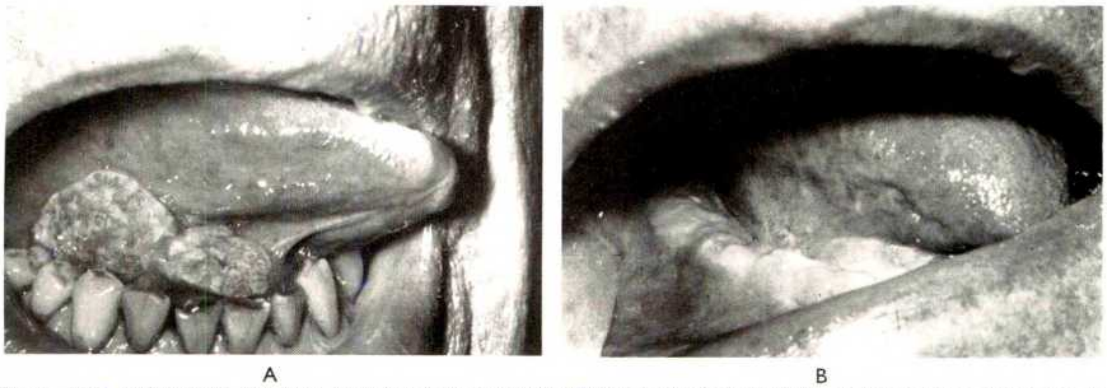


FIG. 3.—Male, aged 62 years. Squamous carcinoma of the mouth floor (A) before and (B) 8 years after a radium implant. Patient remains well after 10 years.

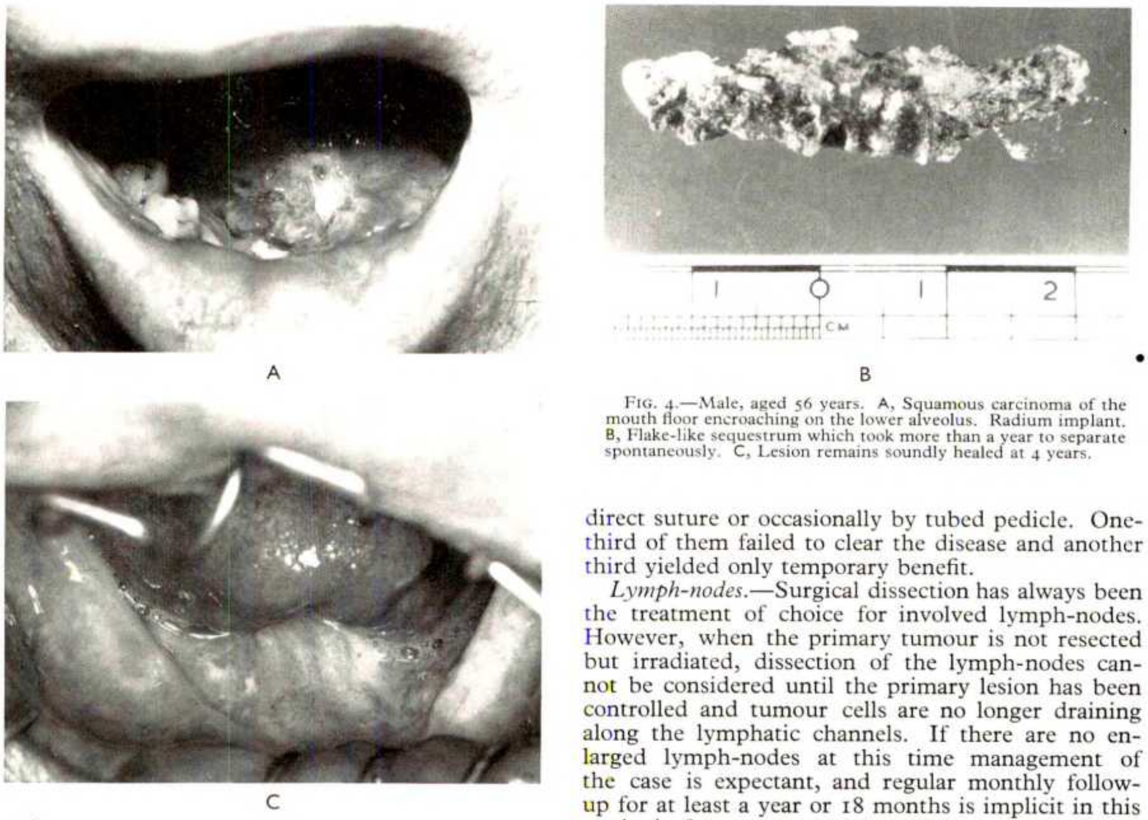
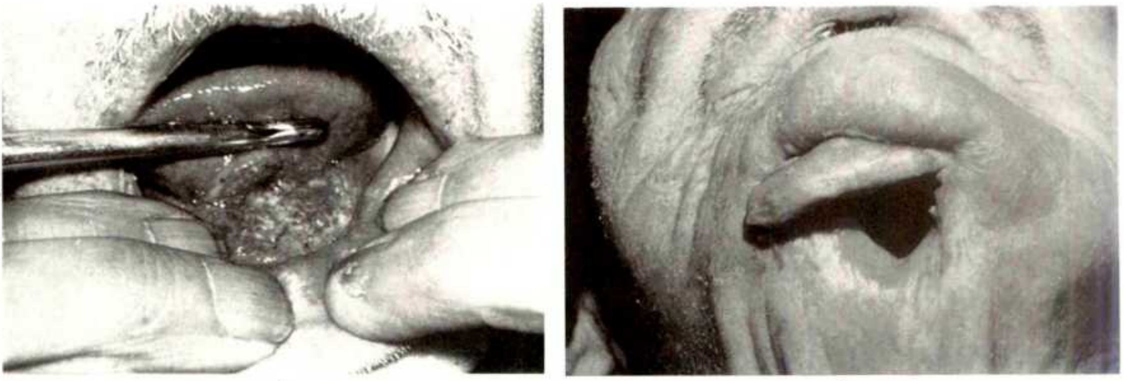


FIG. 4.—Male, aged 56 years. A, Squamous carcinoma of the mouth floor encroaching on the lower alveolus. Radium implant. B, Flake-like sequestrum which took more than a year to separate spontaneously. C, Lesion remains soundly healed at 4 years.

During the period under review only 68 resections of mandible were carried out and, of these, only 4 were elective. The rest were for persistent or recurrent tumour after teletherapy or radium implantation, sometimes with bony necrosis. Most were in the nature of palliative procedures, closure being by direct suture or occasionally by tubed pedicle. One-third of them failed to clear the disease and another third yielded only temporary benefit.

Lymph-nodes.—Surgical dissection has always been the treatment of choice for involved lymph-nodes. However, when the primary tumour is not resected but irradiated, dissection of the lymph-nodes cannot be considered until the primary lesion has been controlled and tumour cells are no longer draining along the lymphatic channels. If there are no enlarged lymph-nodes at this time management of the case is expectant, and regular monthly follow-up for at least a year or 18 months is implicit in this method of management. Any patient who for some reason cannot attend for follow-up provides one of the exceptional indications for elective block dissection. In cases presenting with the lymph-nodes already involved the nodes may be given holding teletherapy as soon as the radium needles have been removed from the primary site, and block dissection then follows as soon as the primary tumour is healed. When massive and perhaps inoperable nodes are



A B

FIG. 5.—Male, aged 74 years. A, Large midline carcinoma of the mouth floor and alveolus. This was treated by cobalt teletherapy and radium implant. B, The tumour was destroyed, but sequestration of the entire midarch of the mandible occurred. The fistula eventually closed with minimal surgery, and the patient died 4 years later without local recurrence or involved nodes.

Table V.—FIVE-YEAR SURVIVAL RATE RELATED TO THE SITE OF THE LESION

SITE OF LESION	5-YEAR SURVIVAL RATE (per cent)		
	Male	Female	Total
Buccal mucosa	47	42	45
Lower alveolus	30	40	33
Mouth floor	26	36	27

Table VI.—FIVE-YEAR SURVIVAL RATE RELATED TO ALVEOLAR INVOLVEMENT

ALVEOLAR INVOLVEMENT	NO. OF CASES	SURVIVORS	
		No.	Percentage
Alveolar mucosa free	114	55	48
Alveolar mucosa involved	230	67	29

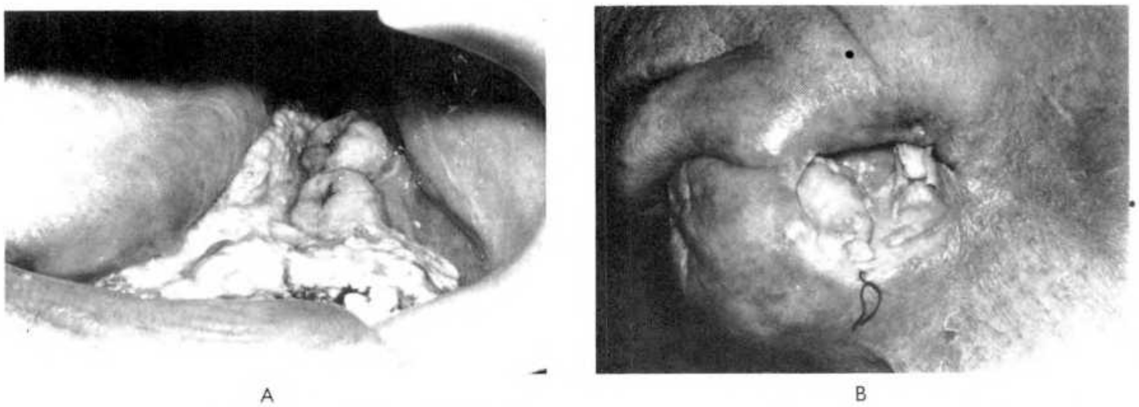
present from the start, treatment is usually by teletherapy to both the primary tumour and the nodes, and the tendency in these cases with a poor prognosis is to concentrate a high dosage on the involved nodes, giving less regard to the rest of the neck. Occasionally, inoperable node masses have been implanted with radium. Operable nodes are always dissected for choice, and if histology confirms the presence of metastases radiotherapy to the neck is usually given postoperatively.

Neck dissection was carried out in 58 of our 356 cases, but in the earlier years of the review many of these were partial (suprahyoid dissections). The effect of this conservative policy towards the lymph-nodes upon the 5-year cure rate is considered below.

Results and Discussion.—The results of therapy in this series of cases are analysed in *Tables V* and *VI*. Despite its limitations the 5-year survival rate has been taken as the index of success and all patients dying within this period are assumed to have died from the disease. In view of the high average age of the patients this assumption does, of course, give a pessimistic picture of the results of therapy. Nevertheless, we feel that it affords a more direct means of comparison than do other devices which seek to make actuarial allowance for the short life expectancy of patients of this seniority. The overall 5-year survival figure for the group works out at 34 per cent. In *Table V* the results are given according to the location of the tumour.

It is impossible to tabulate a satisfactory comparison between the results of interstitial therapy and those of teletherapy. The cases with the best prognosis were on the whole selected for implantation, and teletherapy was very much a second choice, used mostly for advanced or inaccessible lesions and for poor-risk patients. Radium implantation and radical surgery can, in fact, be applied to much the same range of cases; where one modality is possible, so in general is the other. If the gum is involved, however, the generalization obviously breaks down, for such tumours cannot be implanted. Thus, radium implantation was used in 65 per cent of tumours involving only the soft tissues, whereas of lesions spreading to the alveolus, only 20 per cent could be so treated and these were obviously cases where the encroachment was relatively slight. Clearly, by reducing the available treatment alternatives the proximity of the mandible could affect the prognosis, and *Table VI* divides the whole material into two groups: those where the tumour did and those where it did not encroach upon the gum. The difference in the cure rate is striking—a reduction from about 50 per cent in patients with no involvement of the alveolus to less than 30 per cent in patients in whom the alveolus was affected. It is true that there is a certain bias, for the second group contains fewer small lesions. Breakdown into stages makes some of the groups very small, but the diminished cure rate when alveolar involvement occurred seems to be present at all stages.

Lymph-nodes.—In an attempt to assess the importance of the lymph-nodes to success or failure we have reviewed the fatal cases, subdividing them according to whether the patient died with the primary tumour active, with a healed primary but active lymph-nodes, or with both the tumour and the nodes active. Only 21 patients, or about 6 per cent of the whole material, fell into the second group and it therefore appears that if the primary disease is controlled the nodes can usually be successfully dealt with also. Of the 21 patients, 7 had inoperable nodes when first seen, 2 were unsuitable for block dissection (extreme age in 1, simultaneous reticulum-cell sarcoma in the other), 4 had inadequate surgery (resection without block or suprahyoid block dissection), and in 7 there was failure of follow-up. At best, therefore, 11 patients *might* have been saved by elective block dissection, no more than 5 per cent of the patients dying of the disease or 3 per cent of the whole material. This must be set against the morbidity and possible mortality associated with a policy of routine elective block dissection applied to all the remaining cases (Martin, 1951, Jesse, Barkley, Lindberg, and Fletcher, 1970).



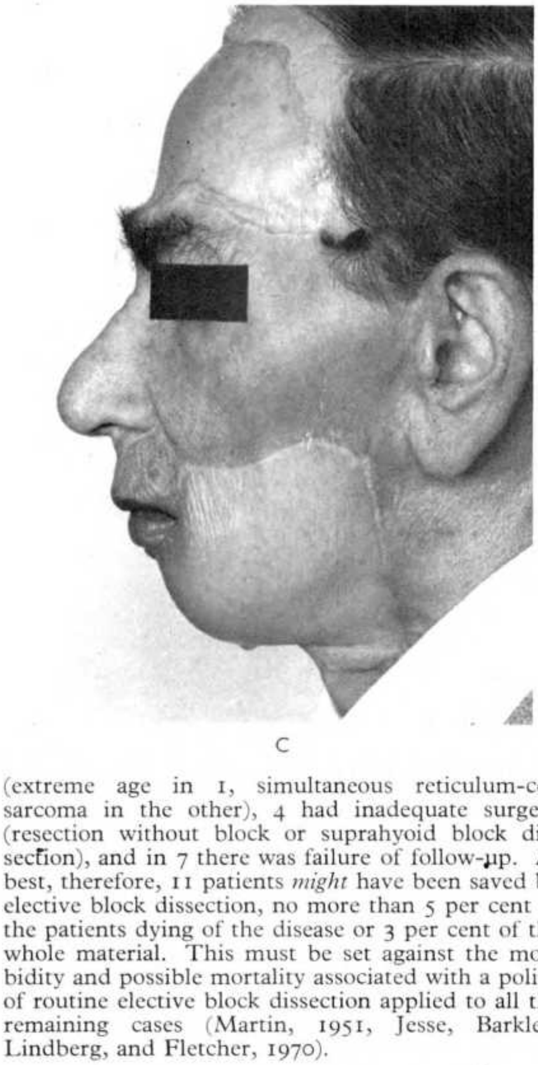


FIG. 6.—Male, aged 65 years. A, Very extensive carcinoma of the mouth floor, alveolus, and buccal mucosa, with submandibular infiltration. The lesion healed completely after treatment with high-energy electrons, but at 3 years the patient developed a large fistula exposing a necrotic mandible (B), necessitating hemiresection of the mandible with the whole thickness of the cheek and mouth floor. The histology was entirely negative for tumour. Repair with forehead and deltopectoral flaps was carried out. The patient remains well (C) at 5 years after therapy.

A purely statistical survey of the material is of limited value when discussing the place of block-dissection. Closer individual study of the cases suggested that certain groups can be distinguished. We have already alluded to patients unable to attend for follow-up. For patients presenting with manageable primaries but considerable node involvement there is much to be said for immediate radical monobloc surgery as the treatment of choice. Patients who present with a moderately large or a very anaplastic primary lesion well away from the midline and who respond well to irradiation should perhaps be given the benefit of an elective block dissection even if no nodes are palpable.

Conclusion.—Our main conclusion and the chief reason for Part II of this paper is that *for tumours involving the lower alveolus* radiotherapy is less effective than for other mouth sites, and the results may well be inferior to those of radical surgery. During the past 5 years we have made a gradual transition to surgical management of this particular group, and the techniques employed are set out in Part II. A provisional assessment will be made, but it is of course too early to know whether our hopes of improved results will be fulfilled.

II. PRINCIPLES AND EVOLUTION OF SURGICAL MANAGEMENT

Most patients with mouth cancer are elderly and many are enfeebled. The overriding need to achieve resection and reliable closure in one stage has already been stressed. In the following section we outline the search for techniques which can accomplish this aim without loss of their radical nature.

Requirements of Curative Resection.—

Primary Tumour.—The importance of wide soft-tissue clearance of the growth was stressed by Trotter (1913), and Gardham (1953) emphasized that this wide clearance must be in depth as well as surface extent. Lederman (1964) pointed out that growths of the posterior part of the mouth floor may penetrate direct to the submandibular triangle behind the free edge of the mylohyoid diaphragm (*Fig.* 7).

If the alveolus is involved two new routes of spread are opened up. Spread along the fascial planes of the periosteum has long been recognized (Polya and Navrath, 1903). Moreover, in the elderly edentulous patient the alveolar bone is absorbed and the inferior dental canal is no longer sited deeply in the mandibular body but comes to lie directly beneath the alveolar mucosa (*Fig.* 8). Consequently the perineural lymphatics of the inferior dental nerve readily become involved by the tumour. Southam (1970) recently confirmed these findings in 4 out of 15 cases where the nerve was submitted to histological examination. Thus when the alveolus is involved by growth extensive resection of the mandible becomes mandatory and excision must include at least the whole length of the inferior dental canal (*Fig.* 9).

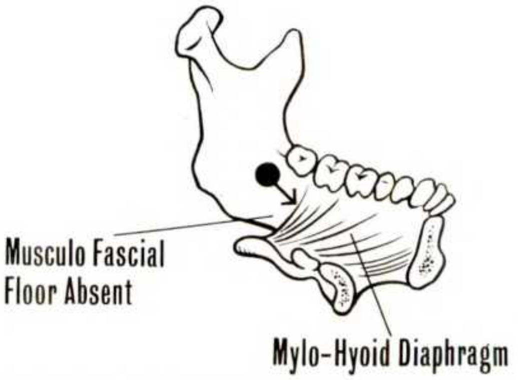


FIG. 7.—Direct spread of tumour involving the palatoglossal sulcus.

Nodes.—Since the radical procedures to be described necessarily enter the neck it is usually desirable to include neck dissection in the operation. The cervical nodes must be excised in continuity with the specimen to avoid rupturing the fascial planes and lymph-channels and so spilling tumour cells. It is therefore essential that the neck dissection, which is usually done at the start of the operation, should enter the correct muscle plane in the submental and submandibular regions, as will later be described.

In general surgeons have become disenchanted with the suprahyoid and other partial neck dissections, both as methods of exposure and as curative procedures. Complete block dissection of the affected side, including the whole submental triangle, has become the accepted operation. Although some surgeons have not hesitated to perform simultaneous bilateral block dissections (Frazell and Moore, 1961; Spiro and Frazell, 1968), there is no strong case for prophylactic dissection on the contralateral side unless both sides of the neck have to be opened up for the resection of the primary lesion. If enlarged nodes are present bilaterally an acceptable modification is to preserve the internal jugular vein on the less affected side (*Fig.* 10). In other cases it may be possible to delay the contralateral dissection for 3 weeks and thus avoid the undoubted risks of a simultaneous double dissection, for staged bilateral dissection with removal of both jugular veins (*Fig.* 11) has been shown to be a safe and worth-while procedure (Frazell and Moore, 1961). Undoubtedly there is a strong stimulus to strive for a complete clearance of these mouth tumours in that the disease seldom extends below the clavicle and definitive cure is a reasonable hope.

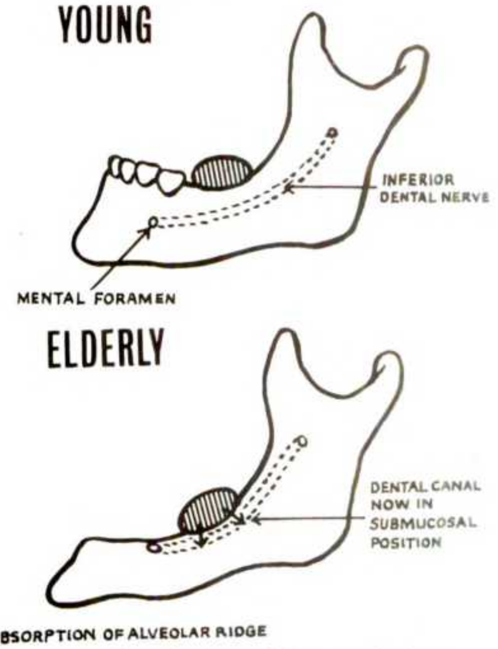

YOUNG
INFERIOR DENTAL NERVE
MENTAL FORAMEN
ELDERLY
DENTAL CANAL NOW IN SUBMUCOSAL POSITION
ABSORPTION OF ALVEOLAR RIDGE

FIG. 8.—Changes in the mandible as a result of age.

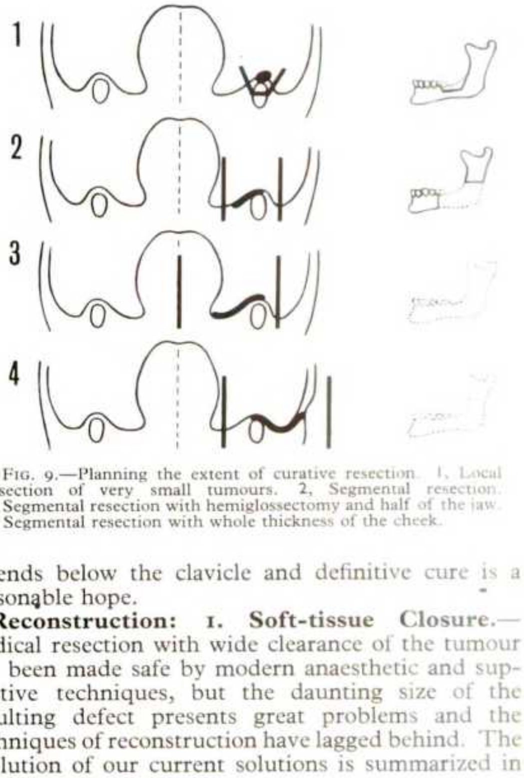


FIG. 9.—Planning the extent of curative resection. 1, Local resection of very small tumours. 2, Segmental resection. 3, Segmental resection with hemiglossectomy and half of the jaw. 4, Segmental resection with whole thickness of the cheek.

Reconstruction: 1. Soft-tissue Closure.—Radical resection with wide clearance of the tumour has been made safe by modern anaesthetic and supportive techniques, but the daunting size of the resulting defect presents great problems and the techniques of reconstruction have lagged behind. The evolution of our current solutions is summarized in the following paragraphs.

Attempts at Direct Suture.—

Local flaps: In the past intra-oral closure was often attempted by mobilization and suture of the surrounding mucous membrane. However, there is rarely enough mucosa to carry out direct suture, or to allow closure by a transposition flap, without producing unacceptable tension and distortion.

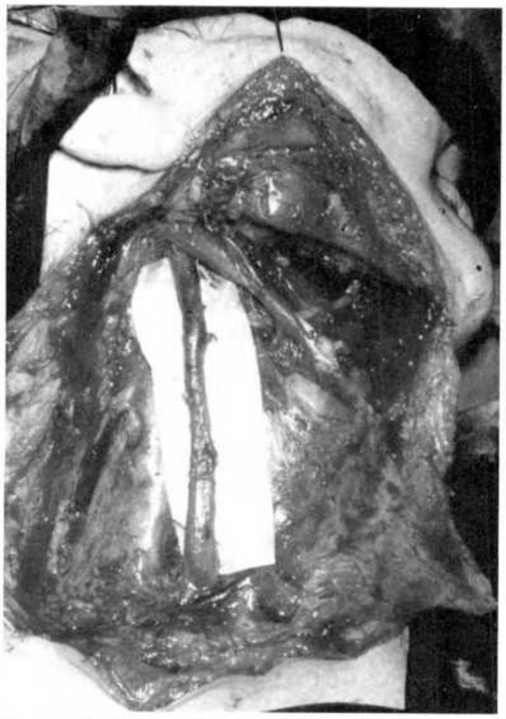


FIG. 10.—Simultaneous bilateral neck dissection. Conservation of the internal jugular vein on the less affected side.

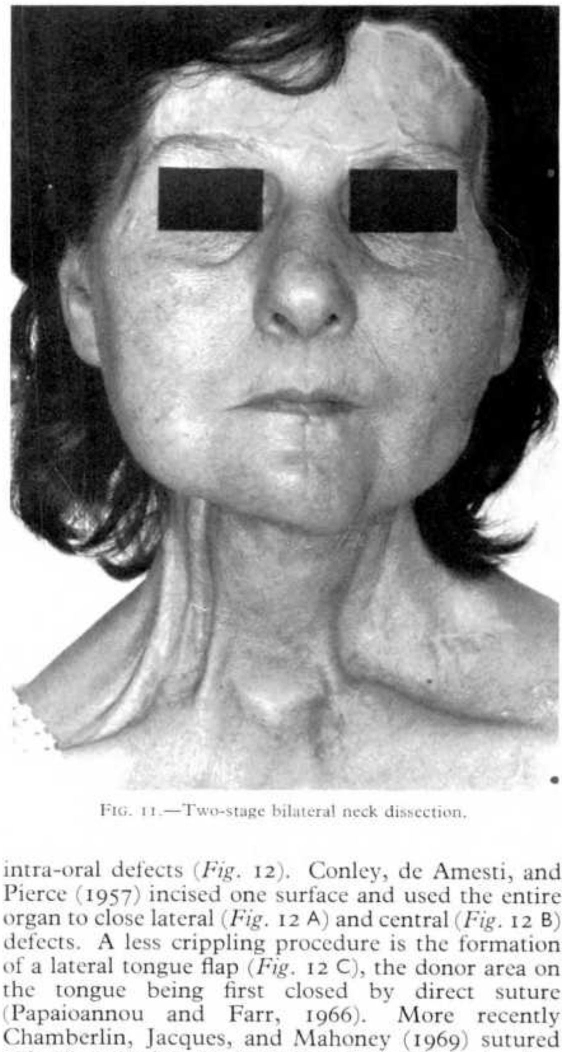


FIG. 11.—Two-stage bilateral neck dissection.

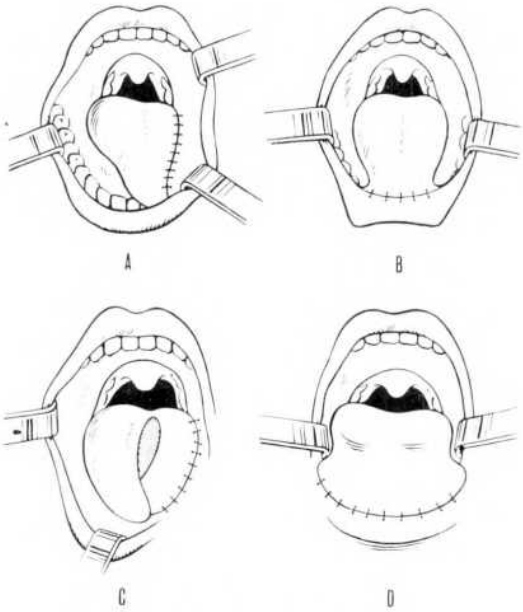


FIG. 12.—Use of the tongue in repair (*see* text).

Tongue flaps: The tongue is a highly mobile structure and it is therefore not surprising that numerous techniques have been described for using it to cloak intra-oral defects (*Fig.* 12). Conley, de Amesti, and Pierce (1957) incised one surface and used the entire organ to close lateral (*Fig.* 12 A) and central (*Fig.* 12 B) defects. A less crippling procedure is the formation of a lateral tongue flap (*Fig.* 12 C), the donor area on the tongue being first closed by direct suture (Papaioannou and Farr, 1966). More recently Chamberlin, Jacques, and Mahoney (1969) sutured only the anterior third of the defect and used a free skin-graft to close the posterior defect. Alternatively they cauterized the area to prevent adhesion of the remaining mobile tongue. In the case of very large defects or for dehiscence of a wound (provided that the tongue has not been exposed to a high dose of radiation), the entire organ can be split and unfolded to provide a large musculomucosal flap to close the defect (*Fig.* 12 D). These methods, however, lead to great difficulties in swallowing and speech owing to distortion of the tongue which interferes grossly with oral mechanics even when healing takes place by first intention. Worse, primary closure often fails and large salivary fistulae with their attendant miseries are not uncommon.

Free grafting: The possibilities of skin-grafting of mucosal defects had been realized by Schnitzler and

Ewald as long ago as 1894, but the inlay technique was first used by Moszkowicz in 1917 and developed by Esser in 1917. Pickerill in 1918 and Blair in 1925 extended its use. This technique became the standard method of repair in the fifties for post-excisional mucosal defects. Edgerton (1951), Figi and Masson (1953), Conway and Murray (1953), and Coleman (1958) developed these techniques, but Fister and Sharp (1963) described peripheral loss of these grafts and Edgerton and Desprez (1957) described total loss.

Many modifications of techniques were explored. Ward and Robben (1951) sutured a free graft under the overlying skin some 10 days before excisional surgery. Corso and Gerold (1962) buried a rubber tube covered by a free graft at the time of operation and 8 days later incised the area, exposing the new sulcus. This method, however, has greater application in the construction of a sulcus or mobilization of the tongue as a secondary procedure. It is now accepted that, even with the addition of muscular flap supports, the take of these grafts cannot be guaranteed, especially if preoperative radiation has been given. Even if an adequate take of the graft is achieved the skin has limited elasticity and will tend to contract (Fister and Sharp, 1963).

Causes of Failure.—Complications such as wound infection, fistulae, and strictures were common. Attempts at closure were often abandoned and skin-to-mucosa suture was performed, leaving a large fistula. The unfortunate patient was then sentenced to a lengthy follow-up period for the tissues to recover and to see if there was any recurrence of the tumour before definitive reconstruction was commenced. This commonly consisted of various forms of tube pedicles of abdominal skin laboriously conveyed to the defect, using the wrist as a temporary host. Meanwhile, with the passage of time secondary contracture of the edges of the defect had taken place, tissues had become distorted, the tongue had become fixed or prolapsed through the wound, and the remaining mandibular fragments had been dragged into malposition by the unopposed action of the pterygoid muscles and the contracting scars. Over the surface of these thick scar bands at the edges of the defect the skin was chronically infected and sodden from constant contact with saliva, rendering the area unsuitable for the reception of skin-flaps. The dire need became apparent for reliable techniques of immediate primary closure of the post-excision defect if patients were to have a reasonable quality of life postoperatively.

The Search for Safe Regional Flaps for Immediate Closure.—The use of *regional flaps*, as against flaps from distant areas, for repair promised an obvious advantage, namely, the importing of well-vascularized tissue, which is of special value when irradiation has been the primary method of treatment. The adjacent skin of the neck seemed the obvious choice, and a succession of different neck flaps has been described (*Fig.* 13). These may be conveniently grouped as follows:—

Group I: Simple skin-flaps either based laterally to form a transverse flap (*Fig.* 13 A), superolaterally to give an oblique flap (*Fig.* 13 B), or superiorly to give a vertical flap (*Fig.* 13 C).

Group II (*Fig.* 13 D): The broad-based vertical flap resulting in a large skin defect in the neck. Bakamjian and Littlewood (1964) closed this by a second skin-flap from the chest.

Group III (*Fig.* 13 E): Conley (1960) used a flap based posteriorly on the region of the nuchal line to produce a 'nape of the neck flap' but found it difficult to mobilize.

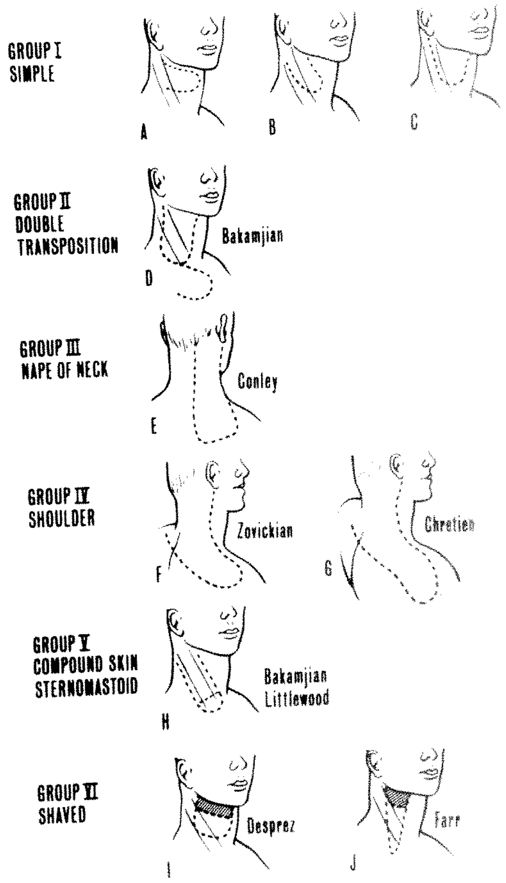


FIG. 13.—Neck flaps used for intra-oral repair.

Group IV: Zovickian (1957a, b) after a preliminary undermining procedure raised a flap of shoulder skin (*Fig.* 13 F). Chretien, Ketcham, Hoye, and Gertner (1969) used an even longer more mobile flap but numerous delay procedures were required (*Fig.* 13 G).

Group V: Bakamjian and Marshall (1963) described the use of a strap flap, based superiorly on the occipital and posterior auricular arteries and including the sternomastoid muscle, to close palatal defects. Littlewood (1967) adapted this technique to the closure of intra-oral defects (*Fig.* 13 H). (The skin in this composite flap procedure is 4 cm. wider than the muscle and extends distally on to the chest.) Unfortunately, preserving the vessels and the muscle may compromise the neck clearance.

Group VI: In order that primary intra-oral closure could be accomplished Desprez and Kiehn (1959) used a broad, superiorly based flap (*Fig.* 13 I) which they turned in below the mandible, removing enough of its epithelium to allow suture. However, the large defect in the neck needed a skin-graft for closure.

Farr, Jean-Gilles, and Die (1969) modified the technique and used a smaller, wedge-shaped flap (*Fig.* 13 J) which allowed immediate closure of the neck skin. The failure rate with this flap has proved unacceptably high (30 per cent in Farr's (1970) cases) unless there is a preliminary delay procedure.

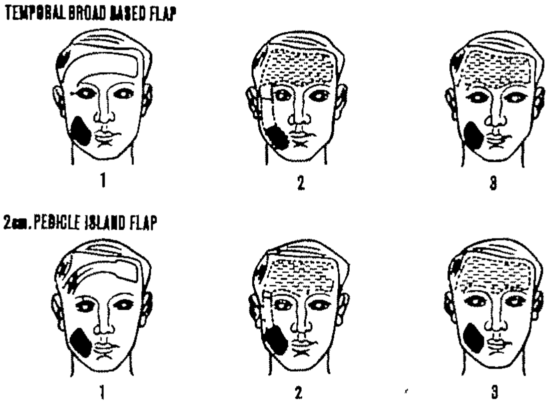


FIG. 14.—Forehead flaps based on the superficial temporal artery for replacement of intra-oral lining. 1, Mucosal defect. 2, Forehead flap turned down and passed into mouth. Split skin to forehead. 3, Pedicle returned to forehead.

For midline resections (central arch carcinomas) a submental flap based on the lower border of the mandible has been used. The flap was passed under the skin adjacent to the proposed defect, thus producing a lined flap to be used some 15 days later in the reconstruction (Edgerton, 1951; Ward and Robben, 1951; Zovickian, 1957a, b).

All these flaps have serious drawbacks. The skin of the neck is often hair-bearing, it may have been irradiated, and, as Ward and others (1959) have pointed out, such skin may slough if merely raised, let alone transposed. Moreover, all these techniques leave a temporary salivary fistula, the closure of which is not always the simple out-patient procedure that some authors have suggested it is. The greatest objection of all, however, to the use of cervical skin is the difficulty in providing really safe cover for the carotid system exposed by the neck dissection.

Development of the Island Forehead Flap.—Blair (1925), Conway and Murray (1953), Ward and others (1959), and McGregor (1963a, b) made a positive advance by establishing the value of a flap of forehead skin with a broad-based lateral pedicle (*Fig.* 14). This flap is passed through a surgically produced fistula into the oral cavity, with a suture line above the level of the salivary reservoir, thus giving complete salivary seal. Polya (1926) used the 'biological' flap of Monks (1898) and Esser (1917) to carry forehead skin to line the oral cavity on a vascular pedicle, consisting of only the anterior superficial temporal vessels. Kernahan and Littlewood (1961) demonstrated the possibilities of a narrow flap with a 2-cm. pedicle based on the course of the anterior branch of the superficial temporal artery to close skin defects. These techniques have now been combined and adapted for intra-oral closure (Wilson, 1967) (*Fig.* 14 B). The narrow pedicle provides a wide yet freely mobile flap which can be made to reach any required intra-oral site, allowing definitiv suture of nine-tenths of its perimeter at the primar operation. If desired the pedicle of the flap may b shaved of its epithelium so that it heals into the chee 'tunnel'. This avoids, with some cosmetic loss, second operation to divide and return the pedicle and may be useful in the elderly poor-risk patient.

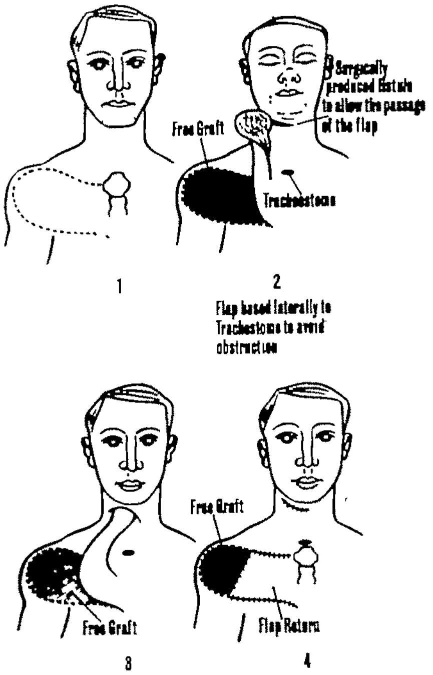
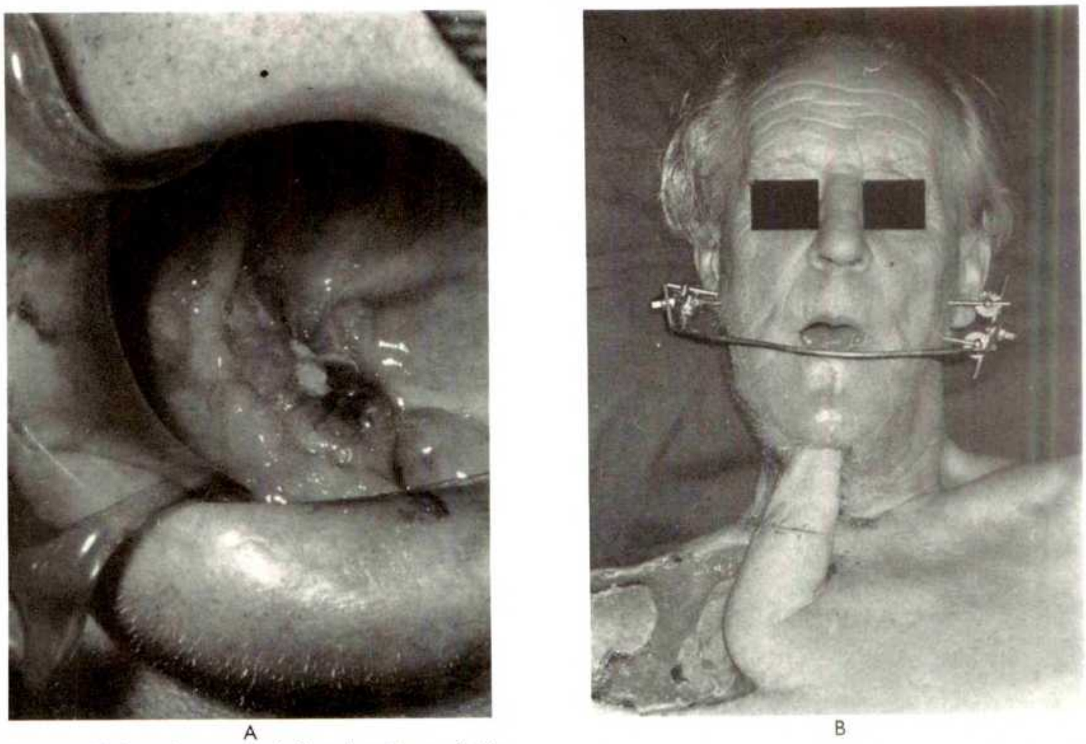

Free Graft
Surgically produced fistula to allow the passage of the flap
Tracheostome
1
2
Flap based laterally to Tracheostome to avoid obstruction
Free Graft
Free Graft
Flap Return
3
4

FIG. 15.—Central arch carcinoma; mucosal replacement by deltopectoral flap.

The flap is well vascularized, with an excellen anastomosis across the midline (Corso and Gerold 1962), so that the entire forehead may safely be used giving ample tissue to close either a central, lateral, o posterior defect. Delaying, as suggested by Millar (1964), is quite unnecessary and is unwise, for th flap may then become stiff and oedematous and mor difficult to handle.

Some advanced tumours require a wide *en blo* resection including the overlying skin, creating whole-thickness defect. To close such a gap in on stage, skin cover, as well as the forehead flap fo lining, must be provided. Edgerton (1951) use free skin-grafts. Others have resorted to local flaps the drawbacks of which have already been described The large cervical-pectoral flap of Garrett, Giblin and Hoffman (1966) supplies enough tissue but it to may necrose as it is based on the anterior border of th trapezius where the platysma is deficient and vascularization poor (McGregor and Reid, 1966).

Delto-pectoral Flap (Bakamjian).—The delto-pectoral flap of Bakamjian and Marshall (1963) ha proved a satisfactory solution of this problem. I provides almost unlimited skin, and is a significan advance in the management of these cases. It can b used, alternatively, to provide mucosal lining; thi spares the forehead skin but leaves a temporar salivary fistula (*Figs.* 15, 16). However, by shavin a strip of dermis to allow complete closure we have successfully obtained salivary seal with this flap. We have found that the most valuable use of the Bakamjian flap is to close the skin defect in the face (and upper neck) after the mucosal defect has been closed by inserting a forehead flap (*Fig.* 17).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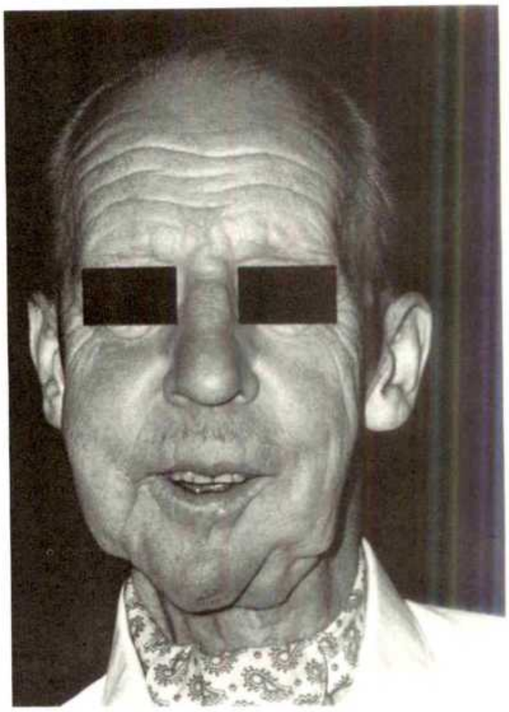
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FIG. 16.—Male, aged 70 years. A, Central carcinoma. B, Use of a deltopectoral flap for mucosal replacement. C, The patient well 2 years after surgery.

If the lower lip with its vermilion border has to be sacrificed it can be replaced by using the Abbé procedure to switch a flap containing the required tissue from the upper lip and incorporating this in the repair. When and how to provide support, e.g., for the chin, are discussed under 'Current Surgical Management'.

Reconstruction: 2. The Mandible.—

Extent of the Problem.—Marginal resections of the mandible do not require any replacement (*Figs.* 18, 19). When, however, the continuity of the mandibular arch is destroyed by segmental resection or hemimandibulectomy the soft tissues collapse inwards, resulting in loss of contour. The lateral (posterior) mandibular segment, if there is one, is pulled upwards and inwards by the unopposed action of the temporalis–pterygoid sling, and the soft tissues contract to produce a deformity which becomes almost impossible to correct. The introduction of a skin-pedicle lining flap helps to prevent gross distortion by interposing a bulk of soft tissue and prevents the formation of tight scar bands between the bone ends. Even so, the loss of mandibular stability inevitably downgrades the functions of speech and mastication (Conley, 1962). Anaesthesia of the lower lip owing to loss of the mental nerve may in some cases interfere with 'lip-seal' and contribute to drooling of saliva. Hence, in these cases, though immediate mandibular support is not essential, an eventual bone-graft is often very desirable.

When the central mandibular arch is removed immediate stable support is vital (*Fig.* 19), otherwise there is no fixed point for a suture to support the tongue and larynx, so that funnelling of the oro-pharynx with dysphagia and perhaps respiratory obstruction will result. Immediate reposition of the excised bone segment seemed an ideal solution. Reposition of the bone, after removing the tumour and exposing the bone to boiling, was described by Orell in 1937. The technique was modified by Harding (1957), who cleared the segment of soft tissue and autoclaved it before reimplanting. The procedure has fallen into disrepute as no bony union takes place and many of the grafts are absorbed. Gaisford, Hanna, and Gutman (1961) had to remove the bone in 3 out of 4 cases in which they used this method.

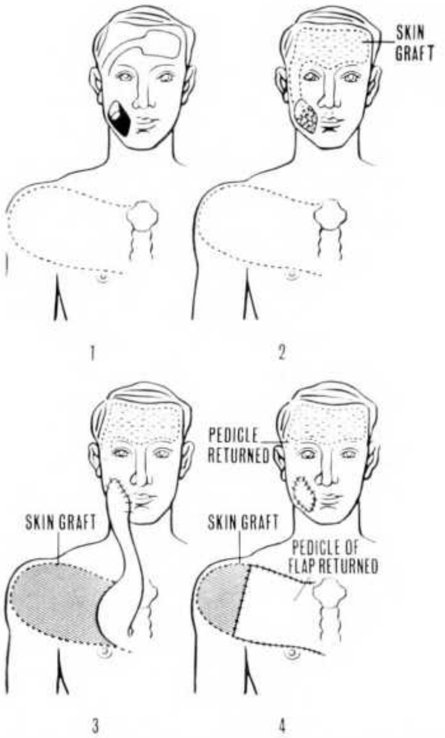


FIG. 17.—Use of an island forehead flap for lining, and a delto-pectoral flap for skin cover.

Immediate block-bone grafting of the defect seemed attractive and was advocated by Edgerton, Ward, and Sikes (1950) and Conley (1953, 1956). The technique was modified by Desprez and Kiehn (1959), who threaded blocks of bone on a Kirschner wire, improving the vascularization and allowing the implant to take up the correct curved form—the so-called 'shish-kebab' technique. Millard (1964, 1965, 1967), and Millard, Campbell, Syockley, and Garst (1969) threaded a Kirschner wire along the medulla of a section of rib, removed wedges of bone from the concave aspect to allow moulding, and slotted the ends into mortices cut in the remaining mandibular segments. This was the so-called 'pig-on-a-spit' method. Fleming and Morris (1969) used a simple bent-rib graft but supported the repair by an external acrylic splint. External splints, however, are ill tolerated by the patient. Cleanliness is difficult to maintain and there is increased risk of infection.

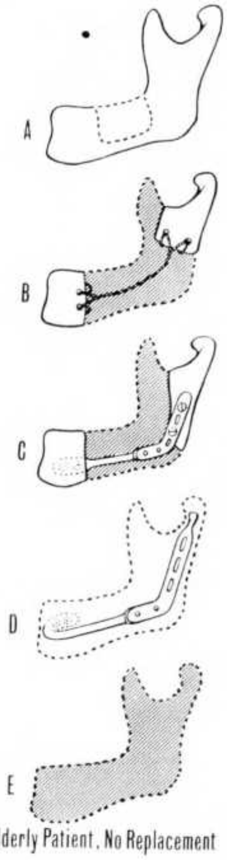


FIG. 18.—Mandibular resection and replacement (*see* text).

In our view, therefore, there are serious disadvantages in immediate bone-grafting in the type of case now under discussion. An immediate and lasting watertight intra-oral closure cannot always be guaranteed, especially if the tissues have been exposed to large doses of radiation. In these circumstances the avascular bone block is frequently lost. Millard (1971) reported a 30 per cent loss of grafts and now advocates a delayed bone-grafting procedure.

Because block-bone is so vulnerable to infection further trial is currently being made of the use of cancellous bone chips, pioneered by Mowlem (1963). These chips are rapidly vascularized even in the presence of infection and intra-oral sinuses. Yoel (1966) applied the chip-grafting technique to post-excisional mandibular defects. He used a perforated stainless-steel trough to support the chips and to give stability. Brånemark, Breine, Hallen, Hanson, and Lindström (1970) used a lighter, perforated, titanium frame filled with the chips, which are easily obtained with a gouge after a 2-cm. trapdoor of compact bone has been raised on the iliac crest. Fortunately, external fixation is not required, as it has been found that the support is adequate and limited stress increases the rate of vascularization of the bone.

Most workers have preferred not to use immediate bone-grafts. Various techniques have been employed to secure immediate stabilization, with the option of eventual substitution of a bone-graft.

Temporary fixation was first achieved by driving a Kirschner wire into the inferior dental canal in the cut end of the mandible (*Fig.* 19 B). Such wires were commonly extruded and postoperative pain from irritation of the inferior dental nerve frequently occurred. Byars (1946) suggested the use of metal bars. Many foreign substances have been used to maintain the position of the fragments and to replace the mandible. The use of stainless-steel plates was described by Edgerton and others (1950) and Philps (1967). Chrome-cobalt prostheses were advocated by Conley (1951) and Kleitsch (1951, 1952), and Ticonium was used by Walsh (1954). Acrylic resins were popularized by Niebel, Healey, Neenan, and Hoffman (1954) and Healy, Subdy, Niebel, Hoffman, and Duval (1954). Inert but weak replacements by Teflon or Silicone were tried by Brown, Fryer, Kollias, Oilwiler, and Templeton (1963) and Small, Brown, and Kobernick (1964).

Titanium now seems to be the material of choice (Cook, 1969, *Fig.* 19 D; Bowerman and Conroy, 1969, *Fig.* 19 E). Time has shown it to be non-irritant to the tissues and it is sufficiently malleable to allow bending to the required contour and fit. The prosthesis can be assembled as desired in the theatre from a kit of parts, which are easily and rapidly riveted together. Both the Bowerman and the Cook prostheses are currently used at Westminster Hospital.

Choice of Method.—The type of reconstruction, if any, to be used will depend, first, on the evaluation of the patient, paying particular attention to age, general condition, and the extent of the tumour. Secondly, it will depend on what sophisticated laboratory facilities and special skills are available to the operating team.

In the elderly poor-risk patient any form of implant is inadvisable. The adequate removal of the tumour with low morbidity is of paramount importance. Gaisford and others (1961) reported that in 89 cases where no reconstruction of the mandible was undertaken the patients willingly accepted their minor disabilities.

In the younger patient where fixation is necessary but metal implants are not available the mandibular ends may be temporarily stabilized quite simply by four strands of stainless-steel wire braided together for strength (*Fig.* 19 C). Fixation by passing each of the four filaments through oblique channels drilled in the outer cortex and twisting them together will give adequate stability and prevent torque. Three weeks later the wire can be replaced by a bone-graft, when the pedicle of the lining flap is returned.

In a carefully selected group of patients definitive bone replacement of a hemimandible can be undertaken as a primary procedure. In this case when the excision is undertaken the articular disk of the temporomandibular joint must be retained. The bone-graft, which is carved to pattern from the iliac crest, will then fuse with the undersurface of the disk, allowing movement in the upper compartment of the joint (Manchester, 1965) and preventing secondary ankylosis.

When the replacement demanded is greater than half of the mandible, the use of a permanent metal prosthesis is recommended as this is superior to multiple segments of bone wired together.

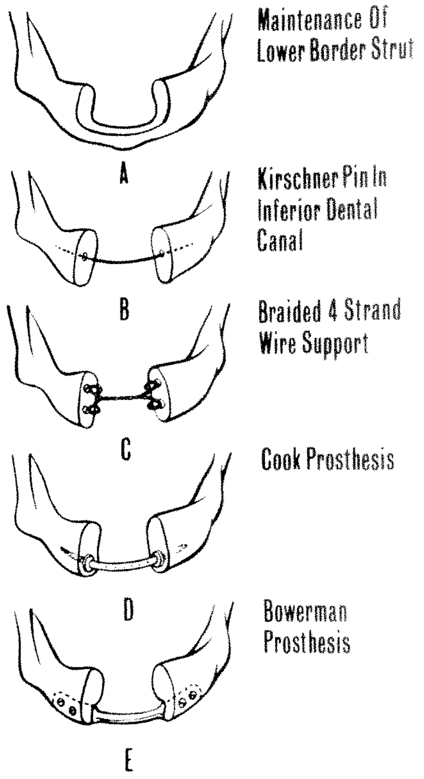


FIG. 19.—Central arch resection; immediate support.

In a few younger patients with firm remaining teeth a 'cosmetic' denture may be well tolerated and give great satisfaction (*Fig.* 20).

To sum up, therefore, a satisfactory routine for soft-tissue reconstruction has been found in the use of the forehead flap for lining and the deltopectoral flap for cover. Support is used only when essential, and, in general, temporary metal support is preferred to immediate bone-grafting.

III. CURRENT SURGICAL MANAGEMENT

In this final section the authors describe the fairly standardized procedure which is now their current practice.

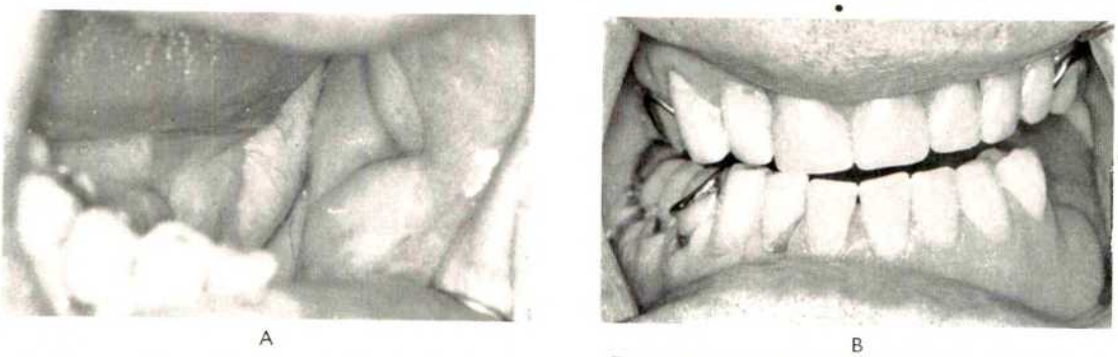
Operability and Planning.—Every effort is made to assess the individual tumour accurately. In addition to the anatomy of the tumour some idea of its malignancy may be gained from its histological picture, growth-rate, and relation of node involvement to primary size. Radiological examination, especially with dental occlusal films, may show destruction of bone, but this confirmatory evidence is often delayed long after clinical involvement of bone has become obvious. In cases with trismus tomography of the base of the skull and pterygoid region may be invaluable. Because distant metastases are occasionally seen, a routine radiograph of the chest is always performed.

Almost all the cases will repay preliminary examination under anaesthesia. At this time confirmatory biopsies of any suspicious areas may be useful, for sometimes this disease has a multifocal nature (the 'field cancerization' of Slaughter, Southwick, and Smejkal, 1953), when under-assessment is easy; and, conversely, some of the apparent surface extent may prove to be leucoplakic or premalignant only.

Extension backwards to the pharyngeal wall, or upwards to the base of the skull, may contra-indicate surgery; so may gross bilateral node involvement or fixity of nodes to the carotid vessels. All these factors must be weighed together, taking into account the age and condition of the patient and the extent to which the operation is likely to palliate if it does not cure. Dental treatment may be given at this preliminary session if desired and prosthetic requirements, if any, assessed.

The superficial temporal artery should be checked for patency, and its course marked out preoperatively.

Preoperative Radiotherapy.—In the past, as recounted above, surgical resection was considered the second resort if full-dose radiotherapy failed. It is still our practice to give preoperative radiotherapy in the belief that it reduces the risk of operative implantation of viable tumour (Henschke, Frazell, Hilaris, Nickson, Tollefsen, and Strong, 1966). Our dose, however, is usually limited to about 4000 rad in 4 weeks and operation follows as soon as the visible reaction has subsided, whatever the response may have been. It is important to base the resection on the original assessment of the tumour, not on its reduced size after irradiation. Clinical photography is invaluable in this respect.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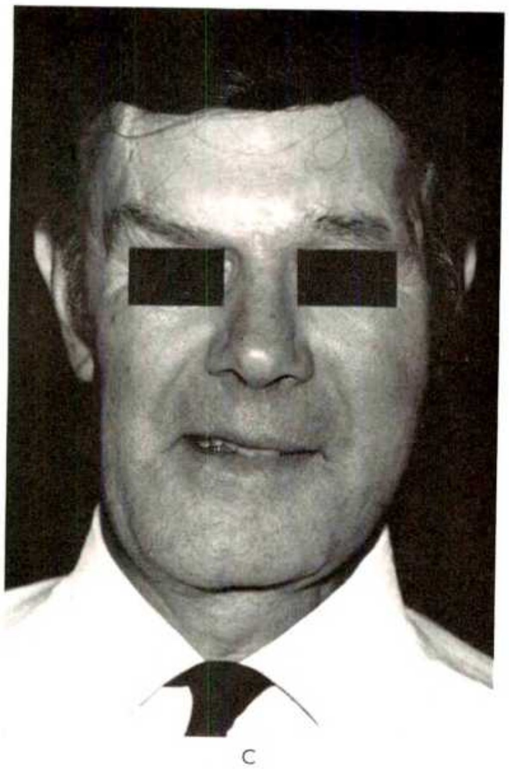
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FIG. 20.—A, Left forehead flap after hemimandibulectomy. B, 'Cosmetic' denture in place. C, Final appearance.

Anaesthesia.—Age, cardiovascular state, and pulmonary function have nowadays receded in importance but they must be assessed by the anaesthetist, who will occasionally report that anaesthesia is absolutely contra-indicated.

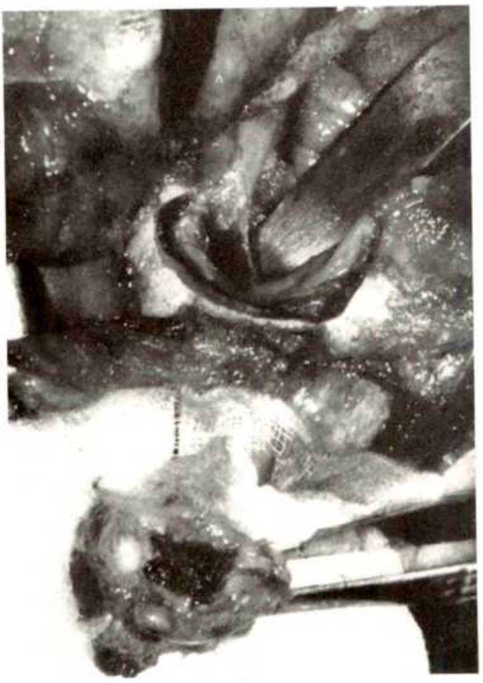
Intubation may present difficulties in patients with trismus and immobile cervical spines, and preliminary tracheostomy is sometimes inevitable. Otherwise, tracheostomy is almost invariably performed at the end of the operation. A simple technique without a Bjork flap is used to ensure rapid healing. An Intracath is inserted into an arm vein at the start of the procedure and pushed on into the innominate vein. This provides central venous pressure readings during the operation and a reliable drip for the vital postoperative days. Continuous electrocardiographic recording is used. Hypotension is almost always used but requires skill and care in elderly poor-risk patients.

General Considerations of Operative Technique.—

Frozen-section histology is used throughout the resection, as the aim is to obtain a clear margin of at least 3 cm., and if possible 4 cm., around the tumour. This certainty of clearance has obviously become more important now that immediate definitive closure is the routine.

Wound contamination: Fischer, Ketcham, Roxanc, and Malygreen (1967) reported that 13 per cent of washings from the neck wounds contained cancer cells. We take the following precautions. Ulcerated tumours are covered with a small wool pledget soaked in mercuric chloride, 1/500, and at the end of the resection the entire wound is either washed thoroughly with water or saline or exposed to half-strength Milton packs for 5 minutes.

Premalignant lesions: Prophylactic excision of areas of mucosa known to be at risk is now both feasible and desirable (Helsper and Fister, 1967; Moore and Catlin, 1967). A free split-thickness skin-graft may be applied to the periosteum and held in position by a dental composition mould kept in place with a Gunning splint or denture fixed to the mandible.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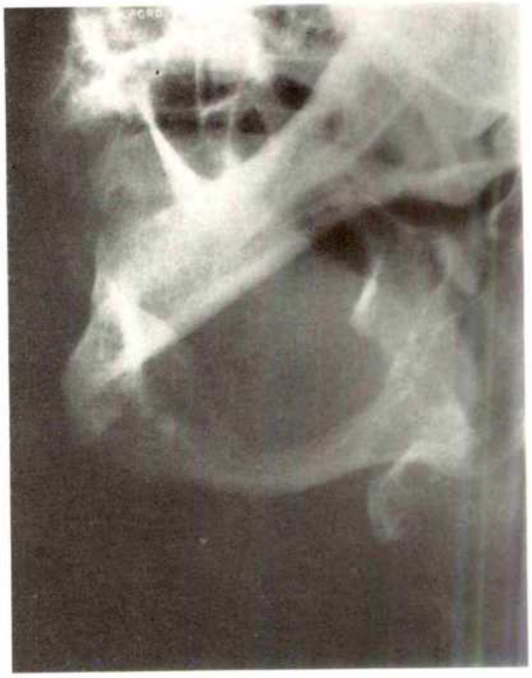
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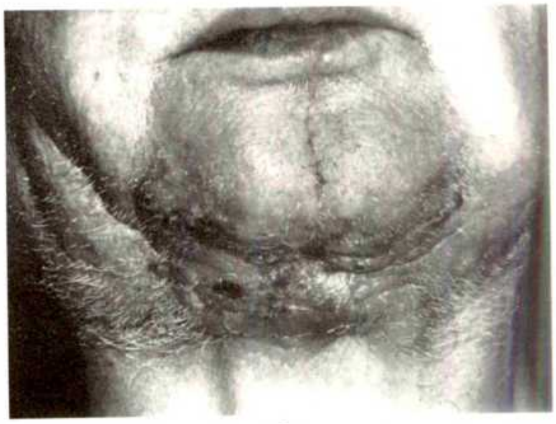
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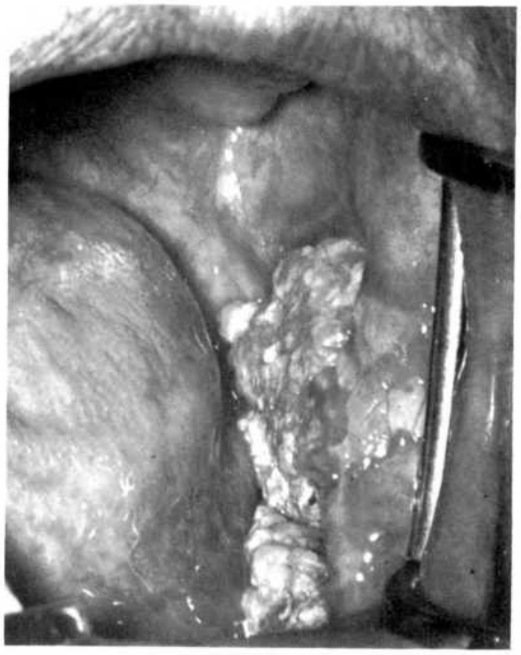
FIG. 21.—Local resection of a small alveolar tumour in an elderly patient. A, Resected tumour is seen above. B, Radiograph showing recurrence anterior to the defect. C, The clinical recurrence.

Local excision of small carcinomas: Local removal with an area of underlying alveolus was described by Rankow (1968). This procedure (*Fig.* 21) leaves the lower border of the mandible intact so that repair is simple, but it may well fail to allow an adequate clearance. We have seen recurrence of the tumour in the periosteum or along the inferior dental canal (*Fig.* 21 B) and we do not favour this procedure except for exceptionally early or border-line lesions or in extremely poor-risk patients.

The Radical Resection.—This will be described under 'lateral arch tumours' and 'central arch tumours'. In each case extensions to include removal of the tongue and/or skin will be considered.

Lateral Arch Tumours (*Fig.* 22).—As has already been pointed out, the extent of the mandibular resection is never less than from the mental foramen to the inferior dental foramen, but in some cases part of the ramus may be left, though the coronoid process is usually removed (*Fig.* 18) to ensure ample room for the forehead flap as it passes into the mouth. For most tumours, other than small anteriorly situated ones, complete hemimandibulectomy is preferred.

Any of the standard incisions for neck dissection may be used, and should be extended forwards to split the lip in the midline. The incision dividing the free margin of the lip should be V-shaped, otherwise postoperative contracture is liable to lead to unsightly 'notching' of the lip contour. If necessary, the vertical limb of the neck incision may be supplemented by the inferior extension of Martin (1951). If a deltopectoral flap is to be raised some modification may be needed (*see below*). The flaps normally include the platysma, for if the tumour is invading this layer skin resection and replacement are the proper procedures.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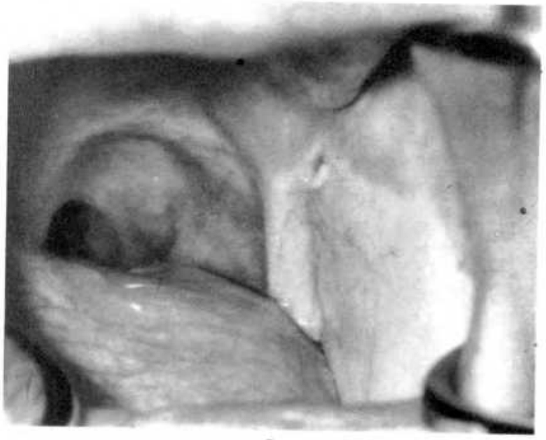
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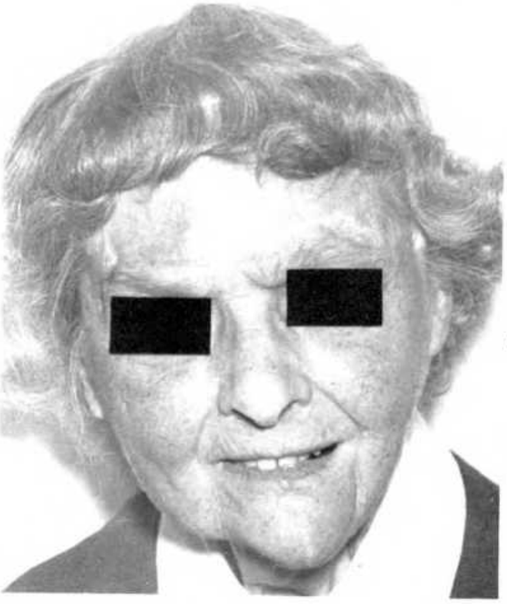
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FIG. 22.—Female, aged 68 years. A, Lateral carcinoma. B, Repair with a forehead flap. C, Final appearance of the patient alive and well after 4 years.

The operation begins with the neck clearance which is normally a total Crile dissection, working from below. The dissection is carried upwards, deep to the anterior belly of the digastric and the mylohyoid muscles, to include the affected area of the mandible and associated soft tissues. Division of the mandible 3 cm. anterior to the tumour permits the posterior segment to be rotated laterally, exposing the lingual sulcus and allowing a planned excision of the entire involved area. The mandible is sectioned posteriorly, preferably above the level of the lingula with its associated dental nerve and vessels. This completes the resection.

If the entire half mandible is to be resected the initial steps of the operation are as already described. However, when the stage of dividing the soft tissues posterior to the tumour is reached the masseter is sectioned to expose the ascending ramus of the mandible. A subperiosteal plane is then sought, stripping the soft tissue upwards to expose the entire bony ramus.

The coronoid process is now revealed with the insertion of the temporal muscle. This muscle is divided close to the bone by sharp dissection to free the coronoid process, and the vascular soft tissues are pushed away from the sigmoid notch. The condylar attachment is now fully in view. An incision is first made in the anterior capsule and, by a combination of pressure by an elevator thrust into the lower compartment of the joint and distraction of the mandible laterally, the mandibular condyle is dislocated. When this has been achieved the insertion of the lateral pterygoid muscle is revealed and is easily divided by sharp dissection. It is important that this dissection be kept close to the bone to avoid injury to the maxillary artery, which is in direct relationship with the posterior surface of the neck of the mandible. After dividing both the lateral and medial pterygoid muscles the specimen may be lifted clear. The cavity is now inspected and haemostasis secured. Irrigation with water or application of a Milton pack is carried out, as has been described.

A pattern is next made of the defect, marking on it the position of entrance of the narrow pedicle which will be on its posterosuperior aspect.

Attention is now directed to the forehead on which the course of the anterior branch of the superficial temporal artery has been marked out before the induction of hypotension. The necessary length of flap is assessed and checked by transposing a tape. The 2-cm.-wide pedicle can then be outlined on the temple and the pattern of the intra-oral defect marked out across the width of the forehead. The flap with its pedicle is then carefully raised to include the galea.

This ensures the continuity of the arterial system, leaving an intact pericranium as a good base for a split-thickness skin-graft. The entire forehead skin should be sacrificed to allow the edges of the repair to be concealed by the hairline, eyebrows, and glabellar crease. The defect is then covered by a single sheet of skin, preferably taken with a drum dermatome to give a graft of uniform thickness and including sufficient dermis to allow the best cosmetic appearance. The freed forehead flap is now folded on itself longitudinally and its folded distal end sutured together at two or three points with heavy black silk stitches, with the ends left long to be used as traction sutures.

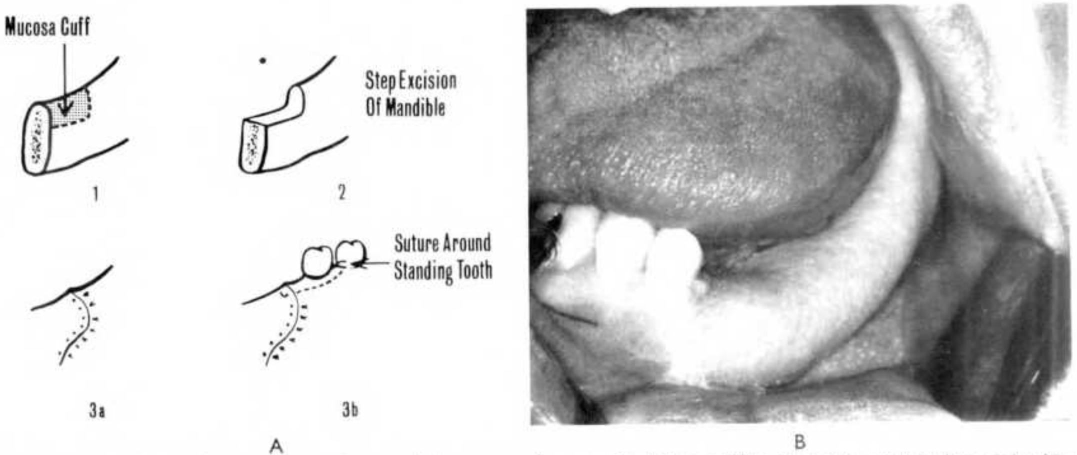

FIG. 23.—A, Technique for securing sound mucosal closure over the cut end of the mandible. B, Shows sound healing of the skin-flap over bone end.

In all females and some males the forehead is thin and the narrow-based flap may be passed easily through the space between the transected temporal muscle and its fascia, inside the zygomatic arch, and thus delivered into the mouth. In males with a bulkier flap a surgical fistula may have to be created around the external surface of the zygomatic arch into the oral cavity. This fistula is created by blunt dissection and stretching, keeping close to the bone to avoid the orbital branch of the facial nerve, the integrity of which must not be jeopardized. The flap is then unfolded and sutured to the defect, commencing posteriorly, using closely placed end-on mattress sutures of o silk, and working towards the midline. In this way the flap creates a new buccal sulcus as a salivary reservoir, above which the suture lines are relatively dry so that the risk of salivary leakage is minimal.

There is a weak point in the closure at the site where the flap is attached to the alveolar mucosa. A modified technique (*Fig.* 23), constructing a 1-cm. shelf of bone by sacrificing the intact alveolar margin, allows a valvular closure and provides bony support to the anterior edge of the flap, much reducing the risk of breakdown of the wound at this critical angle. The cut end of mandible should be smooth and rounded off carefully, using a bur in the Hall airdrill.

After hemiresection of the mandible an immediate prosthesis is not essential, but in the younger good-risk patient a Bowerman metal prosthesis may be inserted. The new half-mandible is constructed in the correct dimensions from a kit of parts. The upper end of the prosthesis carries a mandibular head which must be accurately fitted into the glenoid fossa. The weight and muscular pull transmitted to the prosthesis tend to dislocate it downwards and this is prevented by constructing a temporalis muscle sling, which is passed through a slot in the upper end of the prosthesis and sutured to the fascia of the pterygoid muscles.

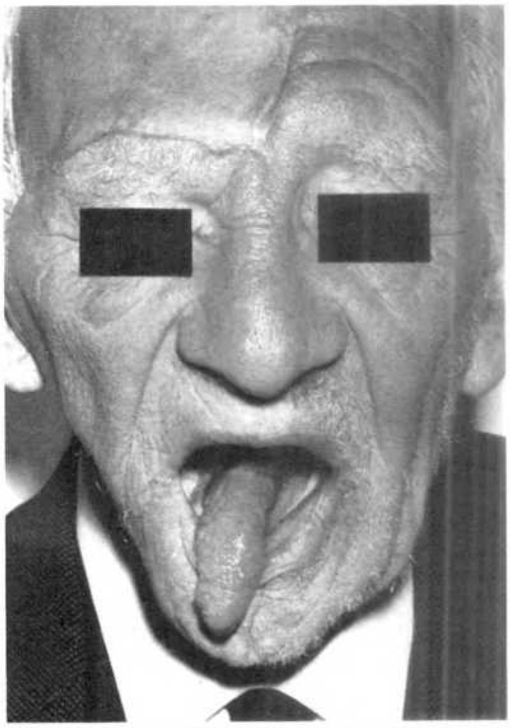

FIG. 24.—Mobile tongue after a right hemiglossectomy and hemiresection of the mandible. N.B. The appearance of the forehead is improved if the whole width of skin is taken. This is now our regular practice.

The lower end of the prosthesis is then bolted to a prepared flattened surface on the *lingual* aspect of the symphysial region of the mandible. The wounds are closed in layers. Suction drainage is provided.

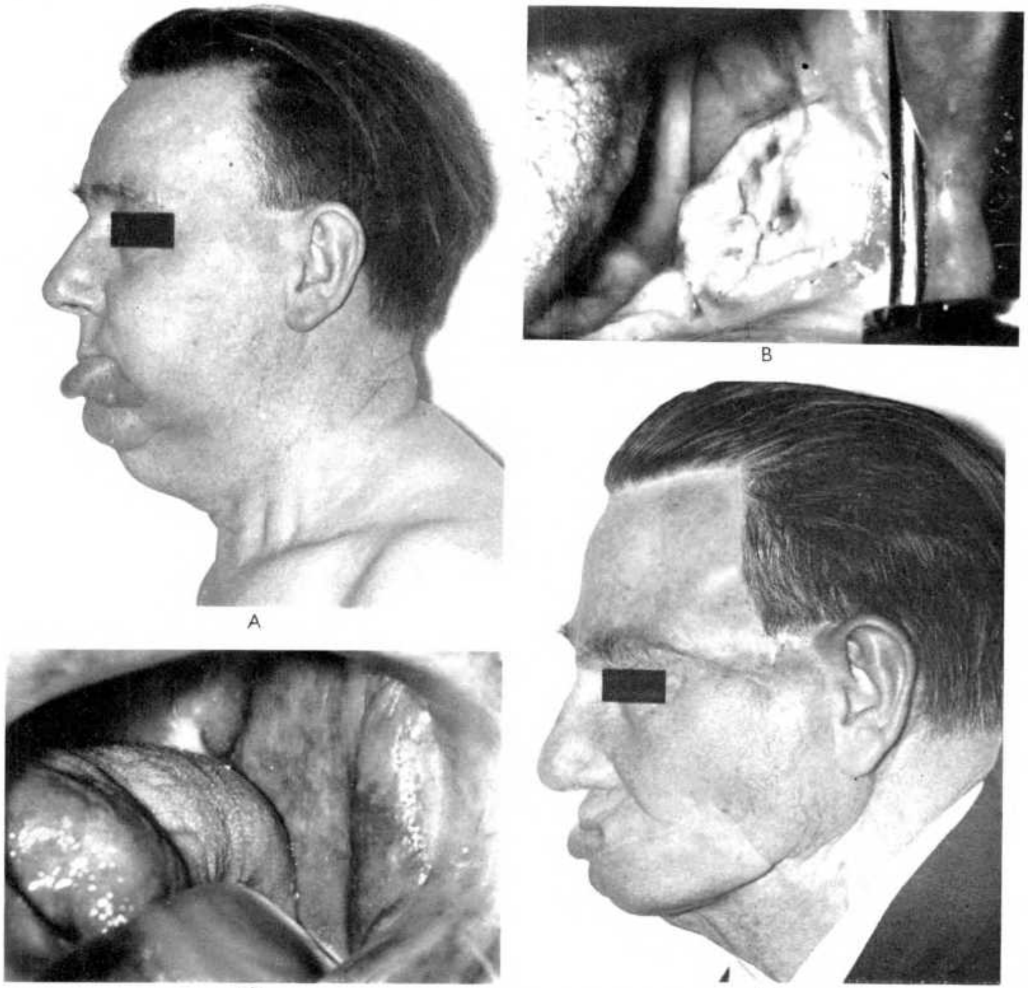

FIG. 25.—Male, aged 72 years. A, Lateral carcinoma involving the whole thickness of the cheek and lip. B, View of the lesion. C, Mucosal replacement by forehead flap; Bowerman prosthesis; deltopectoral flap for skin cover. D, The patient well 2½ years after surgery.

Hemimandibulectomy associated with hemiglossectomy: The half-tongue must be included in the resection in large tumours of the alveolus if they are found to trespass on the territory of the floor of the mouth within 1 cm. of the tongue. Only slight modification in surgical technique is required. The lingual artery is tied, as well as the facial artery, during the neck dissection, which is then carried upwards in a deeper plane, i.e., deep to the hyoglossus muscle, on the surface of the geniohyoid and geniohyoglossus. The lingual and hypoglossal nerves must, of course, be sacrificed. The tongue is split in its avascular midline plane, and the half-tongue becomes part of the *en bloc* resection.

In the reconstruction it is important to recreate a mobile tongue tip (*Fig.* 24) by suturing together the edges of the tongue wound for about 3 cm. backwards from the tip. Also, if the excision extends to the posterior third of the tongue some direct closure posteriorly may be obtained. The temporal flap can now be laid in to complete the reconstruction of the half-tongue and form a new floor to the mouth. This technique allows the formation of a mobile tongue which will not only play its part in speech and deglutition but also facilitate oral toilet. The importance of this aspect of tongue functions—to remove food débris from the mouth—was first emphasized by Aird (1958).

Carcinoma of the lateral alveolus involving the skin (*Fig.* 25): The resection in this case must include the involved skin along with at least a 2–3-cm. margin of healthy tissue, preferably checked by frozen section. The resultant defect constitutes a large fistula which must be closed by a pedicle skin-flap. In our hands, as has already been indicated, the island temporal flap supplies the best watertight lining to the mouth and the Bakamjian deltopectoral flap produces immediate unlimited skin cover. It will usually reach upwards to the level of the zygoma without difficulty. This flap (*Fig.* 17) is based on the lateral border of the sternum and in width extends from the clavicle to the nipple. It includes the upper three perforating branches of the internal mammary artery and, to accommodate shoulder abduction, it is highly elastic.

The flap is raised *to include the fascia of the pectoralis major*. It is then transposed to cover the defect as completely as possible and sutured in place. The intervening part of the flap is tubed to avoid a raw surface. The defect on the chest can be closed by an immediate or delayed free skin-graft. If neck skin has been sacrificed the flap can, to varying degrees, be set into the neck defect. It thus ensures secure cover for the exposed carotid vessels (*Fig.* 26).

Involvement of the posterior tongue and pharynx: The patient may experience difficulty in swallowing after extensive excisions of the tongue or pharynx necessitated by extension of the alveolar tumour. Cricopharyngeal myotomy at operation relaxes the sphincter-like action of the lower section of the inferior constrictor muscle, opening the upper end of the oesophagus to facilitate swallowing (Mladick, Horton, and Adamson, 1971).

Central Arch Tumours.—Tumours involving the symphysial region of the mandible require special consideration. The defect produced is much more crippling. A totally anaesthetic lower lip is often unavoidable, and the two cut ends of bone, if left free, will be pulled upwards and inwards by the pterygoid muscles. Moreover, the tongue tends to fall back, obstructing the airway. Some form of fixation is therefore imperative, and a reliable skin-flap for lining, with if possible complete salivary seal, is vitally important.

Though a deltopectoral flap can be used to supply the lining it does produce a temporary fistula and its central position brings the pedicle over the tracheostome, interfering with the airway (cf. *Fig.* 16). The narrow-based forehead flap for lining is much to be preferred. Particular attention must be paid to a maximum insert of the flap to give a complete salivary seal.

It is our practice to insert an immediate metal spacer to maintain the position of the bony fragments and to support the anterior deep tissues of the neck and the tongue. If salivary seal cannot be guaranteed, or if the more refined prostheses are unavailable, the braided stainless-steel wire technique already described provides a simple method of obtaining at least a temporary fixation. When the pedicle of the flap is returned at 3 weeks the wire can, if desired, be replaced by a bone-graft, using a sheet-lead pattern taken from the operative specimen to ensure an exact replacement.

Better immediate fixation is obtained by a Cook or a Bowerman prosthesis (*Fig.* 27). The former (Cook, 1969, *Fig.* 19 D) screws into the cut ends of the bone by special swivelling screws; the latter (*Fig.* 19 E) is bolted to the *lingual* aspects of the two halves. Both types are made of titanium and may be bent to the required curve.

The excision in the region of the symphysis menti of necessity divides the genioglossus, geniohyoid, mylohyoid, and anterior belly of the digastric muscles—the central component of the so-called 'hyomandibular complex' of Edgerton and McKee (1959). The anterior support of the hyoid bone, larynx, and tongue is thus destroyed. If the larynx cannot rise the patient may be unable to open the upper end of the oesophagus to allow the swallowing of food. If the glottis cannot be closed owing to post-surgical glottic ptosis, aspiration of fluids will occur. Only minimal support is at first supplied by the skin-flaps, and therefore a temporary suture of catgut or silk from the mandible to the hyoid bone (*Fig.* 28 A) is essential (Jabaley and Hoopes, 1969). A more refined 'scaffolding' has been described by Desprez and Kiehn (1959), using fascial strips passing from the lateral border of the mandible, looped around the hyoid bone, and sutured to the central area of the mandible (*Fig.* 28 B) or mandibular prosthesis (*Fig.* 28 C). The creation of this double sling simulates the action of the mylohyoid diaphragm, combining vertical and forward traction. The procedures described allow adequate support of the tongue and prevent it from falling backwards, ensuring good airway after the tracheostomy tube has been removed. In our experience fascia is at risk from infection and should be used only if closure can be guaranteed (*Fig.* 29).

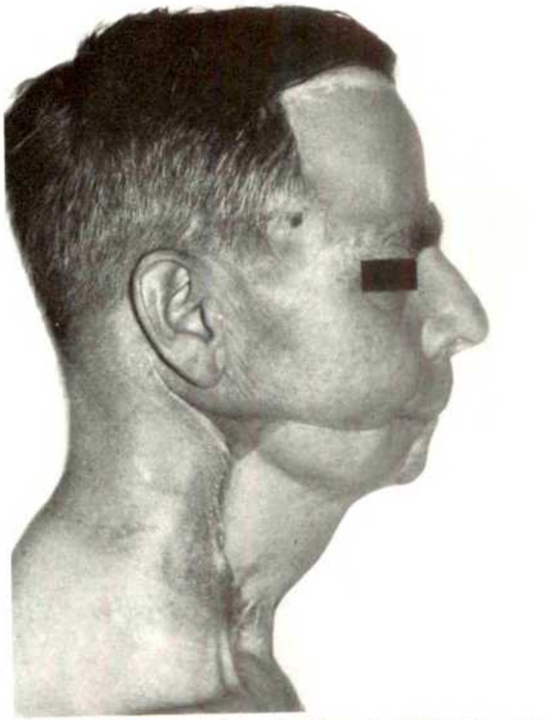
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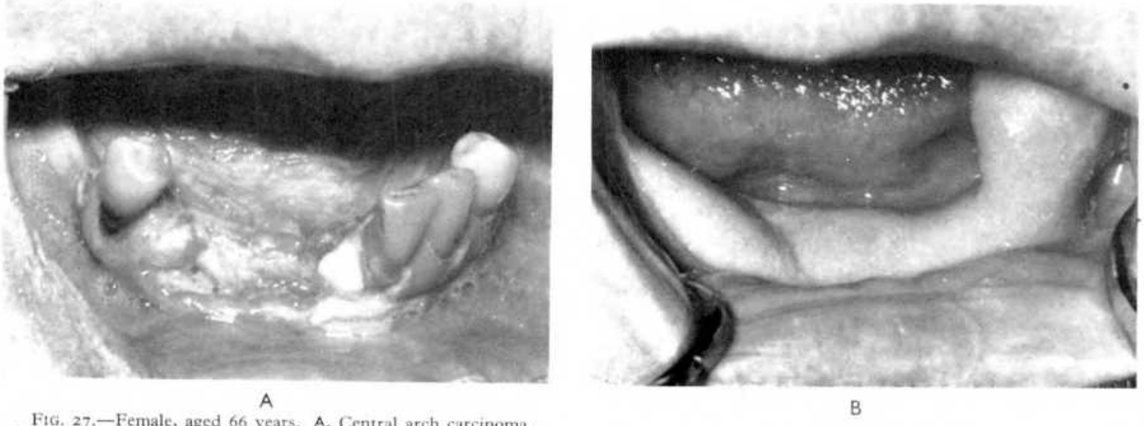
FIG. 26.—Deltopectoral flap set into the neck after skin resection to ensure good cover for the great vessels.

Central arch resection with anterior glossectomy: Extensive tumours in this region involve the mouth floor, which must be excised in continuity. Should the tumour extend to within 1 cm. of the anterior edge of the base of the tongue, the anterior tongue should be amputated and included in the specimen. The previously described methods of reconstruction allow repair of this defect and disablement is often surprisingly small.

Central arch tumour involving the skin: In advanced cases the tumour may ulcerate through the skin of the face. A wide monobloc resection of the involved area is performed. The defect in the facial skin is repaired by a deltopectoral flap, as already described.

Post-operative management: Bulky dressings of the wound are ill tolerated in this group of patients. The only pressure applied is a tie-over support of the forehead and deltoid skin-grafts.


A

B

C

FIG. 27.—Female, aged 66 years. A, Central arch carcinoma. B, Mucosal replacement by a forehead flap; Cook prosthesis. C, The patient well 2½ years after surgery.

Reliance is placed upon suction drainage. Two fenestrated wide-bore rubber tubes are carefully placed under the skin well clear of the carotid arteries, brought out through dependent stab incisions, and sutured firmly in place. These tubes should be connected without delay to two separate suction pumps.

In the elderly or poor-risk patient, continuous electrocardiographic monitoring is required for the first 3 days. A temporary defunctioning of the oropharynx by a nasopharyngeal tube is of great benefit, or occasionally gastrostomy may be preferable. A simple tracheostomy is routinely carried out. The tracheostomy is maintained for 5 days, preventing obstruction of the airway, reducing the dead space, aiding respiration, and facilitating bronchial toilet for the control of infection.

Many of the patients with advanced tumours have malnutrition, not necessarily obvious, from pain and trismus; hence postoperative nutrition may be a problem. Nothing can be given by mouth, although cleansing is essential, and feeding is by the intravenous route. Intravenous alimentation to ensure a calorie/nitrogen ratio sufficient to generate the protein required for the process of tissue repair is aimed at, and added vitamins, especially ascorbic acid, may be needed. The entire oropharyngeal cavity is at rest, healing is therefore rapid, and all tubes may be removed by the ninth postoperative day and a soft diet commenced. Most patients are allowed out of bed on the second day to sit in a chair, for early ambulation, especially in the elderly, is beneficial to the morale and reduces the complications. With good nursing care the morbidity of these admittedly major procedures can be kept to an acceptably low level.

RESULTS

We conclude with a brief report on 82 consecutive radical resections, all involving one or both of the pedicle flaps described in this paper. Lesser procedures are excluded from this review. Ages of the patients ranged from 34 to 85 years, but 40 patients were over 60 years old, including 12 over 70. More than half of the tumours were recurrent after radiotherapy or surgery and almost all were extensive and adherent to, or involving, bone. For most of these patients radical surgery remained the sole chance of survival.

In all the cases the diagnosis was histologically confirmed; there were 77 squamous carcinomas, 2 osteosarcomas of the mandible, 1 fibrosarcoma, 1 melanoma, and 1 adenoid cystic carcinoma arising in the midline mouth floor of a man with untreated tongue-tie, so that diagnosis had been delayed. The site of origin of the tumour was obscure in some of the advanced cases, and reliance had to be placed on the patient's recollection. The presumed locations are shown in *Table VII*.

The intra-oral defect was repaired in 78 cases by a forehead flap, and in the other 4 a deltopectoral flap was used. Of the forehead flaps, 74 were based on a narrow (2-cm.) arterial pedicle; a broad pedicle was used only if the artery was not palpable or had been sacrificed in the excision. There was major partial loss of the forehead flap in only 3 cases (1 of these was a haemophiliac) and minor marginal loss with delayed healing in a further 7, but no patient failed to obtain at least temporary intra-oral seal.

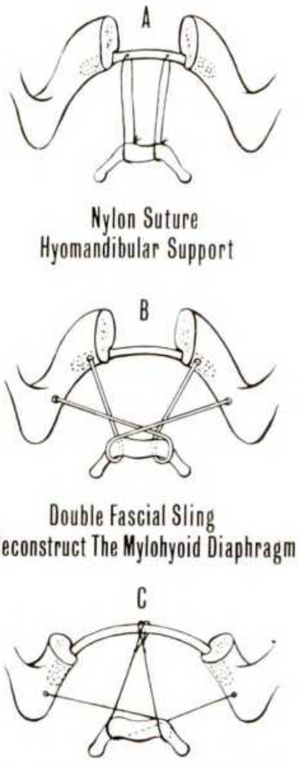


FIG. 28.—The hyomandibular sling.

Table VII.—SITES OF ORIGIN OF TUMOURS

Site of Origin	*No. of Cases*
Tonsillar area	4
Retromolar triangle	13
Lateral arch and mouth floor (includes 3 sarcomas)	34
Central arch and mouth floor	8
Buccal and labial mucosa	11
Tongue	12
	82

Resection of the full thickness of the cheek was needed in 17 advanced lesions. For these patients a deltopectoral flap was used to replace the skin, in addition to the forehead flap. In this group there was marginal necrosis of the deltopectoral flap in 2 patients and partial loss in 1 other patient whose flap was constructed on the ninth postoperative day to deal with secondary haemorrhage from a sloughing neck wound.

In all but 3 of the cases major mandibular resection was required. No immediate replacement was needed in 56 patients. No patient of over 60 years had any form of prosthesis after hemimandibulectomy. Where immediate support was essential, either a twisted wire or a Cook or Bowerman prosthesis was used. An immediate bone-graft was not required by any patient, but several cases have since received definitive iliac crest grafts.

Mortality.—No patient died during the operation or in the first 48 hours. Eight patients died in the later postoperative phase, the cause of death being as follows:—

1. Crusting of the trachea, leading to pulmonary collapse on the third day. Autopsy showed that excision of the tumour was complete.
2. Heart failure and pneumonia.
3. Cerebral damage following ligation of the common carotid artery which was involved by the tumour.
4. Coronary thrombosis.

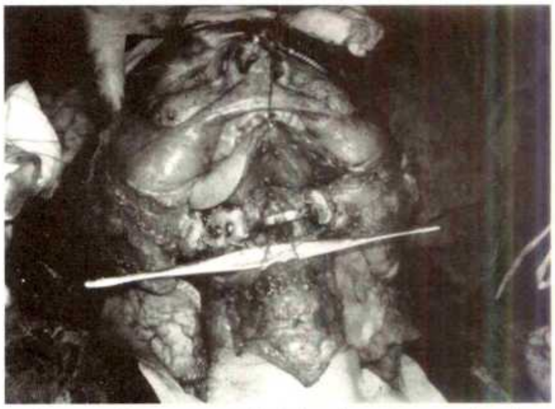


FIG. 29.—Bowerman prosthesis in place after central arch resection. The method of supporting the hyoid is also shown.

5. Coronary thrombosis and aspiration of food. This patient had had a posterior resection and had troublesome dysphagia. We regard this as a preventable death and in such cases, where initial dysphagia is likely, we would now tend to do a gastrostomy at operation.
6. Lung abscess due to aspiration.
7. Death on the fifteenth postoperative day. The cause was obscure but the patient had experienced difficulties with the double deltopectoral flap in relation to his tracheostome. Autopsy was refused.
8. A man of 84 years died of pneumonia after a secondary procedure to resuture his flap.

Status of Survivors and Conclusion.—Although 18 patients have been lost to follow-up and others have been operated on too recently for comment a cautious appraisal is possible. Thirty-nine patients are known to be living with no evidence of disease, including 11 who were operated on 3 or more years ago. This represents a considerable salvaging of patients with advanced disease and in our opinion justifies a continuing trial of radical surgery as the first choice of treatment for tumours involving the lower alveolus.

Acknowledgements.—The authors have the greatest pleasure in acknowledging their grateful thanks to all the other members of the tumour therapy teams at the Westminster Hospital and the Guildford Radiotherapy Centre. The case material presented here is in no sense our own. Patients were, of course, referred to individuals, but all the cases were discussed in joint clinics, where the policies of treatment that we have described were evolved in consultation.

All our colleagues made their cases freely available to us for this presentation. The surgeons include Mr. Gerald Westbury, whose patients contribute largely to this report, and Mr. Kingsley Robinson; the oral surgeons include Mr. John Bowerman and, in the earlier cases, Mr. Peter Cook. We have been fortunate in the high standard of anaesthesia and intensive care afforded by our colleagues of the Magill Department of Anaesthesia—particularly Drs. Wyman, Scurr, Feldman, and Conway, to whom our thanks are due. Almost all the histology has been the work of Professor D. H. Mackenzie, who also attended most of our joint clinics. The radiotherapists, especially Mr. T. M. Prossor and Dr. K. A. Newton at the Westminster Hospital, and Mr. J. J. Richmond and Dr. Helen Mellor at Guildford, merit our special thanks. We are fully aware of the superb quality of the radiotherapy practised at both centres, and are happy to express our sense of indebtedness to these colleagues.

It has been a matter of pride to us over the years that each patient's treatment has been decided by consultation and agreement, and has never been determined by the particular doorway through which the patient was referred to the hospital. For this tradition we owe an immense debt of gratitude to our former teacher and colleague, skilled both in surgery and radiotherapy, Sir Stanford Cade.

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BACTERIAL FLORA IN THE DUODENUM OF PATIENTS AFTER BILIARY FENESTRATION

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Summary

Fasting duodenal aspirates were studied in 15 patients with a biliary fenestration, 5 patients with a single duodenal diverticulum, 1 patient with a biliary fenestration and duodenal diverticulum, and 11 control subjects. A colonic type of bacterial flora, consisting of coliforms, *Clostridium welchii*, and *Streptococcus faecalis*, was found in 10 patients with biliary fenestration, 4 patients with a duodenal diverticulum, the patient with a fenestration and duodenal diverticulum, and in 1 of the control subjects. A high incidence of deconjugation of bile-salts (10 out of 15 patients) and of steatorrhoea (8 out of 15 patients) was noted in the patients with biliary fenestration, as well as in those with a duodenal diverticulum (5 and 3 patients out of 5 respectively). Above-normal serum-folate levels were observed in 3 subjects with coliform colonization.

It is possible that vague abdominal symptoms which may be experienced by patients after biliary fenestration, may be due to the presence of an abnormal bacterial flora in the duodenum.

Biliary fenestration is usually performed in an attempt to avoid postcholecystectomy complications. The operation involves an anastomosis between the common bile-duct and the first part of the duodenum (Magarey, 1966, 1971). It is possible that stasis in the portion of bile-duct distal to the anastomosis may result in the development, or perpetuation, of an abnormal bacterial flora.

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This study compares the bacterial flora in the duodenal aspirate of patients who had undergone biliary fenestration with the flora obtained from patients with a single duodenal diverticulum and with that of control subjects.

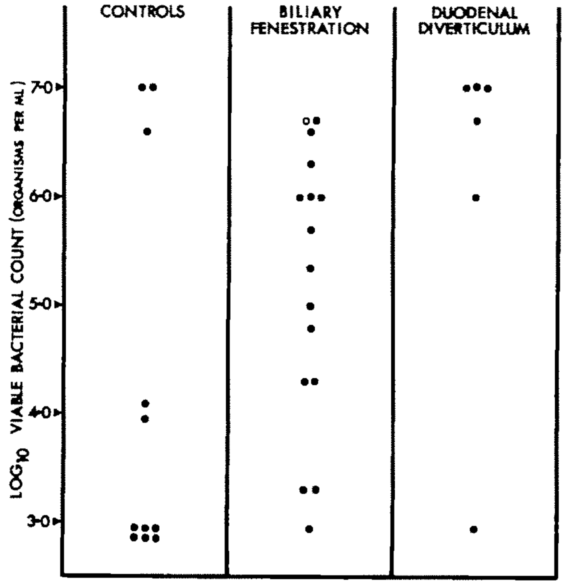

FIG. 1.—Concentration of bacteria in the duodenal aspirates plotted against a logarithmic scale. O, Biliary fenestration and duodenal diverticulum.

MATERIALS AND METHODS

Patients.—Fifteen patients with a biliary fenestration, 5 patients with a duodenal diverticulum, and 1 patient with both a duodenal diverticulum and biliary fenestration were studied.

Forty subjects were selected at random from a total of 448 subjects who had undergone biliary fenestration (Magarey, 1971). Of the 40 patients, 15 agreed to take part in the study. The 15 patients included 11 who complained of intermittent, mild, right hypochondrial pain, dyspepsia, malaise, and diarrhoea; the remaining 4 patients were asymptomatic. The mean age in this group was 55 years (range 40–73 years) and there were 4 males and 11 females. The mean period since operation was 7 years (range 6 months to 10 years).

The operative findings in the 15 patients were: proven cholecystitis (14), cholelithiasis (11), choledocholithiasis (3), and biliary cirrhosis (1). The common bile-duct was stated to have been dilated at laparotomy in 6 patients. There was macroscopic suggestion of pancreatitis in 2 patients. One patient in the series had no evidence of biliary-tract disease. Bacteriological studies were not performed on the gall-bladder or the bile-duct.

The 5 patients with a duodenal diverticulum included 3 who had mild upper abdominal discomfort and diarrhoea. In each case the diverticulum was situated on the pancreatic side of the second part of the duodenum and was approximately 3 cm. in diameter. The mean age of the 3 males and 2 female was 76 years (range 70–88 years).

The patient with biliary fenestration and duodenal diverticulum was a female aged 70 year who was investigated for intermittent diarrhoea.

The 11 control subjects (5 males and 6 females consisted of staff of the hospital. The mean age wa 28 years (range 18–41 years).

Methods.—A sample of duodenal aspirate wa obtained from fasting subjects through a steril open-ended tube which was positioned in th duodenum under fluoroscopic control.

Bacteriological Methods.—In all instance cultural studies were initiated within half an hour o obtaining the sample.

Culture.—Serial dilution of the aspirate was mad in thioglycollate broth. Blood-agar plates were the inoculated with 0·1 ml. of these dilutions an incubated aerobically and anaerobically at 37° C for 48 hours. Anaerobiosis was obtained b flushing with hydrogen in the presence of a col catalyst.

Another aliquot was centrifuged at 2500 r.p.m. fo 10–15 minutes, and the deposit was examined usin a Gram stain. The deposit was cultured on Mac Conkey plates and, where necessary, on anaerobi Nagler plates.

Bacteria were identified by colonial appearanc and biochemistry, and counts were given as th number of organisms per ml. of the aspirate.

Bile-salt Deconjugation.—Qualitative evidenc of bile-salt deconjugation was obtained by thin-laye chromatography on silicic acid using the solven system outlined by Hofmann (1962).

Serum Folate.—Serum folate was estimated b a modification of a microbiological assay usin *Lactobacillus casei* (Baker, Herbert, Frank, Parshe Hutner, Wasserman, and Sobotka, 1959).

Vitamin-B_{12} Studies.—Serum vitamin B_{12} wa estimated microbiologically, using *Euglena gracilis* i a modification of the method described by Hutne Bach, and Ross (1956). ^{57}Co vitamin B_{12} was used t study vitamin-B_{12} absorption; 8-hour plasma level and 48-hour urinary excretion values were estimate (Coupland, 1966).

Faecal Fat Excretion.—Seventy-two-hour faec fat excretion was estimated by the technique describe by Cammidge, using dried faeces (Varley, 1967).

RESULTS

The results of all the investigations are shown i *Table I.*

Bacteriological.—The bacteria isolated from th duodenal samples are listed in *Table II.* Culture wa sterile in 6 control subjects and in 2 patients: 1 wit biliary fenestration and the other with a diverticulum Coliform organisms were isolated in only 1 contr subject, but coliform bacilli (14 patients), *Cl. welch* (4 patients), and *Str. faecalis* (2 patients) wer predominant in patients (*Table I*). The concentra tion of bacteria in the duodenal aspirates has bee plotted against a logarithmic scale in *Fig.* 1. On patient (*Case* 23) had been treated 2 months befor investigation for acute cholangitis complicated b coliform septicaemia; duodenal intubation at th time showed 1×10^8 coliform organisms per m (*Table I*).

Bile-salt Deconjugation (*Table I*).—Thin-layer chromatography demonstrated unconjugated bile-salts in the duodenal juice of 10 patients who had undergone biliary fenestration. In this group duodenal aspirates grew coliform organisms (7 patients), *Streptococcus viridans* (3 patients), *Str. faecalis* (2 patients), and *Cl. welchii* (1 patient).

All 5 patients with a duodenal diverticulum were found to have deconjugated bile-salts in their duodenal aspirate. Coliform organisms were cultured from the duodenal aspirates of 4 patients and *Cl. welchii* from the aspirates of 2 patients; the aspirate from 1 patient was sterile. The patient with a biliary fenestration and a duodenal diverticulum had deconjugated bile-salts in her duodenal aspirate, and both coliform organisms and *Cl. welchii* were grown on culture.

Deconjugated bile-salts were not found in the duodenal aspirates from the control subjects.

Serum Folate.—The mean serum-folate level in patients with biliary fenestration or a duodenal diverticulum did not differ appreciably from that in the control group. However, all 3 patients with folate levels higher than those of the control subjects had coliform colonization of their duodenum.

Serum Vitamin B_{12} and Vitamin-B_{12} Absorption.—A low serum vitamin-B_{12} level and impaired absorption of vitamin B_{12} was found in an 88-year-old male, who had a duodenal diverticulum and a coliform

Table I.—RESULTS OF THE INVESTIGATIONS PERFORMED IN THE PRESENT SERIES

CASE NO.	PERIOD SINCE OPERATION	AGE AND SEX	SYMPTOMS	ORGANISM WITH VIABLE COUNT (log 10 per ml.)	BILE-SALT DECONJUGATION	SERUM FOLATE (mμg. per ml.)	SERUM B_{12} (μμg. per ml.)	^{57}Co VITAMIN B_{12} (per cent excretion in 48 hr.)	72-HOUR FAECAL FAT OUTPUT (g.)
Controls									
1		32 F.	*	Diphtheroids 8×10^3 *Staph. albus* 1×10^3	—	2·5	780	†	21·5
2		41 F.	*	Sterile	—	5·0	600	†	21·0
3		22 M.	*	Sterile	—	11·0	630	†	15·4
4		23 M.	*	Sterile	—	4·5	1000	†	17·2
5		18 F.	*	Sterile	—	7·4	850	†	20·2
6		33 F.	*	Sterile	—	5·7	860	†	15·2
7		23 M.	*	Coliforms 4×10^3 *Str. viridans* 8×10^3	—	9·0	950	†	20·1
8		22 F.	*	*Str. viridans* 1×10^7 *Staph. albus* 1×10^5	—	6·9	1080	†	16·2
9		37 F.	*	*Str. viridans* 4×10^6	—	4·2	520	†	10·2
10		23 M.	*	Sterile	—	6·8	1600	†	6·9
11		31 M.	*	*Str. viridans* 1×10^7	—	1·9	550	†	20·3
Biliary fenestration									
12	9 yr.	44 F.	—	Coliforms 5×10^4 *Str. viridans* 1×10^4	—	2·8	700	28·4	2·9
13	8 mth.	55 F.	—	Coliforms 2×10^4	+	14·1	970	40·3	25·7
14	6 yr.	50 F.	—	*Str. viridans* 2×10^{10}	+	8·5	740	26·3	47·7
15	> 10 yr.	60 F.	—	Coliforms 1×10^6	+	8·1	450	14·6	34·3
16	> 10 yr.	52 F.	—	*Str. viridans* 2×10^6	+	9·9	1180	22·4	31·2
17	> 7 yr.	57 M.	+	*Str. viridans* 2×10^6 *Str. faecalis* 2×10^6	+	6·3	350	14·3	24·9
18	10 yr.	58 F.	—	Coliforms 1×10^6	+	8·0	450	19·8	35·0
19	> 10 yr.	74 M.	+	Coliforms 5×10^5	+	10·1	460	25·7	34·5
20	8 yr.	47 F.		*Str. viridans* 2×10^3	+	3·5	840	14·7	29·9
21	2 yr.	40 F.	+	Coliforms 3×10^6 *Str. faecalis* 2×10^6	+	5·5	500	11·1	3·2
22	9 yr.	73 M.	—	Coliforms 1×10^5	+	11·6	950	29·1	15·0
23	5 yr.	48 F.	+ +	Coliforms 2×10^5 *Cl. welchii* 2×10^4	+	5·9	1120	23·3	7·3
24	8 yr.	58 F.	+	Coliforms 2×10^4	—	8·8	970	13·8	7·3
25	> 10 yr.	55 F.	—	*Str. viridans* 2×10^3	+	9·8	1550	30·1	8·3
26	6 mth.	55 M.	—	Sterile	—	6·3	700	23·3	19·9
Duodenal diverticulum									
27		75 M.	+	Sterile	—	1·7	560	‡	29·3
28		77 F.	+	Coliforms 1×10^7 *Cl. welchii* 6×10^4	+	4·3	300	16·4	26·0
29		88 M.	—	Coliforms 1×10^7	+ + +	21·3	100	4·08	17·0
30		70 F.	+	Coliforms 1×10^6	—	5·2	880	24·7	20·9
31		70 M.	—	Coliforms 1×10^7 *Cl. welchii* 4×10^6	+ +	6·8	640	18·5	26·4
Biliary fenestration and duodenal diverticulum									
32	7 yr.	70 F.	+ +	Coliforms 5×10^8 *Cl. welchii* 3×10^4	+	7·6	850	21·6	57·4

* Symptoms were nil. † Not performed. ‡ Not done.

Table II.—FREQUENCY WITH WHICH BACTERIAL SPECIES WERE ENCOUNTERED

BACTERIA	CONTROL GROUP (11 patients)	BILIARY FENESTRATION GROUP (15 patients)	DUODENAL DIVERTICULUM GROUP (5 patients)	BILIARY FENESTRATION AND DUODENAL DIVERTICULUM (1 patient)
Coliforms	1	9	4	1
Cl. welchii	0	1	2	1
Str. faecalis	0	2	0	0
Str. viridans	4	6	0	0
Staph. albus	2	0	0	0
Diphtheroids	1	0	0	0
Sterile	6	1	1	0

count of 1×10^7 organisms in his duodenal aspirate. Vitamin-B_{12} absorption was, however, corrected when the investigation was repeated with intrinsic factor, indicating that the deficiency was not related to the bacterial colonization. All the other patients exhibited normal vitamin-B_{12} absorption.

Faecal Fat Excretion.—Seventy-two-hour faecal fat excretion was above 22 g. in 8 patients with biliary fenestration, in 3 patients with a duodenal diverticulum, and in the patient with a biliary fenestration and a duodenal diverticulum. Faecal fat excretion was below 22 g. in all the control subjects.

DISCUSSION

The operation of biliary fenestration creates an anatomical abnormality of the biliary tract, resulting in a short-circuiting of bile into the duodenum. Stasis could occur in the portion of bile-duct between the anastomosis and the sphincter of Oddi. It is also possible that this stasis may result in persistence of preceding infection in the biliary tract secondary to past or persisting biliary obstruction (Scott and Khan, 1967) or choledocholithiasis (Elkeles and Mirizzi, 1942; Flemma, Flint, Osterhout, and Shingleton, 1967).

Fourteen out of 15 patients who had had biliary fenestration have been shown to have bacterial contamination of the duodenal content. In 10 of these patients the type of bacterial colonization of the duodenum (coliform organisms, *Cl. welchii*, and *Str. faecalis*) differed from that cultured from the control subjects, and resembled more closely the type of organisms found in the patients with a duodenal diverticulum. A similar colonic type of bacterial flora has been observed previously in duodenal diverticula (Goldstein, Cozzolino, and Wirts, 1963; Goldstein, Wirts, Salen, and Mandle, 1969; Gorbach and Tabaqchali, 1969; Drasar and Shiner, 1969), and in the blind-loop syndrome (Tabaqchali, Okubadejo, Neale, and Booth, 1966; Scott and Khan, 1968). This suggests that a situation similar to duodenal diverticulosis may occur after biliary fenestration. However, 3 patients with fenestration and 5 control subjects exhibited duodenal bacterial cultures of streptococci and staphylococci, as has been observed by Donaldson (1964), Kalser, Cohen, Arteaga, Yawn, Mayoral, Hoffert, and Frazier (1966), Donaldson, McConnell, and Deffner (1967), Gorbach, Plaut, Nahas, and Weinstein (1967), and Drasar, Shiner, and McLeod (1969).

There was a difference between the mean ages of the patients and the control group, but it seems to us unlikely that the older ages of the patients would be responsible for the abnormal bacterial colonization which was found in such a high proportion of the patient group (15 out of 21 patients).

Bacterial colonization with *Str. faecalis* or *Cl. welchii* may be responsible for the deconjugation of bile-salts found in the patients with biliary fenestration or a duodenal diverticulum. These organisms have been shown to be able to deconjugate bile-salts (Norman and Grubb, 1955; Maki, 1966; Midtvedt and Norman, 1967; Hill and Drasar, 1968; Shimada, Bricknell, and Finegold, 1969). Free bile-salts were observed in a few patients whose duodenal aspirate did not culture the organisms mentioned above. It is possible that our bacteriological techniques did not isolate an additional species (*Bacteroides*) which is capable of deconjugating bile-salts. The precautions in our modified method were not a strict as those advocated by Drasar (1967), but a rough correlation of the culture results with the Gram-stained smears did not indicate any significant numbers of unidentified organisms.

Biochemical steatorrhoea was found in 7 of the 1 patients who had deconjugated bile-salts in their duodenal aspirates. Bacterial deconjugation of bile-salts results in a lower concentration of conjugated bile-salts, interference with micelle formation, and malabsorption of fats (Tabaqchali, Hatzioannou and Booth, 1968).

No direct relationship was found between the duration of the postoperative period and the levels for bacterial concentration and type of colonization.

The high serum-folate levels found in 3 patients with coliform colonization of the duodenum confirms the observations of Hoffbrand, Tabaqchali, and Mollin (1966), and Hoffbrand, Tabaqchali, Booth and Mollin (1971), who suggested the possible synthesis of folic acid by these bacteria. On the other hand, other workers have found the folate levels to be normal (Mollin, Booth, and Baker, 1957), or low (Cooke, Cox, Fone, Meynell, and Gaddie, 1963) in such circumstances.

In a series reported by Magarey (1971) 105 of 448 patients who had had a biliary fenestration operation experienced subsequent abdominal symptoms. In only 12 of these patients were the symptoms shown to be related to the biliary tract. The 15 patients in the present series were selected 'at random' from the total of 448 patients on their willingness to volunteer for the investigation; it is possible that this willingness might have been influenced by the occurrence of intermittent symptoms.

Demonstration of an abnormal bacterial flora in the duodenum may be the only method of diagnosing infection in the biliary tree (Engstrom, Hellstrom, Hogman, and Lonnqvist, 1971). It is possible that the findings in the present study indicate that vague upper abdominal symptoms after biliary fenestration may, at times, be related to bacterial colonization of the duodenum. This is partly supported by the fact that 9 of the 10 patients with biliary fenestration and colonization of their duodenum with colonic types of bacterial flora suffered from upper abdominal symptoms (*Table I*). However, there were 2 patients with bacterial flora within 'normal limits' who had abdominal symptoms.

Similar colonization of the duodenum may follow other surgical procedures which are performed when the common bile-duct is explored. This possibility has not been assessed in the present study. Consequently, no comparison can be made between the possible effects of these alternative operations and biliary fenestration.

Acknowledgements.—The authors express their appreciation to the Board of the Queen Elizabeth Hospital for permission to publish this study. Dr. N. D. Hicks, Senior Clinical Pathologist, and his staff were responsible for the haematological studies. Dr. M. L. Wellby, Senior Medical Biochemist, and his staff were responsible for the faecal fat estimations.

This study would not have been possible without the co-operation of these two departments.

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STARCH AND INTRAPERITONEAL ADHESION FORMATION

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Summary

A series of experiments on surgical gloves, an animal model, and human biopsies is reported. These studies demonstrate that contamination of the peritoneal cavity is inevitable when starch-precoated gloves are used, and that small doses of starch contamination may be responsible for human intraperitoneal adhesion formation.

Previous publications are reviewed regarding the harmful effects of starch in humans.

In the past 18 months 3 proved cases of starch granulomatosis peritonei have been treated at the Westminster Hospital; 2 of these cases have been recently reported by Colin and Wastell (1971), and this coupled with the clinical interest in this problem has prompted our work on this subject.

Prior to the introduction of starch/magnesium oxide as a dusting powder for surgical gloves in the late 1940's various other substances had been used as glove lubricants and their harmful effects reported. Shattock (1916) reported a silica granuloma on the lip, and Antopol (1933), Germain (1943), Seelig, Verda, and Kidd (1943), Lichtman, McDonald, Dixon, and Mann (1946), Eiseman, Seelig, and Womack (1947), Saxen and Tuovinen (1947), Eberl, George, May, and Henderson (1948), and Seelig (1948), reported granuloma and adhesion formation in the peritoneal cavity caused by talc. It was therefore a relief when Lee and Lehman (1947) reported the development of a starch glove powder that was claimed to be completely absorbed from the peritoneal cavity without ill effect. This work was further substantiated by MacQuiddy and Tollman (1948) and Postlethwaite, McRae, Williams, Deaton, and Cornatzer (1949).

However, it was not long before reports began to appear of experimental studies and clinical observations suggesting that starch powder produced a granulomatous reaction similar to, but of less intensity than, talc.

In animal experiments granulomas have been produced in a variety of species including rabbits, hamsters, and mice (Willand, Masci and Craver, 1954; Ising, 1960; Myers, Deaver, and Brown, 1960; Myllarniemi, 1966). There have also been numerous reports of starch granulomas in humans, intraperitoneal granulomas having been reported by McAdams (1956), Hyden and McClellan (1959), Myers and others (1960), Blair and Blumenthal (1964), McNaught (1964), Bates (1965), Feegan and Beesley (1965), Cox (1970), Mitchell (1970), Colin and Wastell (1971), Nash (1971), and Neely and Davies (1971).

Three cases of intraperitoneal granulomas have been recorded in gynaecological patients not having undergone previous laparotomy (Paine and Smith, 1957; Saxen, Kassinen, and Saxen, 1963), and it is assumed that in these cases starch entered the peritoneal cavity by way of the Fallopian tubes following vaginal examination using starch-coated gloves.

The development of starch granulomas has not been restricted to the abdominal cavity. Ising (1960) reported finding granulomas in 4 E.N.T. cases, in a breast scar, and also following surgery to the leg and vas deferens. Rock (1967) reported starch granulomas in the middle ear and mastoid following stapedectomy.

There would seem to be two problems associated with the contamination of the peritoneal cavity with starch powder as used on surgical gloves. First, there is the development in the postoperative patient of a fever, abdominal pain and distension, ascites, and intestinal obstruction together with multiple granulomas throughout the abdominal cavity at subsequent laparotomy, the condition resembling carcinomatosis peritonei, as described by Bates (1965), Cox (1970), Mitchell (1970), and Nash (1971). Secondly, there is the less well-recognized presence of starch granules in intra-abdominal adhesions and the suggestion that they may be causative in the production of such adhesions (Myllarniemi, Frilander, Turunen, and Saxen, 1966; Sturdy, Baird, and Gerain, 1967).

The glove powder in general use in this country is Biosorb (Ethicon), which is a mixture of starch granules derived from corn starch pretreated with epichlorohydrin to which is added magnesium oxide to prevent clumping of the starch granules. Magnesium oxide alone has also been incriminated as a peritoneal irritant (Saxen and Saxen, 1965; Myllarniemi and others, 1966).

The dangers of starch granules in the peritoneal cavity are well defined but the exact frequency of the problem is uncertain. A series of experiments have been performed to determine whether starch contamination of the peritoneal cavity is inevitable when Biosorb is used as a surgical glove powder. The adhesion-producing effect of starch contamination of the peritoneal cavity alone and when coexistent with peritoneal trauma has been investigated in an animal model.

EXPERIMENTAL METHODS

Glove Experiments.—

1. Five pairs of standard size 6 surgical gloves precoated with Biosorb were taken. Each glove was slapped twice on to a standard 38-mm. laboratory glass slide. The slides were mounted with a cover-slip using XAM (G. T. Gurr) prefiltered through a Seitz filter to avoid contamination. Microscopic examination of the slides was performed using polarized light.

2. A further 5 pairs of similar gloves were washed in separate large bowls of water by sealing the open end of each glove and by immersion below the surface; each glove was then propelled backwards and forwards twenty times in the water. The gloves were allowed to dry and the next day slides were prepared in the same way as above.

3. Five pairs of gloves were washed twice and slides prepared in the same manner.

After preparing the slides, 2·5 ml. of Lugol's iodine were applied to each glove to confirm the presence of residual starch by blue discoloration.

Human Biopsies.—Omental biopsies measuring approximately 2·5 cm.^{2} were taken from 20 patients at the end of a variety of abdominal operations. The specimens were processed, sectioned, and examined under polarized light.

Animal Experiments.—Female Wistar rats were used throughout the study and were subjected to laparotomy via a 2·5-cm. midline abdominal incision. The animals were anaesthetized with ether and the abdominal incision was sutured using silk in all cases. The animals were sacrificed on the seventh day and autopsy specimens were stored in 10 per cent formol–saline. Surgical gloves were not used in the collection of specimens to avoid starch contamination. Specimens were processed, sectioned, and examined by routine microscopy with polarized light.

1. Six animals had 0·01 g. of Biosorb introduced into the abdominal cavity.
2. Six animals had 0·1 g. of Biosorb introduced into the abdominal cavity.
3. Six animals had 0·25 g. of Biosorb introduced into the abdominal cavity.
4. Six animals had 0·5 g. of Biosorb introduced into the abdominal cavity.
5. Six animals had 1·5 g. of Biosorb introduced into the abdominal cavity.
6. Six animals had a 1-cm.^{2} parietal peritoneal defect performed on the lateral abdominal wall and 0·01 g. of Biosorb introduced into the abdominal cavity.
7. Six animals were given a parietal peritoneal defect alone to act as controls.

RESULTS

Glove Experiments.—

1. Examination of the slides from the unwashed gloves showed the presence of multiple starch granules. The granules being birefringent showed the classic 'Maltese cross' appearance when viewed under polarized light. The starch granules were mainly discrete but there was the occasional clump of three to four granules (*Fig.* 1).

2. The gloves that had had one wash still showed the presence of multiple starch granules but there were slightly fewer than in the unwashed group. There were, however, several larger clumps of starch granules present on all the slides.

3. The gloves that had been subjected to two washings still showed multiple starch granules and even more and larger clumps than in the single-wash group (*Fig.* 2).

Human Biopsies.—Of the 20 omental biopsies examined, all showed the presence of starch-granule contamination.

Animal Experiments.—None of the animals that received 0·01 or 0·1 g. of Biosorb showed any evidence of adhesion formation and only 1 animal receiving 0·25 g. developed an adhesion, this being a small omental adhesion to the abdominal incision. However, all the animals receiving 0·5 and 1·5 g. developed a mass of adhesions involving the liver, omentum, and small and large intestines (*Fig.* 3).

The 6 animals with the peritoneal defect plus the introduction of 0·01 g. of Biosorb showed adhesion formation in each animal. The omentum was found to be adherent to the defect in each case and on microscopic examination a granuloma which included starch granules was demonstrated (*Fig.* 4).

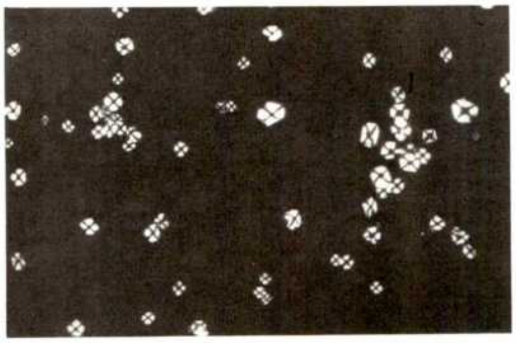

FIG. 1.—Starch granules from an unwashed surgical glove examined under polarized light.

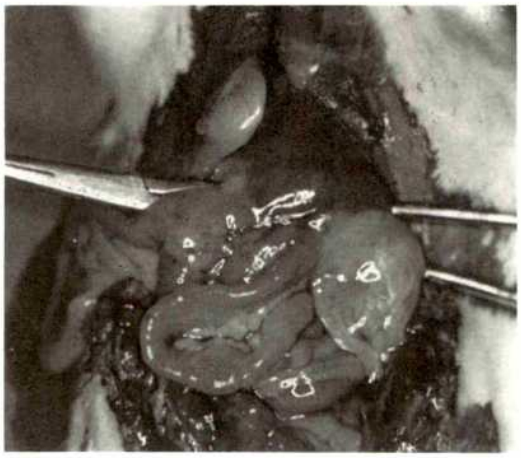

FIG. 3.—Mass of adhesions in an animal having received 1·5 g. of Biosorb intraperitoneally.

The six animals with a peritoneal defect alone showed no adhesion formation to the defect.

DISCUSSION

The standard surgical glove precoated with starch powder would seem inevitably to contaminate the peritoneal cavity with starch granules. Washing the gloves, although reducing the number of starch granules, does not free the outside of the glove from starch. (This finding was confirmed by the use of Lugol's iodine on each glove.) It did, however, cause some clumping of the remaining starch granules, presumably by removing the magnesium oxide in the glove powder. The human omental biopsies taken at the end of laparotomy in a series of patients undergoing abdominal operations also showed starch granules scattered on the serosal surface in every case. It would, therefore, seem to be impossible to avoid some degree of peritoneal contamination when using starch powder in spite of washing the gloves. Perforation of the glove also leads to further contamination and this occurs somewhat frequently; in a series reported by Postlethwaite, Howard, Schanher, and Durham (1949) there was a 16·7 per cent perforation rate in a total of 8893 gloves examined.

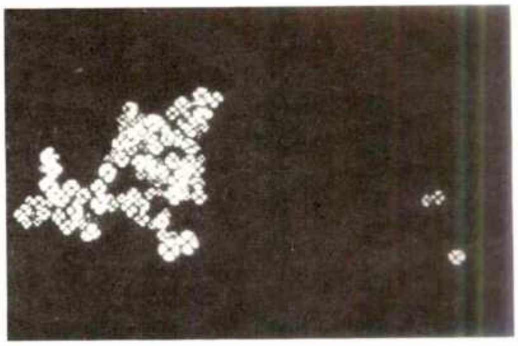

FIG. 2.—A clump of starch granules from a washed surgical glove.

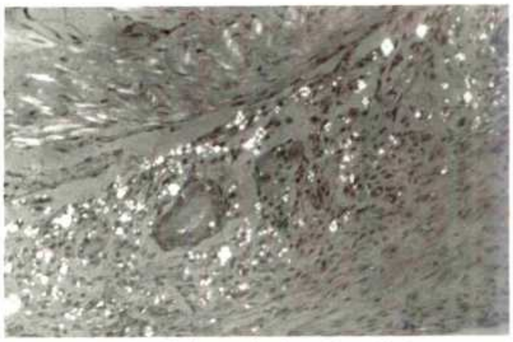

FIG. 4.—Polarized light examination of an adhesion to a peritoneal defect in a rat. Multiple starch granules and a foreign-body granuloma are demonstrated.

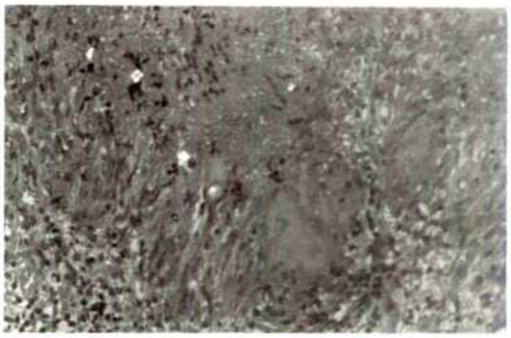

FIG. 5.—Human adhesion biopsy, showing a foreign-body granuloma and starch granules.

The significance of the clumping of the starch granules that occurred after washing is not clear, but it is conceivable that a clump of granules is less easily absorbed and possibly more likely to provoke a foreign-body-type reaction. Lee, Marchall, Collins, and Largen (1952) reported that when lumps of the starch powder were observed, absorption of the powder was delayed and the foreign-body reaction and the adhesions were irreversible. Not every patient develops the acute reaction of granulomatosis peritonei to starch in the postoperative period and the reason for this is not obvious. It has been suggested that a hypersensitivity reaction is to blame, but there is no definite proof of this hypothesis. Intraperitoneal adhesion formation is, however, a serious problem in abdominal surgery and foreign bodies including starch have been incriminated as causative factors in adhesion formation (Adams, 1913; Zachariae, 1954; Bridges, Johnson, and Whitting, 1965). The frequency of starch granulomas in intraperitoneal adhesions requires further investigation. Myllarniemi (1966) was able to show a correlation between dense adhesion formation and the presence of foreign-body granulomas in a series of human adhesion biopsies. We have recently been practising routine biopsy of adhesions and examination under polarized light, and several cases of granulomas in adhesions, with starch granules included, have been demonstrated (*Fig.* 5).

In the animal experiments in this study small amounts of Biosorb (0·01 and 0·1 g.) alone showed no harmful effects, whereas in larger amounts (0·5 and 1·5 g.) adhesion formation occurred in every case. This latter quantity is in excess of any contamination that could occur in a human situation, but nevertheless demonstrates that Biosorb is able to provoke adhesion formation at least in this quantity and in this animal model.

What was interesting was that adhesion formation occurred in all the animals with the small amount of Biosorb (0·01 g.) when coexistent with a peritoneal defect, whereas the defect or Biosorb alone at this dosage failed to produce adhesions. In the human situation injury to the peritoneum and contamination with starch are both inevitable in abdominal surgery, and the combination of these factors may be a more potent cause of intraperitoneal adhesion formation than is at present realized. Following abdominal surgery temporary fibrinous adhesions occur and resolve spontaneously. The presence of a foreign body and granuloma formation may prevent this natural resolution and promote the development of a permanent fibrous adhesion.

The frequency of reports on the harmful effects of starch in the abdominal cavity and the demonstration that contamination of the peritoneal cavity is inevitable when coupled with the high incidence of postoperative intraperitoneal adhesions leave us to question the advisability of using starch-precoated gloves in surgical practice.

Acknowledgements.—We wish to thank Mr. R. Thorley and Miss P. Brock for their technical assistance in the preparation of this article.

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EXPERIMENTAL INVESTIGATION OF THE USE OF CYANO-ACRYLATE ADHESIVE TO PREVENT BILIARY LEAKAGE IN PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY

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SUMMARY

A simple modification of the technique of percutaneous transhepatic cholangiography to prevent leakage of bile or blood has been investigated.

Isobutyl 2-cyano-acrylate monomer has been used to obliterate and seal the tract left when the needle and polythene tube are withdrawn, thus effectively preventing leakage.

PERCUTANEOUS transhepatic cholangiography was first described in 1921 by Burkhardt and Muller in Germany. In 1937 Huard and Do-Xuan-Hop punctured the intrahepatic biliary tree and injected Lipiodol. Carter and Saypol in 1952 used a water-soluble contrast medium. Since then the method has been widely adopted, particularly in South America (Alvarez and Jensen, 1953; Sobredo and Garcia Siguero, 1954).

The number of different techniques described to date suggest that none has been entirely satisfactory, although the method is well established as a very valuable adjunct in the differential diagnosis of the jaundiced patient. All authors agree that the serious hazards in the procedure are bile leakage and biliary peritonitis. Haemorrhage is a secondary hazard. The reported incidence of complications from bile leakage varies from 5 to 50 per cent. The Shaldon modification (Shaldon, Barber, and Young, 1962), introducing a fine polythylene tube over an even finer needle, is regularly used at St. George's Hospital, London. The investigation is only

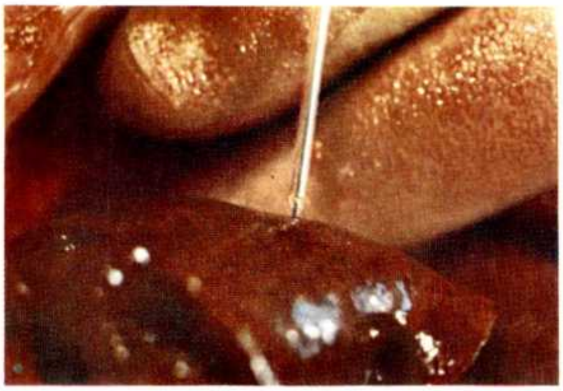

FIG. 1.—Introduction of the catheter.

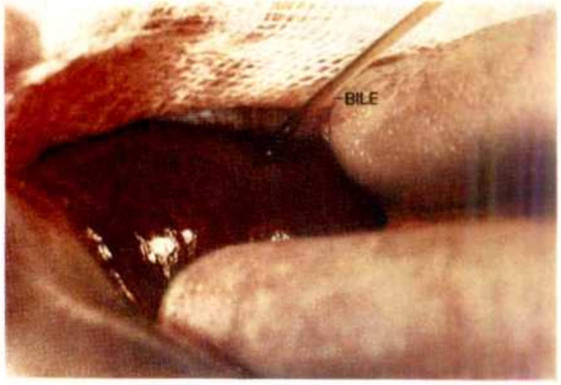

FIG. 2.—Aspiration of bile after withdrawal of the needle.

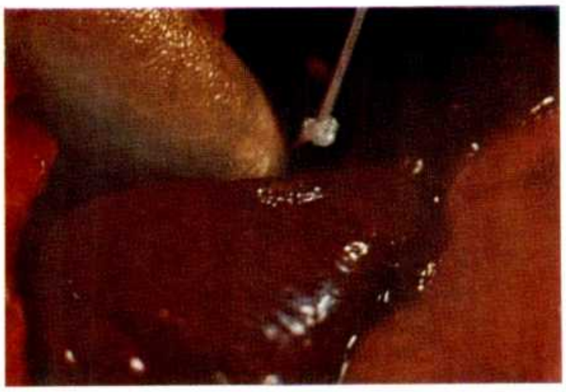

FIG. 3.—Simultaneous withdrawal of the catheter and injection of IBC-2.

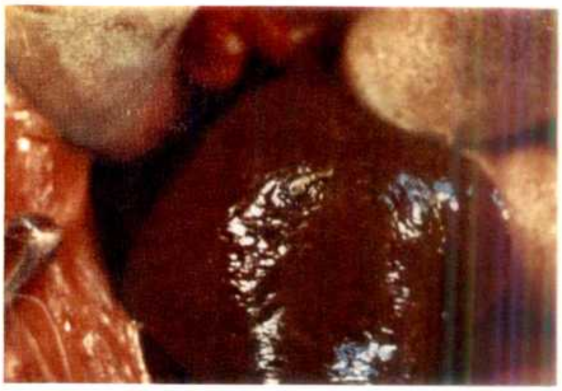

FIG. 4.—After removal of the catheter the tract left by it in the liver is totally obliterated by IBC-2.

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performed immediately before the operation. This principle is widely accepted because of the hazards mentioned above.

Experimental work has been carried out to test the possibility of using isobutyl-2-cyano-acrylate monomer (IBC-2) to obliterate completely the tract left behind by the introduction of the needle and catheter, thus totally preventing leakage of bile or blood.

MATERIALS AND METHODS

Twelve rabbits were operated upon and their common bile-ducts ligated. The rabbits weighed an average of 3 kg. General anaesthesia was used. At the end of the fourteenth postoperative day transhepatic cholangiography using Shaldon's modification (Shaldon and others, 1962) was performed either percutaneously (4 animals) or under direct vision (8 animals).

After the successful introduction of the catheter (*Fig.* 1) the needle is withdrawn and continuous aspiration of bile performed (*Fig.* 2); 8–10 ml. of 45 per cent Hypaque are introduced as the contrast medium. Aspiration of the Hypaque from the bile-duct system is not necessary, as more radiographs can be taken later on for further information if needed.

When the cholangiography is finished, a clean plastic syringe is attached to the end of the plastic catheter.

Stage A: A slight retraction of the polyethylene tube is made, thus removing the tube from the biliary-duct system. Aspiration with the clean syringe must show no trace of bile.

Stage B: Simultaneous withdrawal of the polyethylene tube and injection of the IBC-2 are performed (*Fig.* 3). The tract in the liver substance left behind by the tube is totally obliterated by the cyano-acrylate adhesive (*Fig.* 4).

RESULTS

No operative or postoperative complications occurred. In all 12 rabbits the method proved reliable and effective. The monomer satisfactorily obliterated the site of the needle puncture, and in no instance was there bile leakage, even with external pressure applied to the liver.

DISCUSSION

Cyano-acrylate monomers have been extensively investigated by several workers, and the tissue reaction to these substances has been studied. They have also been cautiously used in some surgical operations.

The response of liver tissue to cyano-acrylates is a localized acute inflammatory reaction. Degeneration or necrosis of the liver tissue in contact with the polymer is slight (Ota and others, 1968). Infiltrating cells are giant cells and lymphocytes. Within a wee after the application a fibrinous membrane is see covering the polymer, and 2 months afterwards thi membrane becomes fibrous.

The biodegradability of this polymer has bee studied with special staining techniques using oil re O, osmic acid, and Nile blue sulphate (Pani, Gladieux and Brandes, 1968). The removal of the polymer i very gradual. It has been reported to be still demonstrable in small amounts for up to 2 years.

The mild histotoxicity of cyano-acrylates is not very serious limitation to the proposed use of thi material since the polymer plug can be removed i those cases where operation is performed.

The factor of carcinogenicity must be borne i mind as no report of very long-term observation is ye available.

In the experiments reported the use of cyano acrylate monomer has proved an effective method o preventing bile leakage or haemorrhage. The metho itself has been shown to be experimentally saf provided that the polyethylene tube is withdraw from the bile-duct system (as shown by aspiration before the monomer is introduced.

Acknowledgements.—The continuous help an assistance of Professor David Slome, the Bernar Baron Professor of Applied Physiology of the Roya College of Surgeons of England, and Mr. Rodne Smith, Consultant Surgeon, St. George's Hospital London, are gratefully acknowledged.

The adhesives were generously supplied b Ethicon, Edinburgh.

The author is also grateful to the Institute of Basi Medical Sciences of the Royal College of Surgeons o England for the grant which made this research wor possible.

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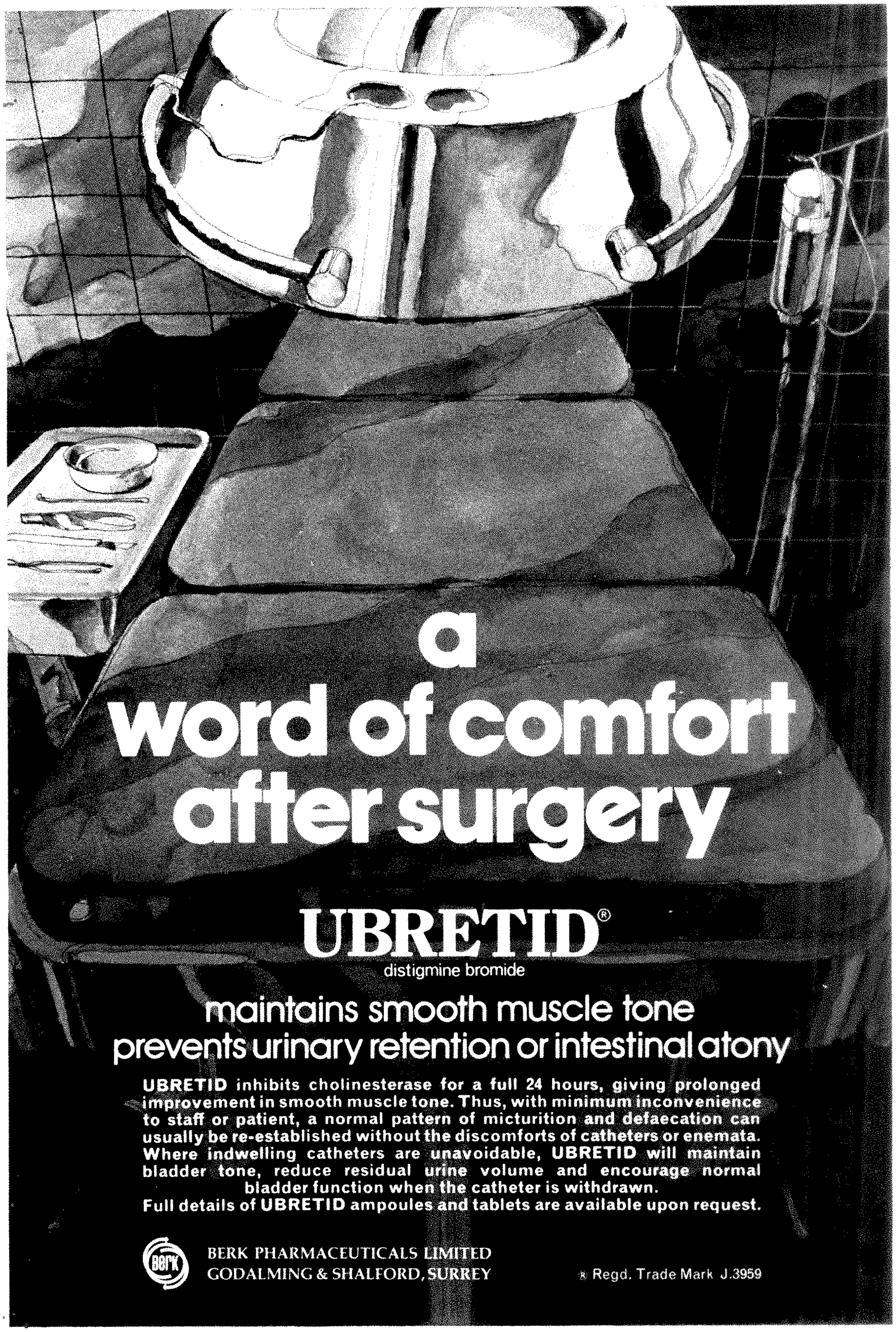

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KOCHER'S PERAMPULLARY APPROACH FOR COMMON BILE-DUCT CALCULI

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SUMMARY

Supraduodenal choledochotomy for common bile-duct stones carries the risk of biliary leakage, a predilection to stricture, and no certainty that all the stones are removed. Stones left behind after the first exploration and new stones formed later require secondary surgery, which is often difficult and has an even greater risk of serious complications.

Perampullary exploration, on the other hand, does not carry an increased initial risk of death or of the complications of biliary fistulae and retained stones of which none occurred in this series. Late complications of stricture and secondary unpassable stones similarly did not occur.

Neither method is free from the risk of postoperative pancreatitis (1 per cent in this series), but there is no evidence that perampullary exploration carries a greater risk than supraduodenal exploration. Even so, it is considered wise to give propantheline for 72 hours after perampullary exploration to reduce this risk.

It has been suggested that a wide, poorly competent, distal common-duct orifice might predispose to ascending cholangitis. No case in this series developed such cholangitis, nor has any case developed stenosis at the sphincteroplasty which might encourage cholangitis. In fact, in the 3 cases that came to post-mortem examination at intervals of 2 and 3 years the sphincteroplasties were still widely patent. Boulter (1961) suggested that sphincterotomy increased the flow of bile in the physiological pressure range and thus might be an additional benefit from the procedure.

GALL-STONES in the common bile-duct as well as in the gall-bladder are not infrequent in gall-stone disease. Rains (1969) stated that between 4 and 7 per cent of all patients with gall-stone disease have stones in the common duct. In the present series almost 20 per cent had such stones. Their removal by standard methods is not always complete and Glenn (1952) cited a figure of 9·7 per cent of cases needing further surgery, while Hughes, Hannan, and Mulvey (1948) found an incidence of 24 per cent. A single exploration of the common bile-duct was stated by Glenn (1967) to carry a mortality of 6 per cent—a figure that is likely to be compounded if more than one exploration is necessary.

The approach to the common duct through its supraduodenal part is the recommended method in the United Kingdom (Rains, 1969). On the Continent of Europe an approach across the duodenum through the ampulla of Vater is popular. The supraduodenal common duct is prone to stenosis when injured, and, after being opened, frequently needs drainage to the exterior. Drainage of the common duct after perampullary exploration is naturally directly into the duodenum and requires no external drains.

Perampullary exploration would have much to recommend it, provided that it was not more dangerous, more liable to sequelae, or less efficient than the supraduodenal route. The procedure can, moreover, be so arranged that should any stones be left behind or new stones form they can discharge spontaneously into the duodenum without hazard to the patient or need for further surgery.

TECHNIQUE

The method used to explore the common-bile duct in this series is, in essence, that of Kocher (1911) with a sphincteroplasty at the end of the procedure, of the type recorded by Rothwell-Jackson (1968).

The abdomen is opened by any standard method, that of Kocher being used in this series. It is essential that the whole of the second and the beginning of the third parts of the duodenum are mobilized completely as the ampulla of Vater lies farther along the second part of the duodenum than is commonly thought (Cattell and Warren, 1956). If the gall-bladder has not been removed already the cystic duct is defined and ligated close to the gall-bladder. A cholangiogram is now performed by inserting a small catheter into the common duct through the cystic duct. Having proved the presence of stones and their number, the duodenum is opened over the ampulla, which often can be located by gentle palpation. Occasionally it is difficult to locate the ampulla when it is of the flat type. Then the passage of a fine bougie through the cystic duct and down the common duct to cause the ampulla to protrude into the duodenum aids the manœuvre. Of the alternative incisions into the duodenum, a single longitudinal incision along the border has been preferred in this series. A suitable probe is inserted into the ampulla and into the common bile-duct, taking care not to misdirect the probe into the pancreatic duct. The distal common duct is opened along its length, lying within the wall of the duodenum against the probe, with diathermy, to a size sufficient to allow mobile stones to fall into the duodenum and to accept Desjardin's forceps to remove any other stones. It is important to define the pancreatic duct at an early stage lest it be damaged by instruments or sutures placed at the sphincteroplasty. Irrigation of the common duct is performed to be sure that it is clear of stones and 'mud'. If there is doubt, a cholangiogram is made by inserting a fine catheter into the common duct through the ampulla. To prevent back-flow of the contrast medium the lips of the incision into the duct are held together over the catheter with non-toothed tissue forceps.

When the common duct is clear beyond doubt its incised wall is united to the cut duodenal mucosa to form a standard sphincteroplasty, using interrupted sutures of 00 chromic atraumatic catgut. The final opening into the duodenum must be equal in size to the widest part of the common duct so that any new stones which are formed can pass into the duodenum freely. It is not necessary to insert any drains into the common duct.

The duodenum is closed longitudinally in the line of the original incision in two layers; the inner of 0 chromic atraumatic catgut and the outer by 000 silk sutures placed singly close together. The operation is completed by cholecystectomy if the gall-bladder has not been removed previously, and the subhepatic space is drained as appropriate.

Postoperatively nasogastric suction is maintained until clear bile is withdrawn, usually for 48 hours. Propantheline, 30 mg., is given intramuscularly every 8 hours, starting at the end of the operation and continuing for 72 hours to reduce stimulation of the pancreas and to diminish the risk of pancreatitis.

Table I.—CAUSE OF POSTOPERATIVE DEATH IN 107 CASES UNDERGOING PERAMPULLARY EXPLORATION OF THE COMMON BILE-DUCT

Cause of Death	*No. of Cases*
Pancreatitis	1
Acute duodenal ulcer	1
Staphylococcal pneumonia	1
Pulmonary embolism	2
Cardiac infarction	3
Total	8

Table II.—COMPLICATIONS OCCURRING AFTER PERAMPULLARY EXPLORATION OF THE COMMON BILE-DUCT

Complication	*No. of Cases*
Early	
Subhepatic abscess	2
Late	
Recurrent stones	1

CLINICAL MATERIAL

Of 361 cases of gall-stone disease who were treated between 1958 and 1965, 107 (29 per cent) had stones in the common bile-duct; 5 of the 107 had previously had a cholecystectomy when no common-duct stones had been suspected. All the common-duct stones were removed by the perampullary route; 7 cases (6·5 per cent) died in hospital from causes associated with the operation in general (*Table I*).

The remaining 100 cases comprise 71 women aged 22–86 years and 29 men aged 27–78 years. Of these, 1 woman, aged 44, died on the second postoperative day from fulminating pancreatitis, which was proved at autopsy. This patient had had 11 months of recurrent biliary colic, frequently with transient jaundice and, on the occasion that brought her into hospital, pancreatitis. She recovered well from the pancreatitis, the jaundice, disappeared and, after intravenou cholangiography, she was explored 2 weeks afte admission. A single stone impacted in the ampull of Vater was removed. At operation the pancrea was indurated but not actively inflamed. Her initi recovery was uneventful until 48 hours after operation, when she developed fulminating pancreatiti from which she did not recover. It may be tha perampullary exploration of the common duct i inappropriate after pancreatitis. However, in thi series one 60-year-old woman had had precedin pancreatitis severe enough to produce anuria wit added obstructive jaundice and staphylococca pneumonia, yet she recovered from subsequen cholecystectomy and perampullary removal of he common-duct stones 19 days after admission withou event. Similarly 2 other women and 4 men had ha preceding pancreatitis and all recovered from operation without trouble.

Two cases developed subhepatic collections of pu without bile. Both required drainage and bot recovered slowly without subsequent biliary troubl (*Table II*). One woman, who had previously had colostomy after rectal excision, has passed gall-stone through her colostomy on three occasions; altogethe 11 stones were passed, the largest being 6 mm. i diameter. She is known to have a double-barrelle cystic duct–common duct junction and is, presumabl forming new stones in the cystic duct remnant. A the new stones have passed without discomfor jaundice, or pancreatitis. Another woman claims t have had jaundice and to have passed stones pe rectum. Neither her family doctor nor the hospita has seen her during one of these episodes and sh does not have the stones to prove the point. Moreover, intravenous cholangiography shows an apparently normal common bile-duct.

Two cases have had later laparotomies; 1 for diverticulitic stricture of the colon in a woman of 7 and the other a vagotomy for oesophagitis in woman of 65. In both cases examination of th common-duct area showed nothing abnormal.

Three cases have since died from other causes an at necropsy (at 2 years in 1 case and 3 years in th 2 cases) the common duct was found to be empty an to have a wide entrance into the duodenum.

Of the survivors, none has had further biliar disease over a minimum of 6 years and a maximu of 13 years.

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TRAUMATIC RUPTURE OF THE ILEUM

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Summary

Three cases of patients who sustained rupture of the ileum following blunt trauma to the abdomen are reported. The onset of symptoms was delayed for a period which varied between 5 and 12 hours after the injury.

As so many of these patients are either asymptomatic or have minimal symptoms for the first 6 hours after the injury it might be advisable to admit all cases of abdominal injury to hospital for observation.

Laboratory investigations of the haemoglobin, white-blood count, and serum amylase contributed nothing to the early diagnosis of the condition. Plain radiographs of the abdomen show gas under the diaphragm in only 34 per cent of cases of traumatic rupture of the ileum.

Needle aspiration of the abdomen for liberated intestinal contents was not carried out in this series. In other series this procedure was found to be accurate in 90 per cent of cases of traumatic rupture of the small bowel. This is the only investigation which can be regarded as making a useful contribution to the early diagnosis of the condition.

Laparotomy was carried out between 5 and 15 hours after the injury. There was gross contamination of the peritoneal cavity by intestinal contents. This was due in all 3 cases to a single laceration on the antimesenteric border of the bowel. The lacerations were situated at distances varying between 15 and 22·5 cm. from the ileocaecal valve and were between 1·3 and 2·5 cm. in diameter. These were closed using two layers of chromic catgut. The peritoneal cavity was washed out with saline and Noxyflex.

The death of 1 patient in the series occurred 13 hours after the injury and was due to a myocardial infarct. The mortality-rate of 33 per cent for the series is similar to that described in other reports.

ABDOMINAL injuries due to blunt trauma to the abdomen are increasing in number. The majority of these injuries are the result of the large rise in the number of road-traffic accidents and are commonly associated with damage to solid organs such as the liver, spleen, kidney, and pancreas (Counsellor and McCormack, 1935; Hicken and Carlquist, 1944; Fitzgerald, Crawfurd, and DeBakey, 1960; Williams and Yurko, 1966; Hall and Angles, 1969).

The association between blunt trauma to the abdomen and rupture of the small bowel in patients with coexistent inguinal or femoral hernia is well recognized (Aird, 1937; McAdam and Maggregor, 1969). Rupture of the small bowel occurring as an isolated injury following abdominal trauma is extremely rare (Chambers and Card, 1961). Three cases of this type of injury are reported. Attention is drawn to the mortality-rate of 33 per cent which is due to the difficulty and delay in reaching the diagnosis (Hall and Angles, 1969).

CASE REPORTS

Case 1.—A 49-year-old woman tripped and fell on to her back while at home. A few minutes after the accident she began to complain of lower abdominal discomfort. She was seen within 1 hour of the accident by her family doctor. Apart from finding tenderness in both iliac fossae he could detect no other injuries. The patient was not shocked and bowel-sounds were present. The doctor attributed the abdominal discomfort to a possible crush fracture of a vertebra with girdle-type pain.

Twelve hours later the doctor was recalled to see the patient who was in severe pain. She had vomited several times since the accident and examination at this time revealed that she was shocked and had marked abdominal tenderness. The patient was admitted to hospital 14 hours after the accident.

CLINICAL EXAMINATION.—The patient was in severe pain, dehydrated, shocked, and lying motionless. Her temperature was 37° C., pulse 120 per minute, and blood-pressure 90/50 mm. Hg with cold cyanotic peripheries. The chest was clear. The neck and spine were not tender to palpation. There was no bruising of the abdominal wall. Bilateral scars of two previous inguinal herniorrhaphies were noted. The abdomen was distended with guarding and rebound tenderness in all areas. Bowel-sounds were absent. Rectal examination revealed tenderness in the pouch of Douglas. There were no other injuries.

INVESTIGATIONS.—The haemoglobin was 98 per cent, white-blood count 4500 per c.mm., and packed-cell volume 36 per cent. Electrolytes and urea were within normal limits. The serum amylase was less than 250 Somogyi units. A chest radiograph showed partial collapse of the right lower lobe. Supine and erect radiographs of the abdomen revealed no abnormality.

After resuscitation with intravenous saline, plasma, and blood the patient underwent laparotomy.

OPERATION.—The abdomen was opened using a right paramedian incision. The peritoneal cavity was grossly contaminated by intestinal contents. The liver and spleen were intact. The stomach and duodenum were normal. There was a laceration, 2·5 cm. in diameter, on the antimesenteric border of the ileum, 22·5 cm. above the ileocaecal valve. The perforation was sutured in the transverse axis using two layers of chromic catgut. The peritoneal cavity was washed out with saline and Noxyflex. Corrugated drains were inserted into both the upper and lower quadrants of the abdomen. The patient's postoperative recovery was uneventful.

Case 2.—A 51-year-old man, who had previously been well, was admitted to hospital complaining of abdominal pain and vomiting. Six hours prior to admission he had been assaulted after partaking of a large quantity of alcohol. He had been knocked to the ground and kicked several times in the face and abdomen. He had not lost consciousness. Five hours after the incident he began to vomit and complain of severe abdominal pain.

CLINICAL EXAMINATION.—The patient was in severe pain, lying motionless and sweating profusely. His temperature was 37° C., pulse 120 per minute, and blood-pressure 120/70 mm. Hg with cold cyanotic peripheries. The patient had a right periorbital haematoma and a right-sided epistaxis. The neck and spine were not tender to palpation. The chest was clear. There was no bruising of the abdominal wall and no evidence of an inguinal or femoral hernia. The abdomen was not distended, but there was rigidity and widespread rebound tenderness. Bowel-sounds were absent. Rectal examination revealed tenderness in the rectovesical pouch. There were no other injuries.

INVESTIGATIONS.—The haemoglobin was 88 per cent, white-blood count 5200 per c.mm., and packed-cell volume 43 per cent. Electrolytes and urea were within normal limits. The serum amylase was less than 250 Somogyi units. A chest radiograph revealed no abnormality. Supine and erect radiographs of the abdomen showed free gas under the diaphragm.

After resuscitation with intravenous saline, plasma, and blood the patient underwent laparotomy.

OPERATION.—The abdomen was opened using a right paramedian incision. There was gross contamination of the peritoneal cavity by intestinal contents. The stomach and duodenum were intact. There were no lacerations of the liver or spleen. There was a laceration, 2·5 cm. in diameter, on the antimesenteric border of the ileum, 15 cm. above the ileocaecal valve. This was closed in the transverse axis using two layers of chromic catgut. The peritoneal cavity was washed out with saline and Noxyflex. Corrugated drains were inserted into both the upper and lower quadrants of the abdomen.

In the postoperative period the patient was hypotensive and the blood-pressure could not be raised above 70/40 mm. Hg. The patient died 13 hours after the initial injury.

Post-mortem examination, revealed that death was due to a large anterior myocardial infarct.

Case 3.—A 15-year-old girl was referred to the Casualty Department of the Basingstoke District Hospital by her general practitioner. Two hours prior to being seen she had been kicked in the lower abdomen by a horse. Although she was asymptomatic it was decided to admit her for observation.

CLINICAL EXAMINATION.—The patient looked and felt well. Temperature was 37·2° C., pulse 120 per minute, blood-pressure 100/70 mm. Hg with warm peripheries. The chest was clear. There was no bruising of the abdominal wall and no sign of an inguinal or femoral hernia. There was slight tenderness in the right lower quadrant of the abdomen but no guarding or rebound tenderness. Bowel-sounds were present. Rectal examination revealed no abnormality.

INVESTIGATIONS.—The haemoglobin was 95 per cent, white-blood count 8500 per c.mm., packed-cell volume 42 per cent. Electrolytes and urea were within normal limits. The serum amylase was less than 250 Somogyi units. A chest radiograph and erect and supine radiographs of the abdomen revealed no abnormality.

The patient was admitted to the ward. Hourly observations of the pulse and blood-pressure together with 4-hourly observations of the temperature and respiration were carried out. Twelve hours after the original injury the patient began to complain of abdominal pain.

Examination at this time revealed no change in the vital signs. There was, however, widespread tenderness of the right side of the abdomen with guarding and rebound tenderness. Bowel-sounds were now absent and there was extreme tenderness on rectal examination. Laparotomy was therefore undertaken.

OPERATION.—The abdomen was opened using a right paramedian incision. There was slight contamination of the right lower quadrant by intestinal contents. There were no lacerations of the stomach or duodenum and the liver and spleen were intact. There was a large haematoma in the wall of the caecum. A laceration was found on the antimesenteric border of the ileum, 15 cm. above the ileocaecal valve. The perforation was 1·3 cm. in diameter. This was closed in the transverse axis using two layers of chromic catgut. The peritoneal cavity was washed out with saline and Noxyflex. The patient's postoperative recovery was uneventful.

DISCUSSION

The jejunum and ileum sustain damage at or ne
the points of fixation, such as the ligament of Treit
or the ileocaecal valve (Kennedy, 1952). The middl
4 m. of bowel descends vertically along the medi
border of the left psoas muscle into the depths of th
pelvis and is relatively immune to injury (Cottrel
1954).

Rupture of the bowel may be due to crushin
tearing, or bursting injuries. In a crush injury direc
force is applied perpendicularly to the abdomen. Th
bowel ruptures when it is trapped between th
distorted abdominal wall and fixed structures such a
the spine or pelvis. Tearing injuries occur whe
force is applied tangentially to the abdominal wal
The bowel is torn from its attachments and th
mesentery is frequently lacerated. Bursting of th
intestine is associated with an increase in the intra
luminal pressure exerted by fluid or gas caug
between the angulations of the bowel (Counsello
and McCormack, 1935).

The effects of pressure on isolated segments c
fresh human bowel have shown that the intestin
ruptures at a pressure of 7 or 8 lb. per sq. i
(Andrewes, 1911). It has also been shown that whe
the rate of distension was doubled the pressur
required to perforate the bowel was reduced to 4 l
per sq. in. (Burt, 1931). Further investigations hav
revealed that a low pressure acting suddenly on
loop of fluid-filled bowel will produce rupture, b
there will be no harmful effects when the sam
pressure acts on an empty bowel (Geoghegan an
Brush, 1956).

In the present series rupture of the bowel in *Cas*
1 and 3 was probably due to a crush injury. Th
bowel was lacerated when it was forced against th
spine or side-wall of the pelvis. In *Case* 2 the patie
had partaken of a large quantity of alcohol when th
injury was sustained. The laceration of the bow
was probably due to a combination of a crushing an
bursting injury.

When the bowel ruptures, the serosa splits fir
followed by the mucosa. The submucosa is the la
layer to give way (Hertle, 1907). Rupture of the sma
bowel occurs most frequently on the antimesenteri
border (Penberty and Reiners, 1953; McAdam an
Maggregor, 1969). Lacerations of the mesenteri
border occur much less frequently (Aird, 1937
Mufson, 1939; Payson and Mace, 1962). All th
patients in the present series had sustained laceration
on the antimesenteric border of the bowel.

The high mortality of traumatic rupture of th
ileum has been attributed to the difficulties and dela
in reaching the diagnosis. The majority of patient
are either asymptomatic or have minimal symptom
when first seen (Counsellor and McCormack, 1935
Jordan and McAfee, 1963). Two of the patients i
this series (*Cases* 1 and 3) were seen within 3 hours c
sustaining their injuries. One patient (*Case* 1) ha
minimal symptoms while the second patient (*Case*
was asymptomatic. Both patients were thought n
to have sustained serious injury, but after 12 hou
signs of peritoneal irritation were so advanced th
laparotomy was undertaken. The third patient (*Case*
was not seen until 5 hours after the assault. Sig
of shock and peritoneal irritation were by this time s
advanced that laparotomy was considered mandator

The delay in the onset of symptoms and signs is due to the sequence of events which occur following perforation of the bowel. Leakage of the intestinal contents is restricted by evertion of the mucous membrane through the laceration in the wall of the intestine. This has the effect of 'plugging' the hole in the bowel wall. Leakage is also thought to be curtailed by spasm of the circular muscle above and below the level of the perforation (Fraser and Drummond, 1917). The spasm passes off after 5 or 6 hours and peristalsis is resumed. Contamination of the peritoneal cavity then occurs owing to the effluence of intestinal contents through the perforation (Cope, 1914).

If a patient is asymptomatic or has minimal symptoms following trauma to the abdomen there is a danger that the injury might be regarded as being of no importance. This occurred in *Cases* 1 and 3 in the present series. Hall and Angles (1969) have stated that in cases of abdominal trauma with rupture of the bowel there is an immediate reduction or cessation of bowel-sounds. This sign was said to be present even if the patient was asymptomatic and was, by itself, an indication for admission to hospital for observation. In 2 of the patients in this series bowel-sounds were still present 1 and 3 hours after the intestine had been perforated. This sign is of no assistance in attempting to assess the severity of damage to the small bowel.

Laboratory investigations of the haemoglobin, white-blood count, and serum amylase in the present series were within normal limits. These findings are in accordance with those of Shaftan (1960) and confirm the fact that these procedures are of no value in establishing the diagnosis.

Erect and supine radiographs of the abdomen have shown gas under the diaphragm in only 34 per cent of patients with traumatic rupture of the ileum (Duncan, 1956; Williams and Zollinger, 1957). This sign was present in only 1 patient in the present series. These investigations are of limited value in confirming the presence of this condition.

Diagnostic needle aspiration of the abdomen for liberated intestinal contents has been found to be positive in up to 90 per cent of patients with traumatic rupture of the small bowel (Williams and Zollinger, 1957; Williams and Yurko, 1966). This procedure was not used in the present series. It could only have been used with benefit in *Case* 3. In the other 2 patients peritoneal irritation was so advanced that laparotomy was mandatory. This investigation, if used more often, might establish the diagnosis at an earlier stage of the post-injury phase with consequent improvement in the mortality-rate.

Laparotomy with suture of the perforation and peritoneal toilet must be carried out at an early stage if the patient is to survive. Small-bowel perforations have a mortality of 15 per cent when detected within 4 hours, 44 per cent when detected between 4 and 8 hours, and 70 per cent when detected at 12 hours (Wright, Prigot, and Stein, 1948).

The mortality-rate for traumatic rupture of the ileum has decreased over the past 30 years from 60 per cent (Counsellor and McCormack, 1935) to 33 per cent (Hall and Angles, 1969). A greater awareness of the condition together with earlier diagnosis is needed if the mortality-rate is to show further improvement.

Acknowledgements.—I should like to thank the consultant surgeons to the North Hampshire Group of Hospitals for allowing me to report on patients who were under their care. I should also like to thank Mr. J. F. Newcombe, Consultant Surgeon to the Central Middlesex Hospital, for his advice on the writing of this paper.

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INTRAMUSCULAR MYXOMAS

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SUMMARY

Seven cases of intramuscular myxoma are presented. Although these lesions appear to be malignant macroscopically they are in fact benign tumours. They are well recognized and described in the pathology literature, but are not so readily recognized by surgeons.

A COMPREHENSIVE review of 34 cases of intramuscular myxoma was published by Enzinger in 1965. Over the past 2 years 9 cases have been discovered in patients in the Westminster Hospital group. Their presentations were varied and no tumour was diagnosed correctly prior to excision and histological examination. Three of the examples were in patients who did not present in the past 2 years but whose histological slides were reviewed in that time and the diagnosis changed. One of these cases has not been followed up and there are few historical facts available. This case and another which was a chance finding at post-mortem examination will not be described. The present report concerns the remaining 7 cases of intramuscular myxoma.

CASE REPORTS

Case 1.—*Site: Vastus medialis.*—A 63-year-old female presented in 1961 with a swelling in her right thigh which had been present for 18 months. It had not caused pain or limitation of movement. It felt firm and was fixed in the muscle. At operation the tumour was widely excised. Histology showed a spindle-cell tumour in which the cells were very loosely packed and the whole tumour had a myxomatous appearance. These appearances did not suggest aggressive behaviour but the tumour was infiltrating muscle. At the time it was regarded as a fibrosarcoma. Postoperatively the patient was treated with radiotherapy. Ten years after operation there were no signs of recurrence.

The histology has been reviewed within the past 2 years and the opinion is now that it was not a fibrosarcoma but an intramuscular myxoma.

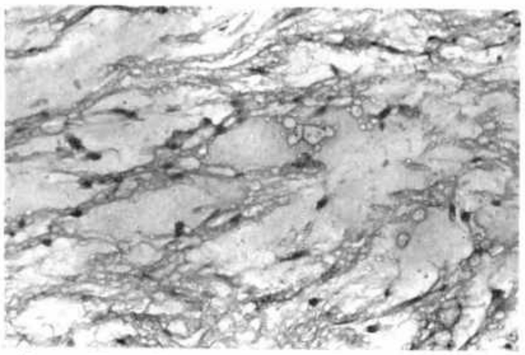

FIG. 1.—*Case* 3. Intramuscular myxoma, showing myxomatous tissue, scattered nuclei, and absence of blood-vessels. H. and E. (× 98.)

Case 2.—*Site: Latissimus dorsi.*—A 73-year-old female presented in 1962 with a swelling in the right side of her neck. On routine inquiry she revealed that she also had a small, painless swelling under her right arm which had been present for 9 months. On examination this second swelling proved to be a firm mass, 3 cm. in diameter, situated in the posterior fold of the right axilla. It was lobulated and had an indefinite margin.

At operation a myxomatous tumour was dissected out of the latissimus dorsi muscle and fat of the axillary fold. It was excised with a wide margin of normal-looking tissue. Histologically it was thought to be a myxomatous tumour, possibly with sarcomatous changes. The patient has been regularly followed up and at 9 years after operation there were no signs of recurrence.

The histology has been reviewed within the past 2 years and a definite diagnosis of an intramuscular myxoma made.

Case 3.—*Site: Gastrocnemius.*—A 65-year-old female presented with a 5-month history of a painless, hard swelling at the back of her right calf which had gradually increased in size. She was otherwise well except for being hypertensive. Clinically there was a well-circumscribed mobile swelling in the superficial muscle of the right calf, approximately 5 cm. in diameter.

At operation there was a swelling in the medial head of the gastrocnemius, measuring 5 × 3 cm. It was excised with a narrow rim of surrounding muscle. During removal the tumour burst and thick white fluid exuded. Histology proved it to be an example of an intramuscular myxoma (*Figs.* 1, 2). There were no signs of recurrence 2 years later.

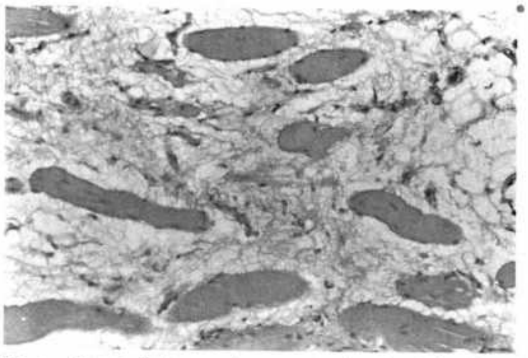

FIG. 2.—*Case* 3. Intramuscular myxoma, showing infiltration of muscle. H. and E. (× 62.)

Case 4.—*Site: Geniohyoid.*—A 44-year-old man presented with a small painless swelling under the chin in the midline, measuring 2 cm. in diameter. It had been present for 8 months and had been troublesome only inasmuch that it interfered with shaving.

At operation the lump was found to be surrounded intimately by muscle of normal appearance. It was excised with a rim of this muscle. Macroscopically it had the appearances of a desmoid tumour, but histology showed it to be an intramuscular myxoma.

The patient made an uneventful recovery and there were no signs of recurrence 18 months postoperatively.

Case 5.—*Site: Rectus abdominis.*—A 54-year-old man was admitted for removal of a small fatty hernia of the linea alba, 2 cm. below the umbilicus, which had been present for 4 months. At operation the lump was excised with a portion of the surrounding rectus sheath. Macroscopically, the lesion was suggestive of a desmoid tumour. Microscopically, it consisted of loose myxomatous tissue containing spindle-shaped and stellate cells. Numerous small blood-vessels were present coursing through the tissue. Mitotic activity was not seen.

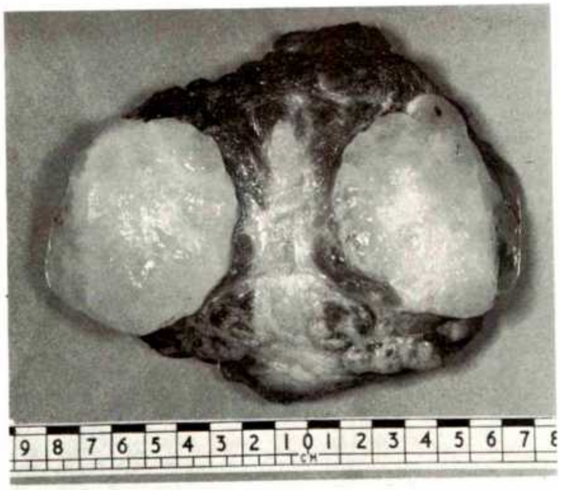

FIG. 3.—*Case* 6. Macroscopic appearance of the tumour.

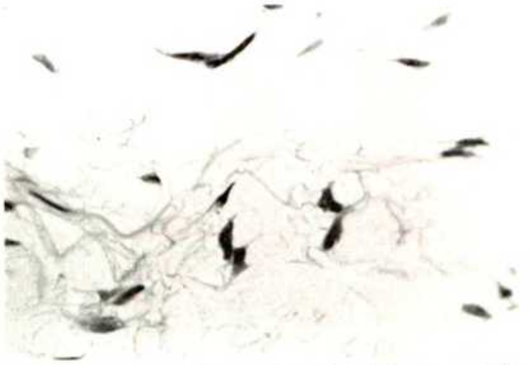

FIG. 5.—*Case* 6. High-power view of typical tumour cells. H. and E. (× 186.)

The tumour was thought to be an atypical intramuscular myxoma as the vascularity was greater than is usually seen. There were no signs of recurrence 2 years postoperatively.

Case 6.—*Site: Gluteus maximus.*—A 73-year-old woman was admitted for a left total hip replacement. Clinical examination revealed a large swelling in the muscles of the left buttock.

At operation through the routine posterolateral incision a large well-circumscribed tumour was discovered within the gluteus maximus muscle. It was 8 cm. in diameter and looked like a well-circumscribed fibrosarcoma (*Fig.* 3). A frozen section was taken and was equivocal, but it was thought that malignant cells were present. A wide excision of the tumour was performed and the wound was closed.

Paraffin sections (*Figs.* 4, 5) showed the lesion to be an intramuscular myxoma. The patient was discharged after 10 days and readmitted 3 months later when a McKee-Farrar arthroplasty was performed. There were no signs of recurrence 1 year later.

Case 7.—*Site: Adductor longus.*—A 45-year-old woman was seen by her general practitioner as she had a small painless swelling on the medial side of her left thigh. She thought that it had appeared after twisting her leg 2 months previously. The doctor diagnosed a haematoma, but as the lump enlarged over the next 4 weeks he referred her to hospital with a diagnosis of possible fibrosarcoma.

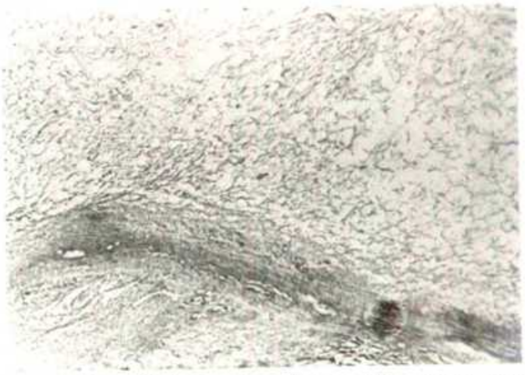

FIG. 4.—*Case* 6. Reticulin stain to show the delicate meshwork of reticulin fibres. H. and E. (× 53.)

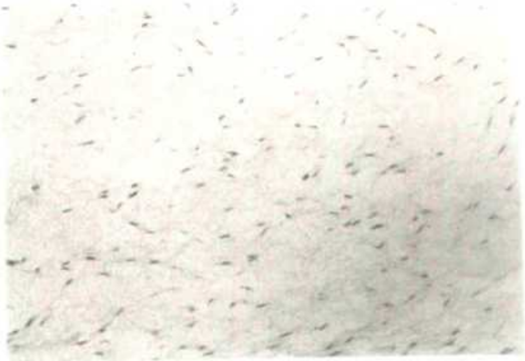

FIG. 6.—*Case* 7. Small numbers of inconspicuous cells scattered in a mucoid stroma. H. and E. (× 53.)

Clinically, there was a non-tender swelling, 4 cm. in diameter, in the left adductor longus which was mobile in the horizontal but not in the vertical plane. The inguinal lymph-nodes were not enlarged.

At operation a swelling within the substance of the adductor longus muscle was discovered. It appeared to infiltrate the muscle locally and it was excised with a rim of normal-looking muscle. Macroscopically, it was an oval cystic lesion measuring 4 cm. in diamater. Histology proved it to be an intramuscular myxoma (*Fig.* 6). There were no signs of recurrence 3 months later.

DISCUSSION

Clinical Presentation.—The sole presenting symptom in all the cases was a painless palpable mass. The interval between the appearance of the tumour and its excision was variable, the average time being 4 months. There was no history of trauma in any of the cases except for 1 patient who had received gold injections in the same area some years ago. All the lesions presented in adults, of whom two-thirds were female.

Pathology.—Macroscopically, the features varied only slightly from case to case. Most of the tumours were rounded masses with a glistening, mucoid, grey/white appearance. On casual examination all were well circumscribed, but closer examination showed them to have infiltrated the adjacent muscle. The size of the different tumours ranged from 2 to 12 cm. in diameter. They appeared in widely differing muscles, although half of them were in the lower limbs.

Microscopically, the tumours were characterized by a small number of scattered inconspicuous cells in abundant mucoid material and a meshwork of delicate reticulin fibres (McKenzie, 1969). In only 1 case was there more than just a sparse vascular network.

Treatment.—The treatment was confined to local excision except in 1 case where radiotherapy was given as the diagnosis was in doubt. There has been no recurrence or metastases in any of the cases, the longest follow-up period being 10 years.

A review of 9 myxomas, of which 7 cases are reported, shows that an intramuscular myxoma is a distinct tumour of benign behaviour. They may resemble mucoid sarcomas, myxoid liposarcomas, and fibrosarcomas. The surgeon must, therefore, be on his guard not to mistake this benign lesion for one o the others mentioned. Frozen sections may b misleading.

Histologically, Stout (1948), Enzinger (1965), an McKenzie (1969) have stated that the precise natur of myxomas is still a matter of controversy. McKenzi (1969) suggested that the myxoma cell may be a altered fibroblast and that transitional forms betwee myxomas and fasciitis may be encountered.

It has recently been reported (Wirth, Leavitt, an Enzinger, 1971) that intramuscular myxomas are a extraskeletal manifestation of fibrous dysplasia. Thi was not evident in any of the cases reported here.

Acknowledgements.—I should like to than Mr. R. Cox for his help with this paper and providin *Cases* 3 and 7; Mr. E. S. Lee for *Case* 2; Mr. B. G Andrews for *Case* 6; Mr. C. Westbury for *Case* 4 Mr. T. M. Prosser for *Cases* 1 and 5. Dr. D. H McKenzie and Dr. J. Earle helped with the patholog and provided the figures.

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EMBRYONIC RHABDOMYOSARCOMA OF THE UROGENITAL TRAC

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SUMMARY

Forty-two cases of embryonic rhabdomyosarcoma of the urogenital tract are reviewed. Their distribution, modes of presentation, clinical features, surgical management, and prognosis are discussed.

EMBRYONIC rhabdomyosarcoma is an extremely malignant tumour of the lower genito-urinary tract which arises from striated muscle. It characteristically presents as a lobular grape-like mass (sarcoma botryoides), an example of which is one of John Hunter's original specimens in the museum of the Royal College of Surgeons of England.

CLINICAL DETAILS

Between 1945 and 1971, 42 patients with embryonic rhabdomyosarcoma of the urogenital tract have been treated at the Hospital for Sick Children, London; 24 tumours arose in the bladder, 9 in the prostate, 3 in the spermatic cord, 4 in the vagina, and 2 in the broad ligament. The median age of the children with bladder tumours was 1 year 9 months, which was significantly lower than that of children with prostatic tumours—3 years and 6 months ($P < 0.05$, Rank sum test)—and also less than that of children with the other types of rhabdomyosarcoma of the urogenital tract (*Fig.* 1). There was no differenc between the sexes in age of presentation.

1. Rhabdomyosarcoma of the Bladder.—O the 24 children with rhabdomyosarcoma of th bladder, 14 were boys and more than 85 per cent wer less than 3 years of age at the time of operation. Th most common first symptom was urinary retentio with strangury due to tumour lobules being pushe down into the posterior urethra. Constipatio occurred in a third of the patients and, in these, recta mucosal prolapse was common. Polyps were passe per urethram in only 2 children and macroscopi haematuria was rare. A baby who was born with th tumour had a distended abdomen, a large tumou arising out of the pelvis, and gross pitting oedema o the lower half of the abdomen and of the right labia The diagnosis could usually be made on clinica grounds when a palpable bladder swelling did no disappear on urethral catheterization. An abdomina tumour was palpable in 22 of the 24 patients afte catheterization. Intravenous pyelography invariabl displayed a dilated upper urinary tract with displacement of the bladder, which contained the characteristic lobulated filling defects (*Fig.* 2).

All the patients were treated by cystectomy wit excision of the posterior urethra in the male and th whole of the urethra in the female, with ileal loo urinary diversion in the later patients in the series. Ureterosigmoid diversion for rhabdomyosarcoma has been disappointing and in the survivors it was later converted to ileal loop diversion. One patient died of cardiac arrest on the operating table; at autopsy a tumour embolus was found occupying the right ventricle and there was tumour thrombus in the inferior vena cava and its pelvic tributaries.

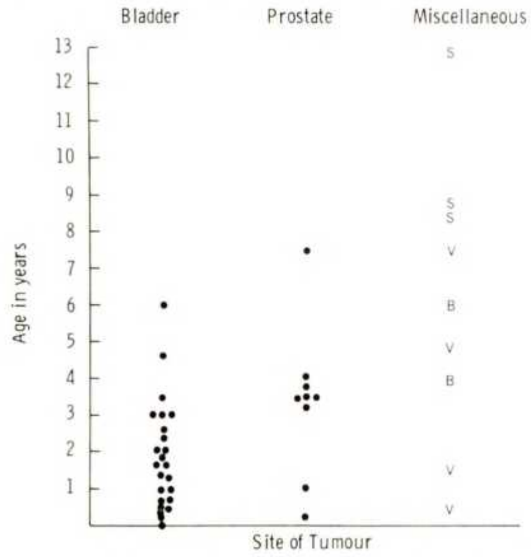

FIG. 1.—Age distribution of children with embryonic rhabdomyosarcoma of the urogenital tract. B, Broad ligament. S, Spermatic cord. V, Vagina.

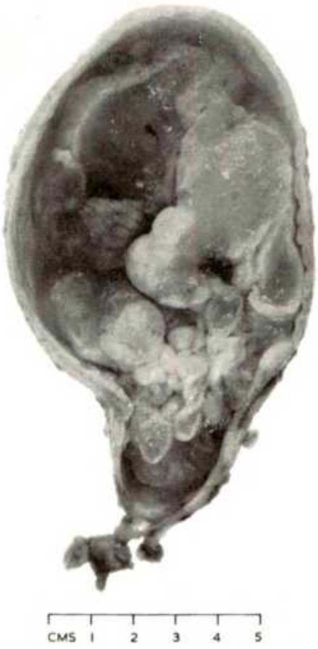

FIG. 3.—Cut section of an embryonic rhabdomyosarcoma of the bladder of the polypoidal type, showing the characteristic polypoidal protuberances in the bladder whose walls are of a normal thickness.

Rhabdomyosarcoma of the bladder has been classified as a polypoid or solid tumour according to the macroscopic appearance at operation or after histological examination. Polypoid tumours (*Fig.* 3) grew principally into the bladder lumen, producing a mass of pearly-grey lobules similar to those which, in the case of rhabdomyosarcoma of the vagina, have been likened to a bunch of grapes (sarcoma botryoides), whereas the solid tumours (*Fig.* 4) grew mainly by extending into the bladder wall, involving the adjacent organs, and, in their late stages of growth, producing a few excrescences into the bladder lumen. There was no significant difference in the age distribution between the polypoid and solid tumours. Seven of the 15 solid tumours occurred in boys as did 7 of the 11 polypoid tumours. Dysuria, pain in

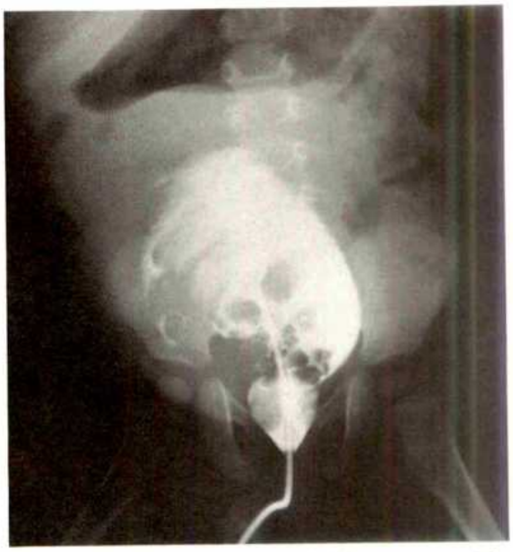

FIG. 2.—Cystogram of an embryonic rhabdomyosarcoma of the bladder, showing the characteristic filling defects in the bladder.

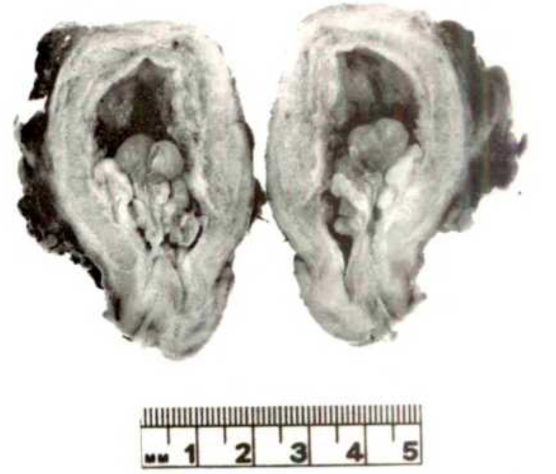

FIG. 4.—Cut section of an embryonic rhabdomyosarcoma of the bladder of the solid type, showing a thick-walled bladder which is involved by the tumour with very few broad-based excrescences.

the lower abdomen, frequency of micturition, and constipation with rectal mucosal prolapse occurred in both varieties, but urinary retention was more common with the polypoid type of tumour. Local recurrence was a constant feature in the patients who died, associated with pulmonary and distant metastases. Of the 24 patients with rhabdomyosarcoma of the bladder who have been operated on since 1945, 11 have survived (for periods of 22, 20, 14, 13, 12, 10, 9, and 5 years, 1 year, and 6 and 3 months, respectively), and in all 11, the tumours were of the polypoid type.

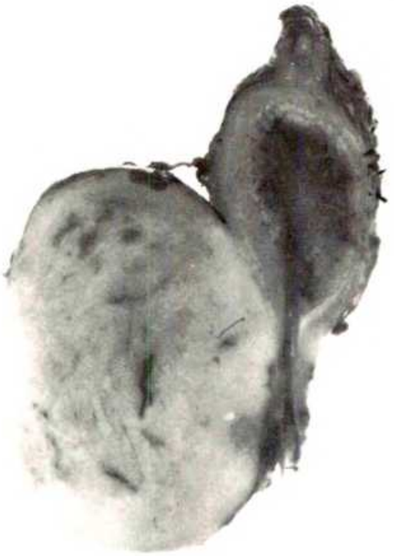

FIG. 5.—Cut section of an embryonic rhabdomyosarcoma of the prostate.

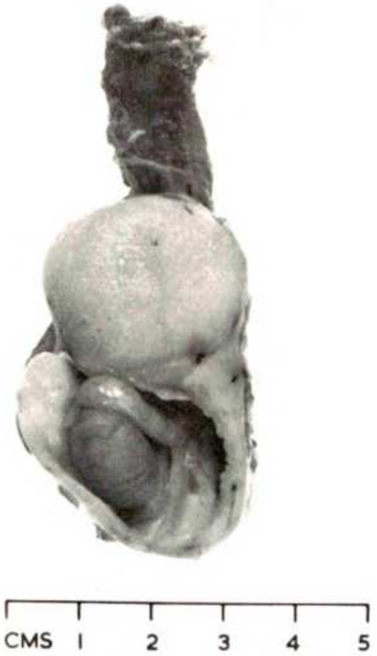

FIG. 6.—Cut section of an embryonic rhabdomyosarcoma of the spermatic cord. There was no involvement of the testis or epididymis by the tumour.

2. Rhabdomyosarcoma of the Prostate (*Fig.* 5).—This tumour usually causes urinary retention at a later age than rhabdomyosarcoma of the bladder, and is accompanied by dysuria, straining on micturition, and dribbling. The median age at the time of presentation was 3 years and 6 months, the youngest patient being 3 months and the oldest 7 years 6 months. The tumour was palpable on rectal examination. Cysto-urethrography helped in revealing the diagnosis, confirmation of which was usually obtained at the time of operation.

Up to 1963, excision of the bladder, prostate, and the posterior urethra was possible in only 3 of the 6 cases and in 2 of these partial excision had been performed at the referring hospital. None of the 6 survived, all having local recurrence followed by distant metastases. Of 3 subsequent patients, suprapubic cystostomy had been performed before referral in 2 as a means of drainage and biopsy. The first child initially did well after excision of the tumour but died 18 months later of local recurrence and distant spread. It is less than a year since the other 2 children had their tumours resected, but at the present time they are thriving and there are no signs of metastases. In both of the longest survivors the tumour recurred 29 months after operation.

3. Rhabdomyosarcoma of the Spermatic Cord.—The common presentation was of a painless lump or lumps in the scrotum, two on the left and one on the right, present for periods of 1 day, 1 month, and 4 months respectively (*Fig.* 6). The lumps were hard or cystic. Orchidectomy with excision of the spermatic cord was performed but lymph-node clearance was not undertaken. In 1 child, because tumour cells were found on histological examination of the veins of the spermatic cord, the testicular vessels were excised up to the level of the renal vein. The para-aortic lymph-nodes were not enlarged. The tunica vaginalis was thickened in all 3 cases, but it was not possible to decide from which para-testicular layer the tumour arose, although it appeared to arise from the tunica in 1 case. One child died within a year of operation without responding to actinomycin D or to radiotherapy, but the other 2 are alive and well 10 years since the time of operation. Both children were given actinomycin D for 10 days postoperatively, and in 1 the course was repeated. These 2 children are probably the longest survivors of this disease.

4. Rhabdomyosarcoma of the Broad Ligament.—Both patients presented with large pelvic lumps. The older girl had severe dysuria and constipation whereas the other had pain in her groin. Intravenous pyelography demonstrated pressure effects of the tumour on the upper urinary tract and a cystogram revealed indentation of the bladder and displacement of the ureters. At operation in both cases a large cystic, very friable, and extremely vascular mass was found arising from the broad ligament. In 1 case this was surgically inoperable and in the other the mass was ruptured on manipulation and was incompletely excised. Postoperative vincristine and radiotherapy did not make any impression on the tumour. Both children died of uraemia within 1 year.

5. Rhabdomyosarcoma of the Vagina.—One 5-month-old child showed typical grape-like masses protruding from the vaginal introitus (*Fig.* 7). The other 3 patients had vulval masses with severe dysuria and considerable vaginal discharge. Two had been treated as vaginitis for prolonged periods of time before a diagnosis was made. The diagnosis of this tumour is based on the demonstration by cystographic and postoperative macroscopic examination of the surgical specimen that the urinary bladder is not involved in the disease. In the youngest child at the time of operation, after the uterus and vagina had been mobilized and the vagina had been opened, it was demonstrated that the tumour was localized to the lower part of the vagina and there was no apparent spread to any other organ. Hence, only vaginectomy was performed and a split-skin graft was applied to the excised defect. In the 6 years since this operation there has been no obvious recurrence of the tumour. In 2 other patients cystectomy, hysterosalpingectomy, and vaginectomy were performed, 1 case also having block dissection of both inguinal lymph-nodes and also removal of the lymph-nodes along the iliac veins. In both patients ileal loop urinary diversion was done. In the fourth patient only biopsy of the tumour was possible as the tumour had metastasized to the lungs. The last 3 patients all died 3 and 2 years and 1 year after operation or biopsy, respectively. There was no response to radiotherapy.

DISCUSSION

There is no agreement about the possible site or sites of origin of rhabdomyosarcoma of the urogenital tract but the following structures have been suggested: Wolffian duct rests, embryonic rests of totipotent cells, misplaced fragments of the embryonic dorsal myotomes, unilateral differentiation in teratomas, and, in the case of the spermatic cord tumours, the cremaster muscle, gubernaculum, and metaplasia from the muscular coats of the vas deferens or epididymis. White (1955) has shown that these tumours are embryonic sarcomata, the tissue consisting of immature mesenchyme which undergoes variable degrees of differentiation to striated muscle, to connective tissue, and possibly to smooth muscle. Some parts of the tumour have a myxomatous structure which does not at first suggest malignancy. In the bladder the growth originates in the submucosal and superficial layers at the base of the bladder and extends down the urethra, right through the membranous portion in the male and the whole length of the female urethra. Ureteric extension is uncommon. Histologically, the tumour is the same whether it arises in the bladder or elsewhere in the urogenital tract. The clinical behaviour of the tumours and their prognosis are very different, the polypoid bladder tumours presenting more often with strangury and urinary retention and having a much better prognosis than the solid variety of bladder rhabdomyosarcoma. This is in complete contrast to the other types, in which, apart from 1 child with vaginal rhabdomyosarcoma and 2 with spermatic cord tumours, all the patients have died from metastases. The tumour recurs locally before there is widespread lymphatic and blood-stream spread, local recurrence being most likely the result of incomplete removal.

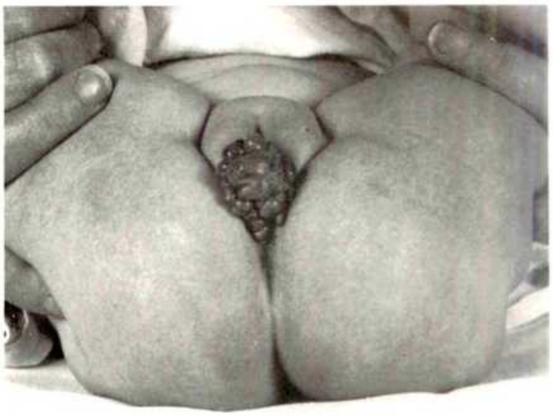

FIG. 7.—Classic sarcoma botryoides in which there are grape-like protuberances of the tumour projecting from the vaginal introitus.

Diagnosis is made on clinical grounds and can be confirmed by endoscopic biopsy. Suprapubic cystostomy should never be performed to obtain a biopsy specimen or for the purposes of temporary urinary diversion. Differential diagnosis is from: (*a*) ectopic ureterocele, especially if complicated by infection or oedema, but the upper-urinary-tract anomaly associated with ureterocele should establish the diagnosis; (*b*) hamartomatous conditions such as neurofibromatosis or haemolymphangioma of the bladder with which there may be associated café-au-lait spots or skin haemangiomas; (*c*) eosinophilic cystitis or cystitis cystica.

Radical lymph-node dissection has not been performed because, apart from spread to lumbar lymph-nodes, there is haematogenous spread to the lungs, kidneys, liver, and bone. Lymph-nodes have not usually been enlarged at the time of operation and microscopic involvement on histological examination has not been a predominant feature in our cases, except with vaginal rhabdomyosarcoma, where spread is early and surgical lymphadenectomy has not been helpful in controlling the disease. Irradiation and chemotherapy have not been helpful in widespread disease or in reducing the incidence of local recurrence. *Figs.* 8 and 9 show the survival periods of the 42 cases of embryonic rhabdomyosarcoma of the urogenital tract in the present series.

Children with prostatic rhabdomyosarcoma presented with signs and symptoms similar to those of adult prostatism. All the tumours were palpable on rectal examination and confirmation of the diagnosis was usually made at the time of operation. Differential diagnosis is from prostatic abscess, in which the child has pyrexia, systemic disturbances, and leucocytosis. Diagnosis can be confirmed by aspiration. The results of treatment of prostatic rhabdomyosarcoma have been disappointing. Of our 9 patients, 5 have died very early after surgery; local recurrence occurred in all 7 cases before distal spread and death ensued. It is less than a year since operation in the remaining 2 cases. These results suggest that surgical extirpation was incomplete and better results may be obtained by a more radical approach.

Arean and Kreager (1965) reviewed 44 patients aged 5–15 years with spermatic cord rhabdomyosarcoma reported in the literature up to 1965. Results were poor, but the 2 survivors in the present series are free of tumour 10 years after surgery. One patient had obvious tumour embolus in one of the veins of the cut end of the spermatic cord. Both were given actinomycin D postoperatively.

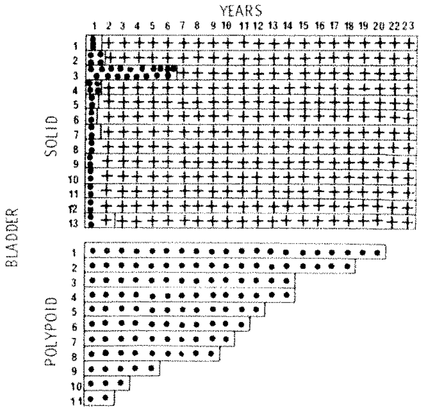

FIG. 8.—Survival times of children with embryonic rhabdomyosarcoma of the bladder. ●, Alive. +, Dead.

One of the characteristic features of rhabdomyosarcoma of the vagina appears to be spread of the tumour to the lymph-nodes, although lymphadenectomy has not improved results. The other feature is its presentation as grape-like masses protruding from the vaginal introitus (sarcoma botryoides). The 5-month-old child who had a simple restricted vaginectomy is alive 6 years after surgery, whereas the other 3 patients died following local recurrence and distant metastases. Earlier diagnosis and treatment may provide long-term survivors. Vaginal discharge in the very young should always be investigated.

Chemotherapy and radiotherapy have not been used prophylactically, except when there has been doubt about complete excision of the tumour. Neither treatment has substantially altered the prognosis although in cases with local recurrence there has been some temporary relief of symptoms. Sutow, Sullivan, Reid, Taylor, and Griffith (1970), reviewing survival data on 78 children with rhabdomyosarcoma (orbit 15, head and neck 31, extremities 8, sarcoma botryoides 5, genito-urinary other than vagina 7, others, 12), indicated that age, histology, primary site, extent of disease, and treatment each had a significant influence on the prognosis. The best survival occurred in patients with sarcoma botryoides and in children less than 7 years of age and the poorest with alveolar rhabdomyosarcoma.

CONCLUSIONS

Polypoidal bladder tumours have a better prognosis than any of the other varieties of rhabdomyosarcoma of the urogenital tract. The solid bladder and prostatic tumours may do better with wider excision to include possible extra-bladder and extra-prostatic extensions of the tumour. Our patients with spermatic cord tumours have survived for long periods after excision of the tumour together with the cord, testis, and epididymis. Vaginal tumours may do better if diagnosed and treated earlier. Reviewing our cases it is apparent that if local recurrence has not occurred in bladder rhabdomyosarcoma within the first 2 years after surgery the patient has probably been cured. This was so in all our cases, except 1 in whom recurrence was noted 6 years after surgery. Local recurrence usually occurs within the first postoperative year followed rapidly by distant lymphatic and haematogenous spread. Hence, it would seem logical that to improve our results we would have to diagnose these tumours earlier, before they are surgically inoperable, and then to perform radical surgery to extirpate the tumour and its possible sites of recurrence, especially as the tumour when it recurs is not responsive to chemotherapy and irradiation.

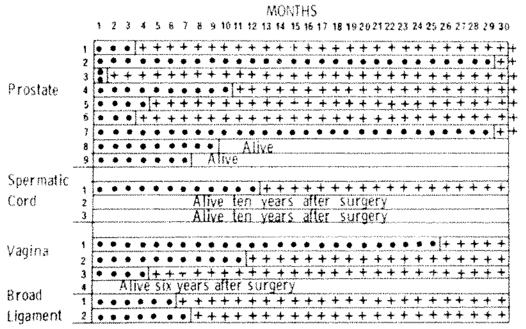

FIG. 9.—Survival times of children with embryonic rhabdomyosarcoma of the prostate, spermatic cord, vagina, and broad ligament. ●, Alive. +, Dead.

Acknowledgements.—I am very grateful to Mr. D. I. Williams, Mr. D. J. Waterson, and Mr. H. H. Nixon for permission to study the patients under their care, and to Professor A. W. Wilkinson and Dr. T. M. Barratt for helpful criticism in the construction of this paper.

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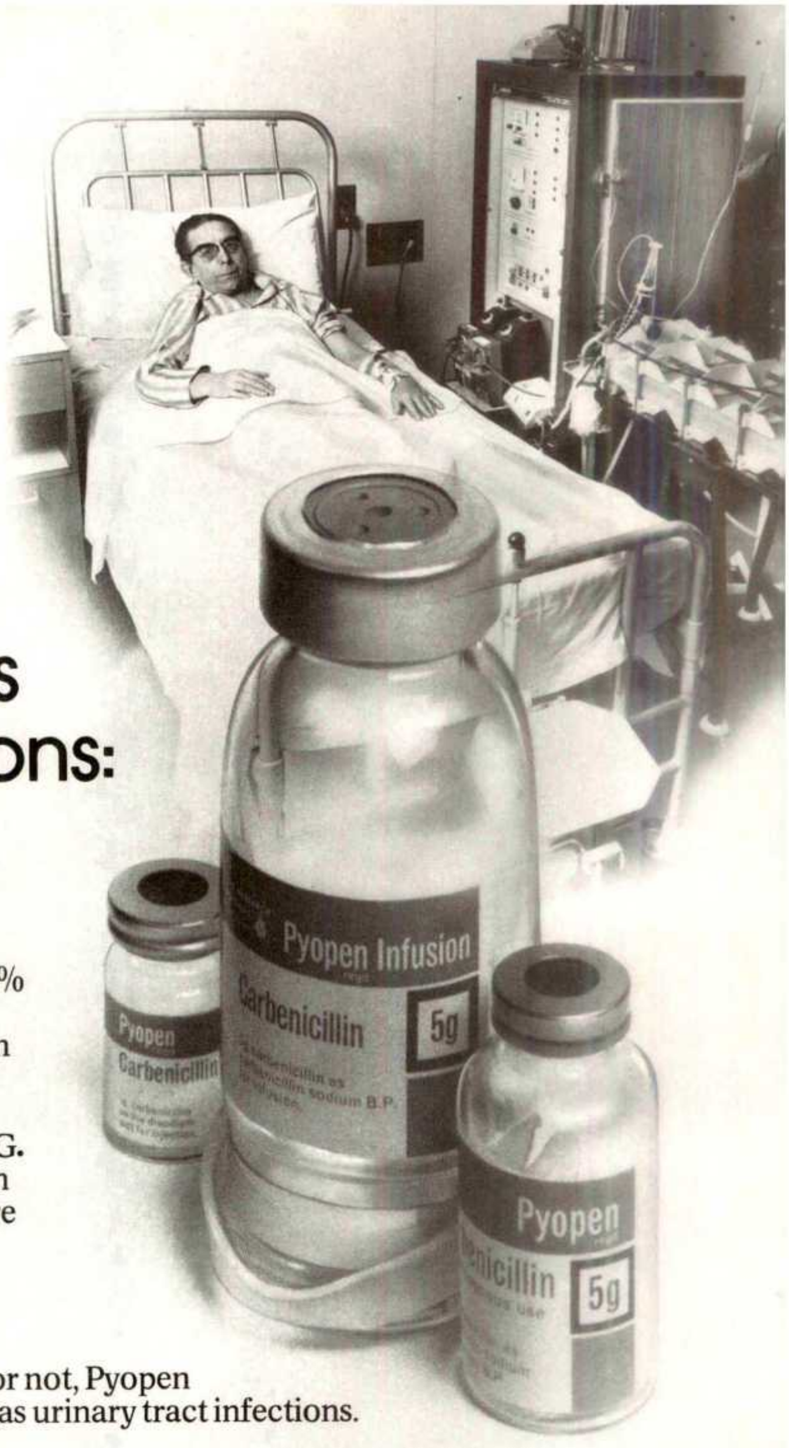

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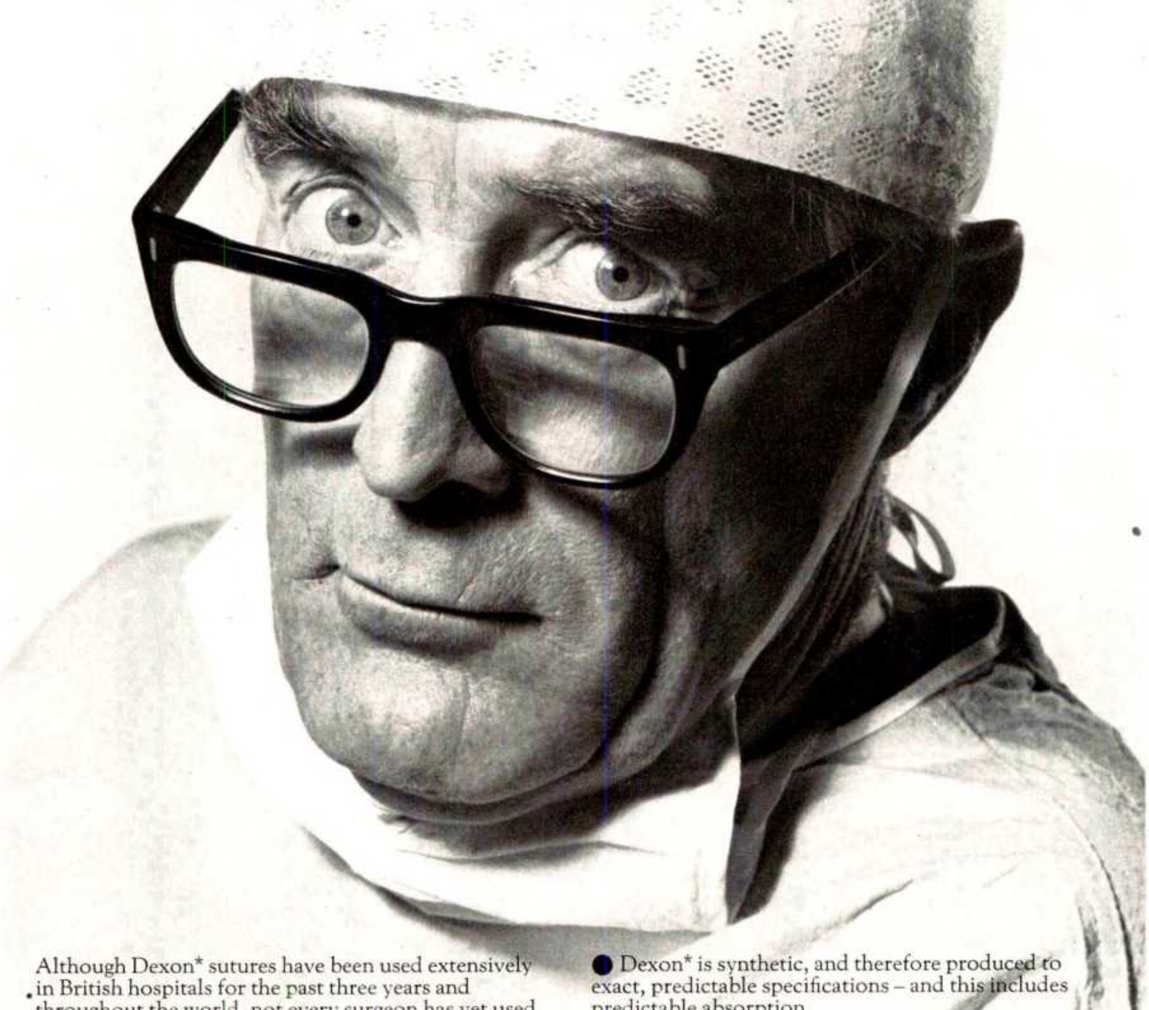

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THE DIAGNOSIS AND PROPHYLAXIS OF PULMONARY COMPLICATIONS OF SURGICAL OPERATION

BY G. LASZLO, G. G. ARCHER, J. H. DARRELL, J. M. DAWSON, AND C. M. FLETCHER

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SUMMARY

Eighty-eight non-bronchitic and 52 bronchitic patients undergoing elective general and plastic surgical operations in two wards were studied for postoperative chest complications, which were diagnosed by increased purulence of sputum and radiological changes at 24 or 48 hours. Eighty per cent of the patients undergoing upper abdominal surgery and 30 per cent of the other patients had chest complications. Postoperative bronchitis or pneumonia severe enough to delay discharge was found in 14 patients (10 per cent). Twice-daily physiotherapy to the chest did not affect the outcome in 86 patients without chronic bronchopulmonary disease. Routine administration of ampicillin to 'cover' chronic bronchitics undergoing general anaesthesia was found to be of no value in a controlled trial of the 52 bronchitic patients. However, bacteriological and radiological studies lend some support to the suggestion that prophylaxis with a bactericidal antibiotic may reduce the incidence and morbidity of postoperative pulmonary infections in patients having upper abdominal operations.

THE importance of infection in causing bronchial and pulmonary complications of surgical operations is uncertain. Administration of prophylactic antibiotics has often been recommended, but early clinical trials showed penicillin to be valueless (Palmer and Sellick, 1952; Thulbourne and Young, 1962). Prophylactic broad-spectrum antibiotics are often prescribed for bronchitic patients with upper respiratory-tract infections, but when the present study was planned their value in the prophylaxis of postoperative chest complications had not been tested. In this paper we report the incidence of bronchial and pulmonary complications of surgical operations, bacteriological studies of sputum, and the results of a trial of prophylactic ampicillin in a group of patients with simple or obstructive chronic bronchitis.

At the same time we noted that the ward physiotherapist spent much time of undetermined usefulness in treating the chests of healthy patients having minor operations. We therefore carried out a survey of all elective admissions to a general surgical unit over a period of 6 months in an attempt to assess the value of standardized routine physiotherapy given to patients without chronic bronchitis or abnormal ventilatory function.

MATERIALS AND METHODS

One hundred and forty male and female patients who were admitted from their homes on two regular admitting days each week to undergo elective operation under the care of one surgical firm were included in the trial. The operations are listed in *Table I*. All the patients were seen by the medical registrar (G. L.) and judged 'bronchitic' (52 patients) or 'normal' (88 patients). He also performed daily clinical assessments but remained unaware how the patient had been treated until after discharge. The patients were allocated at random to 'treatment' and 'control' groups.

Pre- and Postoperative Assessment.—All the patients were assessed by means of a standard questionary, clinical examination, and, in most cases, spirometry.

The questionary was as follows:—

1. Do you ever bring up phlegm?
2. Do you bring up phlegm on most days in the winter for as much as 3 months in the year?
3. Do you ever get short of breath?
4. Do you ever wheeze?
5. Do you smoke? (details).

The 52 patients who gave a positive answer to question 2 were classed as 'bronchitic'. Those in whom 1-second forced expired volume (F.E.V.$_1$) was more than 2 standard deviations below normal for age and height (Ferris, Anderson, and Zickmantel, 1965) were considered to have 'airways obstruction'. At first all those answering 'No' to questions 1–4 who had normal values of forced expired time were not tested by spirometry. Later, F.E.V.$_1$ was measured in all subjects. Patients with reduced F.E.V.$_1$ were all bronchitic.

Sputum.—The patients were instructed to expectorate all sputum before and after operation into special cartons and this was graded daily for volume and purulence according to the criteria of Miller and Jones (1963):—

0	No sputum.
M1	Mucoid.
M2	Suspicion of pus.
P1	Up to $\frac{1}{3}$ pus.
P2	Up to $\frac{2}{3}$ pus.
P3	Pus.

A change of two grades was considered to be evidence of a postoperative chest complication (e.g., from 0 to M2 or from M1 to P1). Any sputum was cultured at least once postoperatively and thereafter if there was any deterioration in macroscopic grade. Duplicate samples of sputum were cultured on blood-agar and chocolate-agar incubated in air. *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* were regarded as potential pathogens. Macroscopic grading was checked by means of films stained with Gram's stain.

Radiological Assessment.—Chest radiographs were taken preoperatively and on the first and second days after operation whenever possible in the X-ray Department rather than in the ward. Preoperative films were taken in the anteroposterior projection as well as in the postero-anterior projection to facilitate comparison with the postoperative films which were taken in the ward. The different focus-film distances used in the department and ward films did not produce any interpretive difficulties. Lateral films were not used.

The results were assessed by a single radiologist (J. M. D.) without access to clinical information. The preoperative radiographs were not used in the preoperative clinical assessment of patient groups but solely as a base-line for subsequent change.

Radiographic lesions were scored as follows:—

0 No lesion.
½ Minimal or 'subsegmental' (shadowing extending over less than one interspace in any dimension).
1 Major or 'segmental' (shadowing extending over one interspace or more in any dimension).

Each lung was divided into six zones and each was scored. Where more than one lesion was seen in the same zone the scores were added. A score of 1 or more on the 2 postoperative days was regarded as significant, i.e., minimal lesions in more than one zone or persisting in two or more films were counted as significant.

Postoperative Clinical State.—Each patient was examined daily; temperature and chest signs were noted.

Procedure for Non-bronchitic Patients.—Patients allocated to the treated group were visited by the physiotherapist once preoperatively for instruction, twice on the day of the operation, and twice daily for 5 days thereafter for breathing exercises, percussion, assisted coughing, and leg exercises. Patients in the control group were visited equally frequently but given leg exercises only. When a chest infection was diagnosed a message was left for the physiotherapist to start treatment whether it had been given previously or not.

Procedure for Bronchitic Patients.—Patients diagnosed as having chronic bronchitis were allocated at random to a group to be given prophylactic ampicillin or to a control group. The allocation of the patient was known to the surgical registrar (G. G. A.) who prescribed the treatment. All the treated patients received ampicillin, 500 mg. by intramuscular injection at the time of the premedication (1–2 hours preoperatively) and 8-hourly thereafter for 5 days. The antibiotic was given orally in the same dose as soon as possible. In the event of clinical deterioration treatment was decided by the house staff in consultation with the surgical registrar. This did not affect the trial since the result for that particular patient was now apparent. In general, wound infections requiring antibiotics became apparent after the immediate postoperative period and did not interfere with the trial. The 'single blind' arrangement resulted in virtually no interference with clinical management of the patients. All the bronchitic patients received physiotherapy, including percussion and postural drainage, three times daily. Those with airways obstruction also received inhalations of isoprenaline before physiotherapy.

Chest complications were classified as follows:—

Type 0 No chest complication.
Type 1 Deterioration of sputum by 2 or more purulence grades on one or more postoperative days—'Bronchitis'.*
Type 2 Deterioration of the radiograph by a score of 1 or more without a change in the postoperative sputum grading—'Collapse'.*
Type 3 Deterioration of both the sputum and the radiograph—'Pneumonia'.*

Infections which persisted after 10 days were classified as 'severe'.

Eighty-eight non-bronchitic patients and 52 patients with chronic bronchitis were included. The incidence of chronic bronchitis was similar to that found in a survey of working men in the neighbourhood (Fletcher, Peto, Speizer, and Tinker, 1970).

Statistical analysis was performed by calculating χ^2 and applying Yates's correction for all 2×2 tables. $P > 0\cdot05$ is rated as not significant (N.S.).

RESULTS

Non-bronchitic Subjects.—Physiotherapy did not reduce the total incidence of chest complications which was diagnosed radiologically (types 2 and 3); physiotherapy was, in fact, associated with rather more frequent sputum deterioration which may have been due to its assisting expectoration (*Table II*).

The site of operation, previous smoking habit, and age were the most important factors influencing the incidence of chest complications (*Table III*). Patients over the age of 40 were more liable to chest complications (55 per cent compared with 31 per cent). Upper abdominal operations carried an incidence of 81 per cent, while the risk from operations at other sites was 29 per cent. Fifty-three per cent of smokers but only 22 per cent of non-smokers developed chest complications. A previous history of occasional expectoration from the chest during respiratory infections was not significantly associated with an increase in complications. No bronchopulmonary complications appeared in a group of 14 patients without malignant disease with no history of sputum production and undergoing non-abdominal operations. When such patients had upper abdominal incisions they fared as badly as the rest. Exclusion of this 'low-risk' group made no difference to the conclusion that physiotherapy was ineffective in preventing chest complications of minor (non-abdominal) surgery. There was a slightly, but not significantly, lower incidence of radiological change in treated patients having abdominal operations than in the control patients (6 out of 12 treated patients; 9 out of 13 untreated patients).

Pathogenic organisms were isolated after operation from the sputum of 11 out of 12 patients with 'pneumonia'. Seven of these infections were classed as severe. In contrast, pathogens were recovered from only 6 out of 12 sputa from patients with postoperative 'bronchitis', and only 2 of these patients had severe infections. Commensal organisms were isolated from 6 patients with postoperative 'bronchitis' and 3 of these cases had persistent infections. Specimens from the remaining 6 patients in this group were lost. No multiresistant organisms were isolated.

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* These terms are used as defined here to facilitate discussion.

Table I.—FREQUENCY OF POSTOPERATIVE COMPLICATIONS AFTER VARIOUS OPERATIONS

OPERATION	POSTOPERATIVE COMPLICATION				
	Type 0 (None)	Type 1 ('Bronchitis')	Type 2 ('Collapse')	Type 3 ('Pneumonia')	Total
Abdominal operations					
Gastrectomy	—	1	1	1	3
Vagotomy and drainage	1	4	4	8	17
Cholecystectomy	1	2	4	2	9
Duodenotomy	1	—	—	—	1
Adrenalectomy	—	—	1	—	1
Appendicectomy	1	1	—	—	2
Epigastric and incisional hernia repair	2	—	—	1	3
Laparotomy	—	1	1	—	2
Colostomy	—	1	—	1	2
Colon operations	1	—	—	2	3
Abdominoperineal resection of colon	—	—	—	1	1
Total	7	10	11	16	44
Other operations					
Rectal	23	4	—	1	28
Herniorrhaphy	15	9	—	2	26
Varicose-vein operations	8	1	—	1	10
Testicular operations	5	1	—	—	6
Minor breast surgery	2	2	1	—	5
Radical mastectomy	—	1	—	1	2
Pituitary implant	1	—	—	1	2
Plastic surgery and node biopsy	14	3	—	—	17
Total	68	21	1	6	96
Overall total	75	31	12	22	140

Table II.—INCIDENCE OF POSTOPERATIVE CHEST COMPLICATIONS IN 86 PATIENTS WITHOUT 'CHRONIC BRONCHITIS' WITH AND WITHOUT PHYSIOTHERAPY

GROUP	NO. OF PATIENTS	POSTOPERATIVE COMPLICATION										NO. OF ABDOMINAL OPERATIONS	
		Type 0	*Type 1*	*Type 2*	*Type 3*	*Types 1 and 3 (Sputum Change)*		*Types 2 and 3 (Radiographic Change)*		*All Types*			
						No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Physiotherapy	44	25	10	1	8	18	41	9	20	19	43	12	27
No physiotherapy	42	23	8	7	4	12	23	11	26	19	45	13	30
Total*	86	48	18	8	12	30	36	20	24	38	44	25	29
		N.S.				N.S.		N.S.		N.S.			

* Two patients included in the survey are omitted from this trial because of departure from the prescribed therapy.

Bronchitic Subjects.—Administration of ampicillin did not affect the incidence of pulmonary complications. The bronchitic subjects, who were all smokers, had the same number of complications as the non-bronchitic smokers. There was no difference between the older and younger patients, nor between those with and without evidence of airways obstruction (*Table IV*).

Pathogens were isolated from only 2 preoperative sputum specimens out of 30 cultured. These persisted after operation but neither patient suffered complications. Unfortunately, a number of postoperative specimens were lost. However, there were more pathogens in the postoperative sputa from the untreated group (9 out of 22; 5 lost) than in the group treated with ampicillin (2 out of 18; 7 lost). In patients having abdominal operations there were 4 out of 6 specimens with pathogens in the untreated group and 2 out of 7 in the ampicillin group. The pathogens in the treated group were both sensitive to ampicillin.

Pathogenic organisms were isolated after operation from the sputum of 6 out of 8 patients who developed 'pneumonia' after abdominal operation. Only 1 patient undergoing a non-abdominal operation developed 'pneumonia' although pathogens were isolated from 6 out of 16 sputa. Thus, although infection with pathogens increased the likelihood of 'pneumonia' after abdominal surgery and ampicillin reduced the rate of isolation of pathogens the antibiotic did not confer any clinical benefit.

There was no association between deterioration in sputum grade and the presence of fungi and coliform organisms which followed antibiotic treatment. No multiresistant bacterial strains were isolated.

All Patients.—*Table V* shows that there was a significant association between the presence of pathogens in the postoperative sputum cultures and the incidence of radiological change.

Pulmonary embolism was diagnosed in only 1 (non-bronchitic) patient in this series; she was the only patient who died of pulmonary complications of surgery.

Table III.—The Effect of Type of Incision, Smoking Habit, and Previous History of Occasional Bronchitis on the Incidence of Postoperative Chest Complications in Patients without 'Chronic Bronchitis'

	No of Patients	Postoperative Complication									
		Type 0	*Type* 1	*Type* 2	*Type* 3	*Types* 1 *and* 3		*Types* 2 *and* 3		*Types* 1, 2, *and* 3	
						No.	Per cent	No.	Per cent	No.	Per cent
Age											
10–39 yr.	39	27	7	4	1	8	21	5	13	12	31
40–80 yr.	49	22	11	4	12	23	47	16	33	27	55
						0·05 > *P* > 0·02		N.S.			
Abdominal operations	26	5	6	7	8	14	54	15	59	21	81
Other operations	62	44	12	1	5	17	27	6	10	18	29
						0·05 > *P* > 0·02		*P* < 0·001			
All smokers†	51	24	14	3	10	24	49	13	25	27	53
Non-smokers	27	21	2	2	2	4	15	4	15	6	22
						P = 0·015		N.S.			
Ex-smokers	10	4	2	3	1	3	33	4	40	6	60
Light smokers	22	10	6	2	4	10	45	6	28	12	55
Heavy smokers	29	14	8	1	6	14	48	7	24	15	52
						N.S.		N.S.			
Occasional phlegm	49	26	12	3	8	20	41	11	22	23	47
Never had phlegm	39	23	6	5	5	11	28	10	26	16	41
						N.S.		N.S.			

* There was a similar proportion of abdominal operations among older and younger patients.

† The effect of physiotherapy was the same in all these groups

Table IV.—The Effects of Ampicillin Treatment, Type of Operation, Age, and Evidence of Airways Obstruction on the Incidence of Postoperative Chest Complications in Patients with 'Chronic Bronchitis'

Group	No of Patients	Postoperative Complication									
		Type 0	*Type* 1	*Type* 2	*Type* 3	*Types* 1 *and* 3		*Types* 2 *and* 3		*Types* 1, 2, *and* 3	
						No.	Per cent	No.	Per cent	No.	Per cent
All subjects											
Ampicillin	25	12	6	3	4	10	40	7	28	13	52
No ampicillin	27	14	7	1	5	12	44	6	22	13	48
Total	52	26	13	4	9	22	42	13	25	26	50
Abdominal operations											
Ampicillin	9	0	2	3	4	6	66	7	77	9	100
No ampicillin	9	2	2	1	4	6	66	5	51	7	78
Total	18	2	4	4	8	12	66	12	66	16	89
Other operations											
Ampicillin	16	12	4	0	0	4	25	0	0	4	25
No ampicillin	18	12	5	0	1	6	33	1	6	6	33
Total	34	24	9	0	1	10	29	1	3	10	29
Age											
10–39 yr.	15	8	3	2	2	5	33	4	27	7	47
40–80 yr.	37	18	10	2	7	17	41	9	24	19	52
Airways obstruction	28*	13	7	3	5	12	43	8	29	15	54
No airways obstruction	24†	13	6	1	4	10	42	5	21	11	46

* Average age 53 yr.

† Average age 40 yr.

The groups are all comparable for age and number of major operations except where noted.

None of the differences in incidence is statistically significant.

Most bronchopulmonary complications occurred on the first or second postoperative day. All of 65 patients in whom radiological changes appeared in the first 48 hours had temperatures above 37·2° C. except 1 case receiving corticosteroid replacement after adrenalectomy. Pyrexia was associated with increased purulence of the sputum in 75 per cent of patients without radiological change. Eighty-four per cent of the patients with pyrexia in the first 48 hours postoperatively had objective signs of chest complications. The correlation of crepitations at the bases with fever and with radiological change was poor.

Severe Complications.—Pulmonary complications prolonged the stay in hospital of 15 patients (11 per cent). None of these patients had received ampicillin; 14 of them had not been graded bronchitic on admission, and the one who had chronic bronchitis was in the control group. Ten were smokers; all but 4 underwent major operations. Details of these patients are given in *Tables VI* and *VII.*

Table V.—THE RELATIONSHIP BETWEEN TYPE OF ORGANISM ISOLATED FROM POSTOPERATIVE SPECIMENS OF SPUTUM AND RADIOLOGICAL CHANGES IN NORMAL AND BRONCHITIC PATIENTS

TYPE OF OPERATION	BACTERIOLOGY	POSTOPERATIVE RADIOGRAPHIC CHANGE		TOTAL NO. OF PATIENTS
		Absent	Present	
Abdominal	Pathogens Non-pathogens	3 7	10 3	13 10
Other	Pathogens Non-pathogens	9 20	3 2	12 22
All operations	Pathogens Non-pathogens	12 27	13 5	25 32
		$P<0{\cdot}05$		

Table VI.—FACTORS RELATED TO THE DEVELOPMENT OF SEVERE POSTOPERATIVE BRONCHOPULMONARY COMPLICATIONS

POSTOPERATIVE COMPLICATIONS	NO. OF PATIENTS	NON-BRONCHITIC	BRONCHITIC	SMOKERS	RECEIVED PHYSIOTHERAPY	RECEIVED AMPICILLIN	PATHOGENIC ORGANISM ISOLATED	AGE RANGE (yr.)	MEAN AGE (yr.)	MAJOR OPERATIONS
Bronchitis	6	5	1	5*	4	0	2	32–64	49	3*
Collapse	2	2	0	0	1	0	—	34	34	2
Pneumonia	7	7	0	5	6	0	7	53–79	61	7
Total	15	14	1	10	11	0	9		53	12

* The 3 patients who developed severe postoperative bronchitis after minor surgery were all heavy smokers (more than 20 cigarettes per day).

Table VII.—RELATIONSHIP BETWEEN THE ADMINISTRATION OF AMPICILLIN AND THE INCIDENCE OF SEVERE BRONCHOPULMONARY COMPLICATIONS IN PATIENTS HAVING MAJOR OPERATIONS

TREATMENT	NO. OF PATIENTS	POSTOPERATIVE COMPLICATION					
		Severe		*Mild*		*None*	
		No.	Per cent	No.	Per cent	No.	Per cent
Ampicillin	8	0	0	7	88	1	12
No ampicillin	35	12	34	17	49	6	17
Total	43*	12	28	24	56	7	16

* One patient who died of pulmonary embolism is excluded from this table.

DISCUSSION

The factors affecting the incidence of postoperative pulmonary complications have been studied and reviewed extensively by Anscombe (1957), Palmer (1962), Collins, Darke, and Knowelden (1968), and Wightman (1968). Our results in untreated patients undergoing abdominal surgery (other than inguinal herniotomy) agree well with those of Collins and others (1968), both as to the incidence of radiological change (55 per cent compared with 68 per cent) and in the number of patients without any evidence of chest complications (20 per cent compared with 14 per cent). We found, as Collins and others did, that smoking and age affected postoperative bronchial infection significantly. It seems that a history of any previous expectoration in a smoker is associated with the same increased risk of postoperative bronchitis as that of regular expectoration for at least 3 months in the winter, which is the accepted definition of simple chronic bronchtis (Medical Research Council, 1965).

Postoperative bronchopulmonary infection is common. Twenty-two per cent of all our patients expectorated sputum containing pus without any radiological change and a further 16 per cent had both purulent sputum and radiological change. Pathogenic organisms were isolated from just over one-third of such patients.

The part played by infection in producing postoperative pneumonia seems to depend on the type of operation. There was a significant association between pathogenic bacteria and radiological shadowing after abdominal surgery, but not after operations where the peritoneum was not opened, when pathogens were often isolated but radiographic lesions were rare. This suggests that postoperative pneumonia is most likely to develop when a pathogenic organism is present in the respiratory tract and there is interference with the breathing. Collins and others (1968) were able to halve the incidence of radiological change by giving adequate doses of prophylactic penicillin and streptomycin, a combination with bactericidal properties similar to those of ampicillin. All their patients had upper abdominal operations and the response to the prophylactic antibiotic was similar regardless of age or 'chest history'.

We were able to reduce the number of pathogenic bacteria isolated by giving ampicillin, although in 2 treated bronchitic patients with pneumonia, organisms showing *in vitro* sensitivity to the antibiotic were isolated during treatment. In our controlled comparison of the effects of ampicillin in bronchitic patients the drug reduced the incidence of postoperative isolation of pathogens but not the incidence of chest complications. Severe complications were, however, commoner in the non-bronchitic patients, none of whom had ampicillin. Combining both groups, severe complications occurred in none of the 25 patients receiving ampicillin, but in 15 out of 113 patients not receiving ampicillin (13 per cent). When upper abdominal operations alone are considered, as in the trial of Collins and others (1968), the differences are more striking, though the numbers are too small to permit statistical analysis (*Table VII*). This study, therefore, lends some support to the suggestion of Collins and others (1968) that broad-spectrum antibiotics may have a prophylactic effect after upper abdominal surgery, since we found pathogens in the sputum of all the severe cases of postoperative pneumonia.

Pseudomonas was isolated on only 2 occasions and no multiresistant staphylococci were found; had these organisms been prevalent at the time of the trial a different conclusion might have been reached. If the source of the pathogens were known other preventive measures, preferable to chemoprophylaxis, might be taken.

There is no general advantage to be gained from giving routine antibiotic 'cover' to bronchitic subjects receiving general anaesthesia for minor operations. It may, however, be advisable to treat the patient perioperatively when pathogens are already present in the sputum, as illustrated by 1 of our bronchitic patients in whom preoperative tetracycline had failed to clear a long-standing pneumococcal infection. Perioperative ampicillin produced a remission without further complications.

Collins and others (1968) stated: 'It is believed that an increase in temperature during the first 48 hours is almost always caused by chest infection.' Infection shown by radiographic changes or purulent sputum accounted for nearly all the pyrexia in the early postoperative period in the present study. Except in 1 patient receiving steroids, the chest radiographs were all normal when the oral temperature was below 37·2° C. in the immediate postoperative period.

Our findings confirm those of Nichols and Howell (1970) that regular twice-daily physiotherapy, including breathing exercises, percussion, and encouragement of coughing, is of no apparent value to non-bronchitic subjects regardless of age, operation, or smoking habits. There is room for investigation of the value of vigorous treatment in the early postoperative period, as suggested by Palmer and Sellick (1962). It is interesting that among the bronchitic subjects who had minor operations, only 1 patient showed collapse radiographically. The more intensive physiotherapy given to this group may therefore have been beneficial, but since the services of trained physiotherapists are always in demand their time should not be spent in useless visits to previously healthy subjects having minor operations.

Acknowledgements.—This study was possible because of the co-operation of Miss J. L. Morris and the qualified staff of the Physiotherapy Department, Hammersmith Hospital, who carried out the prescribed treatment and arranged their schedules to fit in with the protocol.

We are indebted to Professor R. B. Welbourn for critical reading of the manuscript and advice during the initiation of the study.

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MALNUTRITION AND MALABSORPTION IN CROHN'S DISEASE WITH REFERENCE TO THE EFFECT OF SURGERY

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SUMMARY

Sixty-three patients with Crohn's disease showed a high incidence of nutritional deficiencies as judged by laboratory tests. Malabsorption of fat (33 per cent) and vitamin B_{12} (60 per cent) was not sufficiently severe to account for the malnutrition. Malnutrition was especially severe in unoperated patients with active disease, whereas malabsorption was prominent in patients with recurrent disease after resection although they had less active disease and less severe nutritional deficits. Surgery should not be withheld from a malnourished patient for fear of inducing further malnutrition; excision of toxic inflammatory disease will not only improve the immediate outlook but will also reduce the severity of further recurrences. Xylose-excretion tests give a spurious impression of malabsorption in Crohn's disease, possibly as a result of occult renal impairment, and should be abandoned.

NUTRITIONAL disturbance is a common complication of Crohn's disease (Cooke, 1955; Ensrud and Sauer, 1957; Kogan, Schapira, Janowitz, and Adlersberg, 1957; Pimparkar, Mourhan, and Bockus, 1960; Tytgat, Vantrappen, Rutgeerts, and Vandenbroucke, 1967; Dotevall and Kock, 1968; Hertzberg, Myren, and Semb, 1969; Krause, Bergman, and Norlen, 1971). Although the number of possible causes are legion (*Table I*), malnutrition is frequently attributed to malabsorption (Crohn and Yarnis, 1958; Bockus, 1964). However, the role of malabsorption may have been overemphasized because the disease attacks the submucosa rather than the mucosa and frequently spares the jejunum. Kiefer and Arnold (1950) pointed out that malabsorption which resulted from resection of bowel in Crohn's disease was rarely extensive enough to account for the associated malnutrition, and Hoffbrand, Stewart, Booth, and Mollin (1968) suggested that anorexia was a major factor causing folate deficiency in their patients. The importance of impaired dietary intake, fistulous losses, and sepsis in contributing to undernutrition has been stressed by Clark and Lauder (1969), particularly in the postoperative period.

Table I.—FACTORS PRODUCING MALNUTRITION IN CROHN'S DISEASE

- Decreased intake of food
- Presence of active inflammation
  - Increased nutritional requirements
  - Toxic depression of metabolism
- Malabsorption
  - Loss of bowel
    - Inflammation
    - Resection
    - By-pass
  - Stagnant-loop syndrome
    - Stricture
    - Fistula
    - Surgical blind loop
- Gastro-intestinal loss
  - Blood
  - Protein
  - Water and electrolytes
  - Bile-salts
- Minor factors
  - Rapid intestinal transit
  - Impaired bowel function above an obstruction

We have studied an unselected series of patients in order to establish the incidence and severity of malnutrition and malabsorption, as indicated by simple laboratory investigations, and comparisons have been made between patients with active recurrent disease following a bowel resection and those with primary disease.

MATERIALS AND METHODS

Sixty-three patients were studied over a 2-year period; all had symptoms which were sufficiently severe to warrant admission to hospital. The symptoms of those who had suffered a relapse after operation were of comparable severity to the symptoms of patients who had not undergone operation, and the majority of the patients with postoperative recurrences had not been followed up so that they had not been promptly readmitted to hospital. The diagnosis of Crohn's disease was confirmed histologically in 40 patients (63 per cent) and was based on typical clinical and radiological features in the remaining 23, 3 of whom had undergone laparotomy without biopsy. There were 39 females (62 per cent) and 24 males. Their ages ranged from 14 to 71 years with a mean age of 37 years. Only 5 patients were on systemic steroid treatment but 2 others had been given steroid enemata.

The patients were divided into six anatomical groups. Seven patients had diffuse disease which involved the jejunum together with variable amounts of the ileum and colon. Thirteen patients had ileocaecal disease, only 1 of whom had more than 30 cm. of terminal ileum involved. Eight patients had ileocolic disease which involved the terminal two or three loops of the ileum and the ascending colon; one patient had disease extending from the proximal ileum to the splenic flexure. Eight patients had colonic disease which was limited to the right colon in 4 and was total in the other 4 cases. Three patients had disease limited to the anorectal region. Twenty-four patients had been operated on previously; most had undergone ileo-colic resections and had developed recurrent disease in the remaining terminal ileum. Seven patients had been operated on for jejuno-ileitis but only 1 had undergone jejunal resection; 11 patients had undergone surgery for ileocaecal disease, of whom 9 had had resections but 2 had had 40-60 cm. of ileum by-passed and excluded; 6 patients had ileocolic disease and had received more extensive resections; 1 patient had had local excision of disease limited to the descending colon.

The activity of the disease was arbitrarily graded by a system which awarded points for certain clinical and laboratory characteristics. One point was scored for each of the following (Dyer, 1970): symptoms of disease (pain, diarrhoea in an unresected patient, weight-loss, systemic complications); temperature above 37·2° C. during 3 of the first 10 days; haemoglobin less than 11·0 g. per 100 ml.; white-cell count above 11,000 per c.mm.; erythrocyte-sedimentation rate (Westergren) above 20 mm. in 1 hour; serum albumin less than 3·5 g. per 100 ml. Thus patients could be separated into seven grades (0-6).

Haemoglobin and serum albumin were estimated by routine laboratory techniques. Serum folate was measured by the method of Waters and Mollin (1961). Serum vitamin B_{12} was measured by the method of Anderson (1964). Xylose absorption was estimated after an overnight fast followed by the oral administration of 25 g. of D-xylose and 600 ml. of water; urine was collected for the next 5 hours and a blood-sample was taken at $1\frac{1}{2}$ hours. Xylose was measured by the method of Roe and Rice (1948). Faecal fat was estimated by the method of Van der Kamer, Ten Bokkel Huinink, and Weyers (1949). Vitamin-B_{12} absorption was measured by the method of Schilling (1953); after an overnight fast 0·5 μg. of the labelled vitamin was administered with 150 mg. of hog intrinsic factor and a flushing inject of 1000 μg. of unlabelled vitamin was given subcutaneously 2 hours later. Not every patient had every investigation.

RESULTS

Evidence of Malnutrition (*Fig.* 1).—

Haemoglobin.—Seventy-five per cent of the males had a haemoglobin concentration of less than 12·5 g. per 100 ml. and 54 per cent of the females had a concentration below 11·5 g. per 100 ml. The incidence and degree of anaemia were similar in unoperated patients regardless of the main site of disease. In females the haemoglobin levels were significantly higher in those admitted with recurrent disease after operation ($t = 2·38$, $P < 0·025$); in males there was no such difference. There was a progressive fall in haemoglobin associated with increasing activity of the disease ($P < 0·001$).

Serum Albumin.—Forty-four per cent of 59 patients had values below 3·5 g. per 100 ml. Patients with unoperated disease involving the colon with or without associated ileal lesions had a mean level of 3·0 g. per 100 ml. which was significantly lower than the 3·6 g. per 100 ml. which was found in patients whose disease was confined to the small bowel ($t = 2·13$,

$P<0.05$). Although operated patients had a higher mean level than unoperated ones, this did not quite achieve significance ($t=1.84$, $P<0.1$). There was a progressive fall in serum albumin with increasing activity of disease ($P<0.005$). No direct correlation could be demonstrated with blood-urea levels, although subnormal urea concentrations (less than 20 mg. per 100 ml.) were only found in active disease. There was a significant correlation with serum-calcium levels ($r=+0.64$, $P<0.001$), the few patients with divergent results all having steatorrhoea.

Serum Folate.—Sixty-four per cent of the patients had levels below 4·0 ng. per ml. Significant differences could not be demonstrated between patients

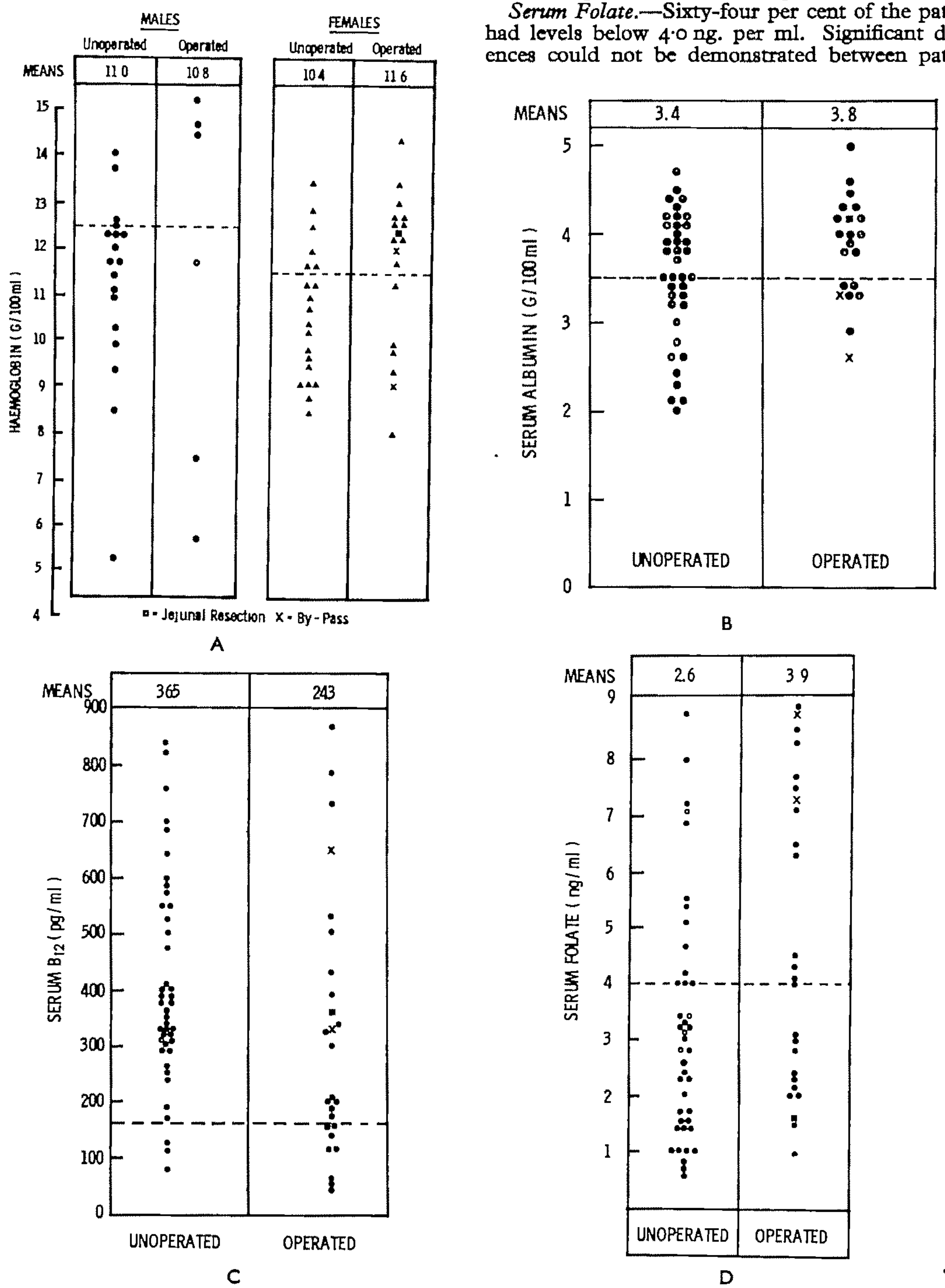

Fig. 1.—Scatter diagrams comparing the levels of (A) haemoglobin (in males and females), (B) serum albumin, (C) serum vitamin B_{12}, and (D) serum folate in patients with unoperated Crohn's disease against levels in patients with recurrent disease after operation. Dotted lines indicate normal limits. ×, Patients with an ileal by-pass. ■, Patients who had had a jejunal resection.

with disease at different sites except that unoperated patients had lower values than patients admitted with recurrent disease after surgery ($t = 2{\cdot}42$, $P < 0{\cdot}02$). There was a progressive fall in folate levels with increasing disease activity ($P < 0{\cdot}002$).

Serum Vitamin B_{12}.—Sixteen per cent of the patients had levels below 160 pg. per ml. Although the mean vitamin B_{12} values were significantly lower in patients who had undergone ileal resection ($t = 2{\cdot}63$, $P < 0{\cdot}02$), 3 unoperated patients had values below the normal range. These patients all had evidence of disease in the ileum and the lowest value occurred in a patient who had had symptoms for over 20 years. Four patients with resections of less than 30 cm. of ileum were not vitamin-B_{12} deficient, whereas 2 of the 3 with resections of more than 100 cm. developed very low levels within 3 years; the third patient appeared to be protected by preservation of the ileocaecal valve and a small cuff of the terminal ileum.

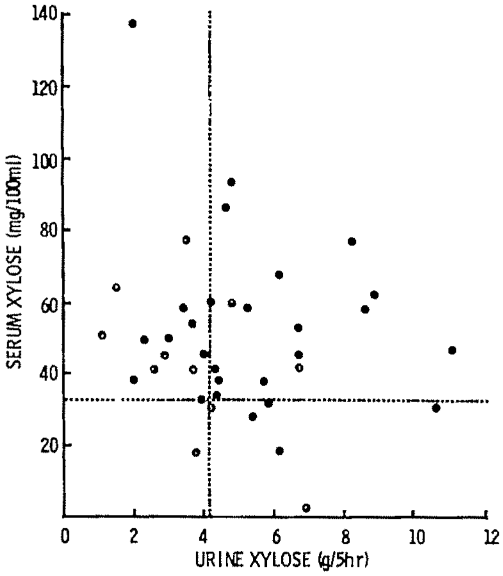

FIG 2.—Comparison of 5-hour urinary excretion of xylose with blood levels at 1½ hours in 38 patients with Crohn's disease. Dotted lines indicate lower limits of normal.

Xylose Tolerance.—This test is an indirect assessment of jejunal function which depends not only on the intestinal absorption of the sugar but also on the excretion of xylose in the urine. Although 43 per cent of 42 patients excreted less than 4·2 g. per 5 hours and 23 per cent of 39 patients had serum levels of less than 32·5 mg. per 100 ml., only 1 patient had both abnormalities (*Fig.* 2), which by these strict criteria indicates that malabsorption of xylose is rare even in the presence of jejunal disease.

Because impaired urinary excretion of xylose is the usually accepted criteria of jejunal dysfunction we have analysed our data further. The mean excretion of xylose for patients with ileocolic or colonic involvement was greater than that for patients with disease confined to the small bowel ($t = 2{\cdot}22$, $P < 0{\cdot}05$), but jejunal disease did not result in a greater impairment of excretion than ileocaecal disease and 3 patients with disease apparently confined to the colon had subnormal xylose excretion (*Fig.* 3). There was no difference in xylose excretion when unoperated and operated patients were compared. Regression analysis showed a significant correlation between increasing blood-xylose levels and increasing activity of the disease ($P < 0{\cdot}025$), and a progressive fall in urinary excretion with increasing activity only just failed to achieve significance ($P < 0{\cdot}1$). Only 2 patients had raised blood-urea levels and only 2 were aged over 65 years, so that neither uraemia nor old age was influencing the results. There was no correlation with faecal fat excretion or with the level of serum folate, a vitamin which is absorbed in the jejunum.

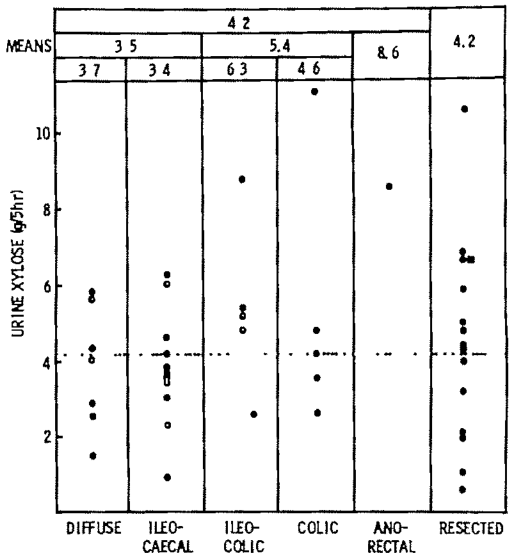

FIG. 3.—Urinary xylose excretion in 42 patients with Crohn's disease after oral administration of 25 g. of xylose related to the site of disease Dotted line indicates 4 2 g. per 5 hours. ■, Patients who had had a jejunal resection.

Faecal Fat.—Thirty-three per cent of 48 patients excreted more than 6·0 g. of fat per 24 hours. Although severe steatorrhoea was commoner after resection (*Fig.* 4), faecal fat excretion was not significantly greater in unoperated patients in this study ($t = 1{\cdot}97$, $P < 0{\cdot}1$). There were no differences in mean faecal fat excretion in unoperated patients with disease at different sites although no patient with disease apparently confined to the colon or rectum had steatorrhoea. The 2 patients with an ileal by-pass did not have steatorrhoea. There was no direct correlation between faecal fat excretion and disease activity or with the serum levels of calcium, magnesium, and cholesterol, nor did urinary excretion of xylose or vitamin B_{12} correlate with fat excretion. The degree of fat excretion did not correlate with the amount of ileum resected, but 1 patient whose ileocaecal valve had been left in situ after a large resection appeared to be protected from steatorrhoea (*Fig.* 5).

Vitamin-B_{12} Absorption.—Sixty per cent of 42 patients had subnormal absorption and operated patients absorbed significantly less vitamin B_{12} than unoperated ones ($t = 4{\cdot}08$, $P < 0{\cdot}001$). However, the incidence and degree of malabsorption did not differ amongst unoperated patients with different primary sites of disease, 48 per cent of whom had subnormal results including 2 of the 4 patients with disease apparently confined to the colon (*Fig.* 6). Only 3 of the 18 operated patients excreted more than 15 per cent of the vitamin; 2 had resections of less than 30 cm. and the third had an intact ileocaecal valve (*Fig.* 7). There is a tendency for vitamin B_{12} absorption to decrease with increasing amounts of ileal resection provided that the ileocaecal valve is removed, although an intact valve does not guarantee normal absorption. Severe malabsorption may also occur with minor resections or even in the absence of operation, but there was no correlation of vitamin B_{12} malabsorption and disease activity.

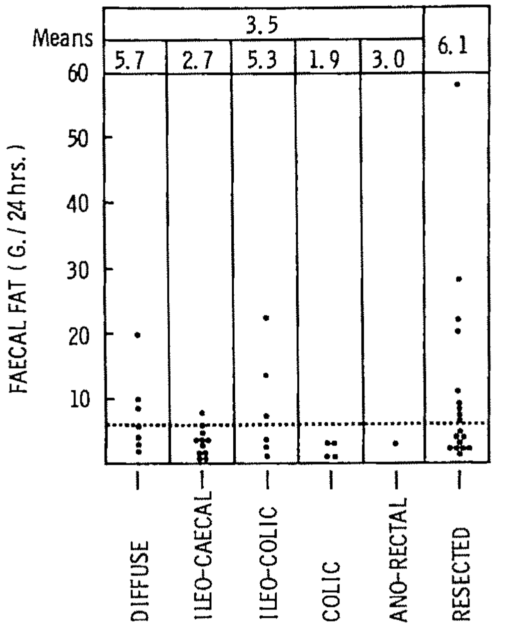

FIG. 4.—Faecal fat excretion in 48 patients with Crohn's disease related to the site of disease. Dotted line indicates 6·0 g. per 24 hours.

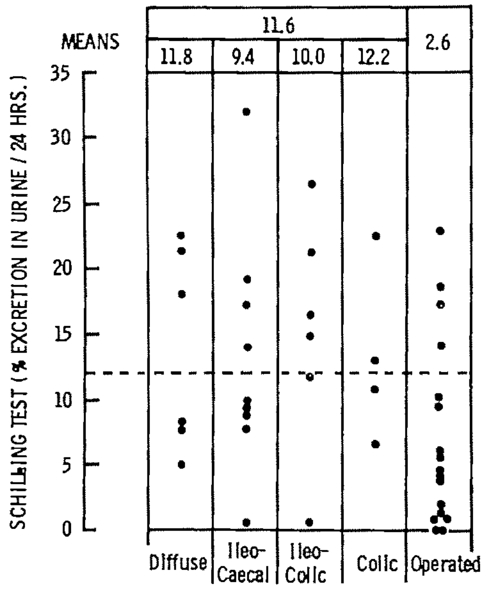

FIG. 6.—Correlation of vitamin-B_{12} absorption (Schilling test) with the site of disease in 42 patients with Crohn's disease. Dotted line indicates 12 per cent absorption.

DISCUSSION

This study not only confirms that there is a high incidence of nutritional abnormalities in Crohn's disease but relates the degree of disturbance to a measurement of disease activity. Although previous workers have noted an association of malnutrition with active disease, the degree of activity has not been defined (Tytgat and others, 1967; Hoffbrand and

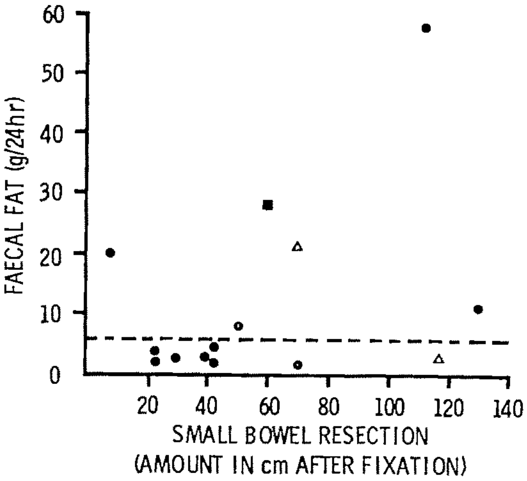

FIG. 5.—Correlation of faecal fat excretion with the amount of bowel resection in 14 patients with recurrent Crohn's disease. ■, Patients who had had a jejunal resection △, Patients whose ileocaecal valve remained in situ.

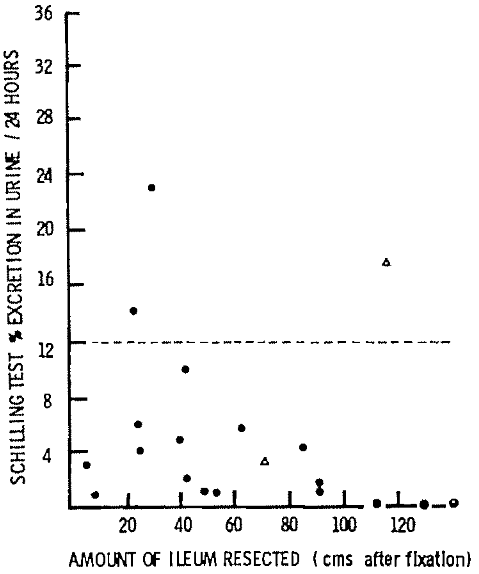

FIG. 7.—Correlation of vitamin-B_{12} absorption (Schilling test) with the amount of bowel resected in 20 patients with recurrent Crohn's disease △, Patients whose ileocaecal valve remained in situ.

others, 1968). Our measurements have shown that active or severe disease is not confined to patients with diffuse jejuno-ileitis (Bockus, 1964), since activity and malnutrition are especially liable to complicate colonic disease; the finding of severe hypoalbuminaemia and the less marked tendency to folate deficiency and anaemia in colonic disease also suggests that malabsorption is not a major cause. Patients with active disease frequently also have profound anorexia and so malnutrition may be the result of starvation. There may also be increased demands for essential nutrients owing to excessive production and loss of inflammatory and other cells so that decreased blood levels may merely represent rapid clearance. Hypoproteinaemia may result from decreased protein synthesis, hypercatabolism of serum proteins, or loss of protein into the bowel (Waldmann, 1970). Our results support the theory of enteric protein loss; the lack of correlation between serum-albumin and blood-urea levels suggests that neither starvation nor decreased protein synthesis is of major importance and that the presence of hypoalbuminaemia is not a reliable index of total protein deficiency. Moreover, some nutritional parameters are interdependent and results should be interpreted with care; hypocalcaemia is usually associated with hypoalbuminaemia because of the loss of the binding protein and rarely indicates malabsorption of calcium with its attendant risk of osteomalacia. Osteomalacia may erroneously be suspected if there is a coincidental increase in serum alkaline phosphatase; this disturbance, however, is usually due to abnormal liver function rather than to disturbed bone metabolism in such patients (Dyer and Dawson, 1972).

The less severe degree of malnutrition in patients who have developed recurrent disease after resection should not be dismissed as the result of selection of patients, because similar indications for admission obtained in all the cases. Moreover, the majority of the patients were often living at a distance from the hospital so that they were not seen at an earlier stage of their illness. Kalser, Roth, Tumen, and Johnson (1960) found that incomplete resection in patients with jejuno-ileitis led to a great improvement in health in spite of the effects of the disease left behind and the malabsorption resulting from surgery. When our patients are graded for disease activity, significantly more unoperated patients have active disease compared with operated ones (*Fig.* 8). Thus, it appears that the total amount of inflamed tissue determines the degree of malnutrition and that reduction of this 'toxic mass' is of prime importance. However, these results should not encourage indiscriminate surgery since adrenocorticotrophic hormone and azathioprine therapy can also dramatically reduce the activity of Crohn's disease within a few days.

The results of the xylose test give very little evidence that jejunal malfunction is important in the genesis of the nutritional disturbance. Thus, although the sugar is predominantly absorbed in the jejunum (Fordtran, Soergel, and Ingelfinger, 1962) changes in renal function and urinary xylose excretion may be of equal importance in giving an abnormal result. This factor has been disregarded by previous workers who have reported variable degrees of 'malabsorption' in Crohn's disease (Benson, Culver, Ragland, Jones, Drummey, and Bougas, 1957; Christiansen, Kirsner, and Ablaza, 1959; Fowler and Cooke, 1960; Shiner, Vakil, and Wilcox, 1962; Dotevall and Kock, 1968; Hertzberg and others, 1969). The recent studies by Kendall (1971), who has shown that intravenously administered xylose is poorly excreted in Crohn's disease, confirm our suspicions of occult renal dysfunction; only 1 of 39 patients had low levels of xylose in both blood and urine whereas active disease was associated with falling urine and rising blood levels. The indiscriminate application of this urinary excretion test is to be deprecated and the presence of a normal blood-urea level is no safeguard against a spurious result.

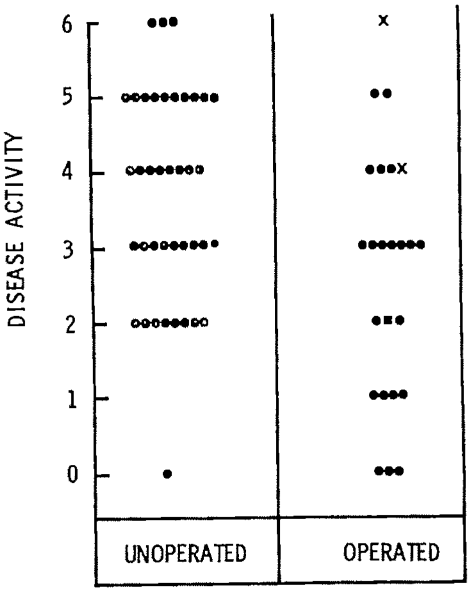

FIG. 8.—Disease activity in 63 patients with Crohn's disease. Twenty-one of the 39 unoperated patients had very active disease (grades 4–6) compared with 7 of the 24 operated patients with recurrent disease ($\chi^2 = 4\cdot54$, $P < 0\cdot05$). ×, Patients with an ileal by-pass. ■, Patients who had had a jejunal resection.

Malabsorption of fat and vitamin B_{12} was attributed to the presence of extensive disease or massive resection (Cooke, 1955; Bockus, 1964). However, our results confirm that malabsorption may also follow relatively small ileal resections and is sometimes a feature of unoperated localized disease of the ileum (Ensrud and Sauer, 1957); this has recently been explained by the discovery that the terminal ileum is the main site of absorption of vitamin B_{12} and conjugated bile-salts (Booth and Mollin, 1959; Lack and Wiener, 1967). The role of bacteria in the production of malabsorption of fat and vitamin B_{12}, as in the stagnant loop syndrome, has been overemphasized, since bacterial overgrowth is variable in Crohn's disease and cannot be directly correlated with malabsorption (Vince, Dyer, O'Grady, and Dawson, 1972). We did not find the severe degrees of steatorrhoea that have been reported by some American workers (Kalser and others, 1960; Pimparkar and others, 1960), possibly because our surgeons have tended to conserve as much bowel as feasible at operation. However, the incidence of malabsorption in our patients was similar to that reported by Hertzberg and others (1969), but their patients were all investigated after operation and there was often no evidence of active recurrent disease. The clinical importance of mild steatorrhoea associated with unresected ileal disease has yet to be established, although the development of megaloblastic anaemia due to malabsorption of vitamin B_{12} is well documented. However, the present study has confirmed that vitamin-B_{12} malabsorption is common in a large series of unoperated patients, the incidence being similar to the 58 per cent noted by Dotevall and Kock (1968). Our findings appear to contradict the work of Schofield (1967), who found that vitamin B_{12} deficiency occurred only after ileal resections of more than 100 cm. and was not a feature of small resections or unoperated disease, but his conclusions were based on serum vitamin-B_{12} levels which usually only become abnormal after massive resection. The results of the Schilling test are unlikely to be abnormal owing to subtle dysfunction such as obtains for the xylose test, because similar results have been found in Crohn's disease using a whole-body counter (Dyer, 1972). Not only may this vitamin-B_{12} malabsorption lead to megaloblastic anaemia in unoperated patients (Dyer, Child, Mollin, and Dawson, 1972), but an abnormal absorption test may also be a valuable sign of early Crohn's disease at a stage when radiography of the ileum is normal.

The relatively minor degrees of malabsorption noted in our patients were insufficient to account for the nutritional disturbances observed and the lack of correlation of malabsorption with disease activity also suggests that malabsorption and malnutrition are unrelated. Our studies suggest that malabsorption is of little clinical significance except in the genesis of vitamin-B_{12} deficiency. On the other hand, it may account for the symptom of diarrhoea which is sometimes due to either steatorrhoea or the cathartic action of unabsorbed bile-salts on the colon (Hofmann, 1967).

Acknowledgement.—This work was supported by a grant from the Board of Governors of St. Bartholomew's Hospital.

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PARTIAL HEPATECTOMY USING A CARBON-DIOXIDE LASER

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SUMMARY

Partial hepatectomy by means of a carbon-dioxide laser has been performed in 13 dogs. The operative technique is described, and its advantages and the absence of morbidity and mortality during the 10 weeks after operation are discussed.

IN a previous report it was shown that incisions of the liver made with a carbon-dioxide laser are accompanied by much less haemorrhage than similar incisions made by surgical diathermy or scalpel. For this reason it was suggested that the laser might be useful in routine hepatic surgery (Hall, 1971). This report describes the successful performance of partial hepatectomy by means of a carbon-dioxide laser.

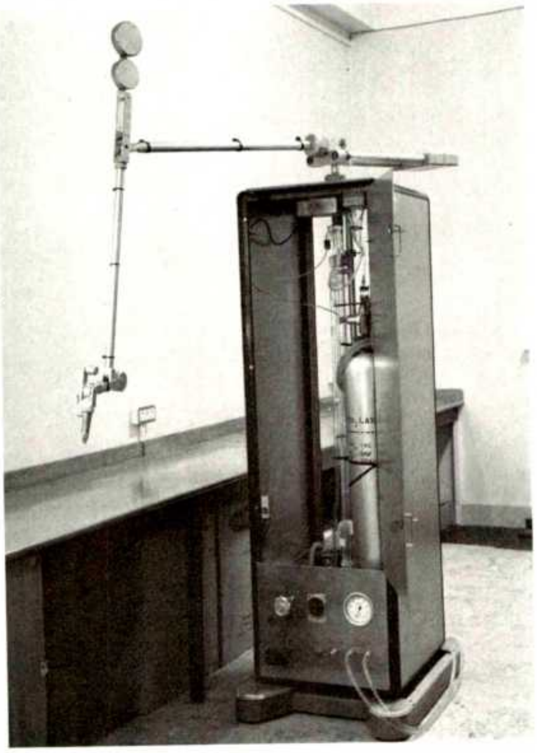

FIG. 1.—Surgical laser. The infra-red beam emerges from the vertical laser (central glass tube) and is reflected along the counter-balanced arm to the focusing handpiece.

THE LASER

The surgical laser (*Fig.* 1) is the first British prototype designed specifically for use in the operating theatre. It provides 35 W. of infra-red radiation (wavelength 10·6 μm.) focused by a gallium-arsenide lens to a spot 0·25 mm. in diameter at the working end of the light, mobile, hand-held instrument (*Fig.* 2). This is held so that the focus of the laser beam is always at the surface of the tissue to be incised. The intense heat at the focus vaporizes the tissue to a depth of several millimetres, the exact depth of the incision depending upon the laser-power density used and the speed at which the beam is moved over the tissue.

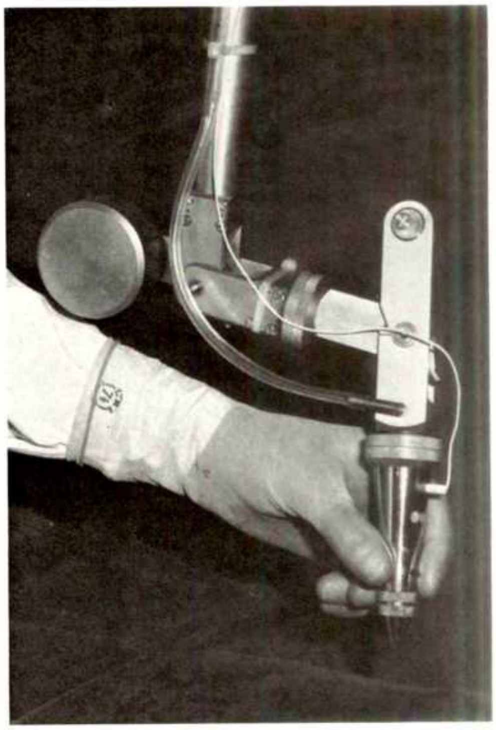

FIG. 2.—Handpiece of the surgical laser.

The laser's action is uniform and gentle (Stellar, Polanyi, and Bredermeir, 1971; Hall, Beach, Baker, and Morison, 1971) compared with the irregular explosive arcing of cutting diathermy. There is no direct contact between the instrument and the tissue so that adhesion of the probe cannot occur. Alternatively, the laser can be held out of focus so that the power is spread over a larger area and heats the tissue slowly rather than vaporizing it, in a manner similar to that of coagulation diathermy.

MATERIALS AND METHODS

Thirteen operations were performed on mongrel dogs weighing 14–18 kg. Full sterile surgical technique was employed under i.v. Nembutal anaesthesia with spontaneous respiration.

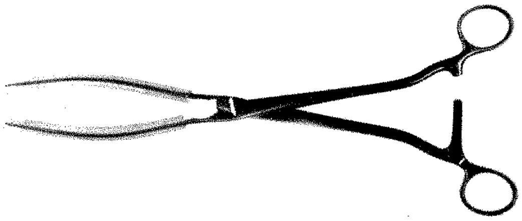

FIG. 3.—Modified Moynihan clamp for atraumatic compression of the liver.

At the commencement of the operation the left femoral artery was catheterized by the Seldinger method to provide continuous monitoring of the systolic blood-pressure.

Upper midline laparotomy was performed using the laser to incise all the layers of the abdominal wall in 10 dogs, bleeding vessels being coagulated with the laser. In 3 dogs scalpel incision was performed, bleeding vessels being ligated in the usual manner. Laser radiation at 10·6 μm. is completely absorbed by water, and therefore several gauze swabs soaked in physiological saline solution were placed behind the liver to protect the posterior abdominal viscera from unintentional exposure.

Blood-flow through the liver must be arrested while resection is performed (Mullins, Jennings, and McClusky, 1968; Hall, 1971). In the first 2 dogs this was achieved by occluding the portal vein and hepatic artery at the porta hepatis with a small Satinsky clamp. However, it was found that such occlusion of the total hepatic circulation could cause severe hyperkalaemia (Hall, 1972) and the method was discontinued. Instead, only the circulation to the portion of liver to be excised was occluded by applying a clamp across the liver lobe. A Moynihan stomach clamp was modified for this purpose (*Fig.* 3) by creating a greater curvature of the blades to fit the contour of the liver and covering them with soft polyvinyl. By this means adequate compression of the lobar vessels was obtained without trauma to the capsule or parenchyma.

Having applied the clamp across the posterior third of the left lobe the anterior half was resected with the laser. The laser beam was moved slowly backwards and forwards across the liver, gentle traction separating the incision so that the laser focus was always at the depth of the incision to vaporize fresh liver parenchyma. This was a simple process that left a dry liver surface, at the centre of which the transected major vessels were clearly visible. These were dealt with in one of two ways.

First, the vessels were sealed by heat coagulation using the laser out of focus. It was possible to coagulate veins up to 5 mm. in diameter by this method and when the clamp was removed no bleeding occurred. This method of laser coagulation was used without any other form of haemostasis in 4 dogs; the swabs were removed from behind the liver and the abdomen was closed without any further precaution or drainage of the operation site.

However, it was considered that this method would not be adequate for the largest vessels that would be encountered in the human liver; the laser would not obviate ligation of these. Thus, in the remaining 9 dogs when resection was complete the open ends of the left hepatic artery and vein and portal vein were oversewn with 0000 Ethiflex sutures. The clamp was then removed and if some of the intermediate-sized vessels bled they were readily coagulated with the laser. No bile leakage was ever observed and the abdomen could be closed without drainage.

Wound closure was completed in 7 dogs using chromic catgut for the peritoneum and linea alba, with silk for the skin. This method was abandoned because of poor healing, and the remaining wounds were closed with interrupted 000 monofilament nylon to the linea alba and skin as two separate layers.

The femoral artery catheter was left in situ at the end of the operation to allow continuous measurement of the blood-pressure during the first 20 hours of recovery. All the dogs were fully recovered and active within 5–15 hours and were returned to normal accommodation after 24 hours. Each dog received Penidural, 1 ml. i.m. immediately, and streptomycin, 0·5 g. i.m. daily for 5 days. The dogs were sacrificed between 5 days and 10 weeks following operation: 1 on the fifth day, 6 on the seventh day, and 2 each at 7, 8, and 10 weeks. Post-mortem examination and liver biopsy were performed in each case.

AUTOPSY FINDINGS

Wound Healing.—All the incisions which had been closed with nylon (2 scalpel, 4 laser) healed well. Those which had been closed with catgut and silk (1 scalpel, 6 laser) were complicated by oedema, serosanguineous discharge, poor skin healing, and breakdown of the deeper layers of the wound. From this small group it appeared on clinical assessment that the healing of laser wounds compared with scalpel incisions was not impaired; the complications were due to the use of catgut.

Liver.—Examination on the fifth and seventh postoperative days revealed no free fluid in the abdomen, no haematoma, and no bile staining of the peritoneum or viscera adjacent to the liver. The liver surface which had been cut by the laser was covered by a layer of pale necrotic tissue up to 2 mm. deep that still had a slightly charred superficial appearance. This layer was soft and easily removed from the underlying liver which was separated from it by a tough fibrous capsule. Histological examination (*Fig.* 4) showed it to be comprised of necrotic liver parenchyma separated from normal liver tissue by a layer of fibrous tissue, polymorphonuclear leucocytes, and macrophages. Sections of blood-vessels which had been sealed by laser coagulation (*Fig.* 5) showed occlusion by a plug of fibrin, the luminal surface of which was covered with intact endothelium.

At 7–10 weeks after operation the peritonal cavity of all the dogs was normal. There were no signs of secondary haemorrhage, bile leakage, or sepsis. Adhesions of the cut liver surface to the stomach and omentum had developed in 2 dogs. In all cases the laser surface of the liver was covered by a capsule that was normal on macroscopic and microscopic examination (*Fig*. 6). The necrotic surface layer was no longer

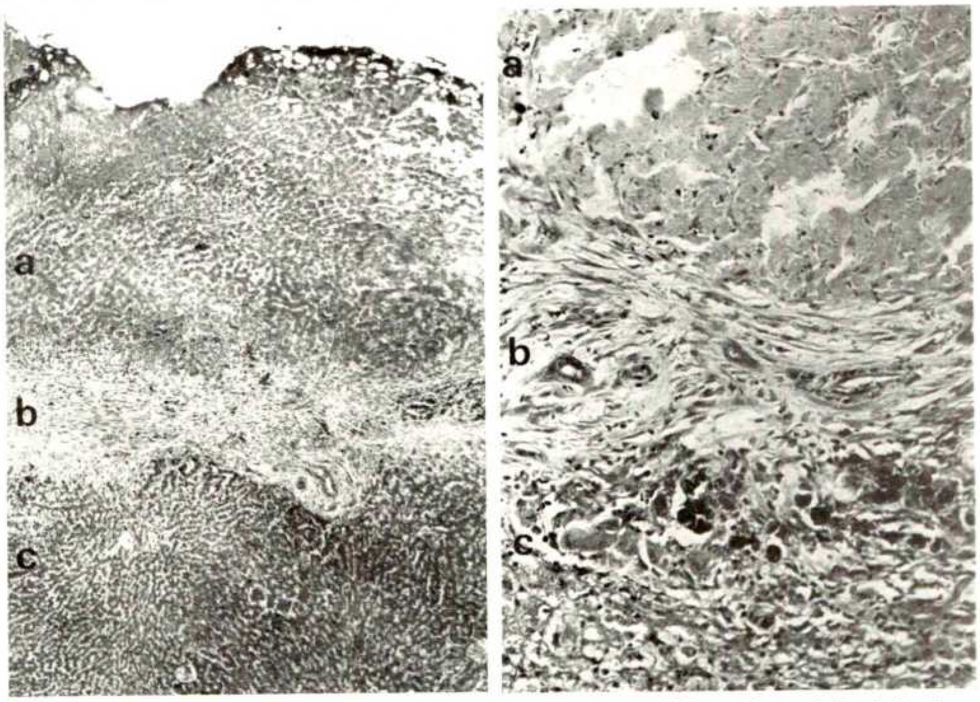

FIG. 4.—Section of the liver 7 days after laser incision. A, × 30. B, × 135. a, Necrotic superficial parenchyma. b, Developing fibrous capsule. c, Normal liver.

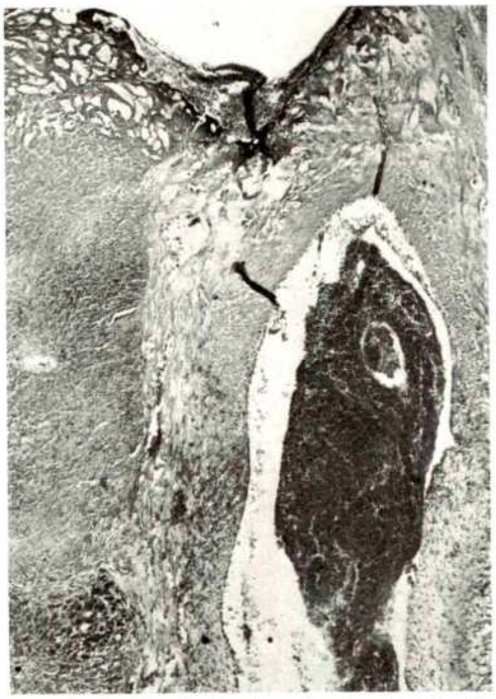

FIG. 5.—Section through a blood-vessel 5 days after it has been sealed by laser coagulation. (× 30.)

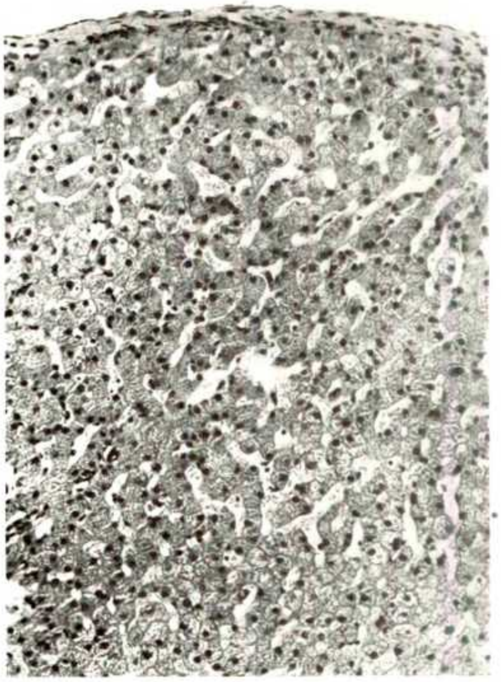

FIG. 6.—Section of the liver 7 weeks after operation showing normal parenchyma and capsules. (× 135.)

present, blood-vessels were closed by fibrous tissue, and the liver parenchyma appeared entirely normal.

DISCUSSION

Since the first recorded partial hepatectomy was performed (Langenbush, 1888) a variety of surgical techniques have been employed (Beck, 1902; Wangensteen, 1951; Nakayama, 1957; Balasegaram, 1968; Smith, 1969).

The particular asset of the laser for hepatic surgery is the primary sealing of the smaller arteries and veins which are present throughout the liver substance that are not large enough to warrant ligation but require haemostasis by other means. The laser overcomes this problem by thermal coagulation during the process of the incision and in doing so it is superior to conventional diathermy. The same process also closes the bile-ducts.

The use of the laser thus enables translobar resections to be performed with comparative ease, avoiding the necessity of formal hemihepatectomy and permitting bilateral or multiple liver resections at one operation. The practical application of this in clinical surgery has been discussed previously (Hall, 1971).

This present study, which includes long-term survival, shows that partial hepatectomy using a carbon-dioxide laser is a simple, safe operation accompanied by a minimum of haemorrhage, no bile leakage, sound healing, and no late complications.

Acknowledgements.—We are very grateful to Lord Brock, Director of the Department of Surgical Sciences, Royal College of Surgeons of England, for providing the facilities for this study; to Miss M. Jacques, Mrs. C. Hill, and Mr. J. Manders of the same department, and Mr. J. Watson of the Buckston Brown Farm, Downe, Kent, for their technical assistance; to the Department of Health and Social Security for a grant for the laser construction and animal expenses.

We also wish to thank Dr. A. Levine and the staff of the Histopathology Department of the Royal Marsden Hospital for preparing the histological material, and Mr. K. Morman of the Institute of Cancer Research for the photomicrographs.

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THE EFFECT OF INCREASED OXYGEN IN ACUTE LIMB ISCHAEMIA

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SUMMARY

Acute hind-limb ischaemia was produced in anaesthetized, ventilated dogs. During ischaemia the femoral venous oxygen tension fell markedly and both oxygen extraction and consumption appeared to increase. Oxygen at 2 ATA produced a relatively small increase in oxygen availability to the ischaemic tissues; femoral venous oxygen tension rose by 20 mm. Hg but oxygen extraction and consumption remained elevated.

THE clinical use of hyperbaric oxygen in the treatment of peripheral ischaemia is largely empirical. There is a need for more critical examination of the relationship between high arterial oxygen tension and ischaemia, particularly since the former is associated with vasoconstriction under normal circumstances (Bird and Telfer, 1966). The present study examines the effect of hyperoxia in acute ischaemia of the canine limb with particular reference to blood-flow and oxygen exchange.

MATERIALS AND METHODS

Studies on 10 large dogs were performed within one of the large compressed-air chambers at the Western Infirmary, Glasgow. Anaesthesia was induced with sodium thiopentone (2·5 mg. per kg.) and maintained with trichlorethylene. Intermittent suxamethonium chloride was given as required to prevent reflex movement. The dogs were intubated and intermittent positive-pressure ventilation was established using a Palmer pump, the stroke volume of which was adjusted to maintain the arterial carbon-dioxide tension (Pa_{CO_2}) between 35 and 45 mm. Hg. The inspired oxygen concentration was measured with a paramagnetic oxygen analyser (Servomex OA 101 Mk II). A catheter inserted in the brachial artery.

was advanced to lie in the mid-aorta proximal to the site of arterial ligation. Arterial blood samples were withdrawn from this site and pressure recordings were made using an ink-jet recorder (Elema Schönander Mingograph 81). Limb and mid-oesophageal temperatures were recorded on an Ellab TE3 Universal Thermocouple and the latter temperature was maintained constant within ± 1° C.

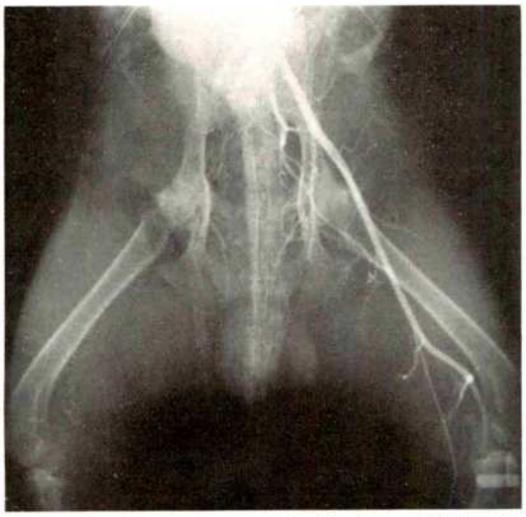

FIG. 1.—Arteriogram demonstrating the degree of ischaemia produced by tightening of the arterial snares on the right side.

The canine hind-limb is well supplied with collateral arterial channels. The lower limb vessels were exposed, therefore, at the root of the aorta, and the circumflex, iliac, and median sacral vessels were ligated (there was no resultant significant change in limb blood-flow). Snares placed around the external and internal iliac arteries permitted the establishment of periods of limb ischaemia which could be terminated at will. The degree of ischaemia produced by the occlusion of the snares is illustrated in the arteriogram (*Fig.* 1). A T-tube was inserted, at the level of the groin, into the femoral vein of the limb under study and the animal was heparinized (100 mg. per kg. i.v.). Blood-flow was measured by first clamping the proximal limb of the T-tube and then collecting the effluent venous blood over a period of 30 or 60 seconds. Blood removed in this fashion was retransfused. The bulk of the blood passing out of the limb traversed the T-tube (*Fig.* 2). Venous pressure was recorded before and after each flow measurement. After the initial surgery the animal was allowed to settle for a minimum period of 1 hour.

Mid-aortic and femoral venous blood samples were withdrawn for measurement of oxygen and carbon-dioxide tension and pH using a triple electrode system (Radiometer Micro Electrode Unit with *p*H Meter 27 and Gas Monitor) calibrated with gases of known concentrations. Correction for the difference in oxygen-tension measurement between gas and blood was made using tonometered blood (McDowall, Ledingham, and Tindal, 1968). Further correction of the blood gases and *p*H was made for any temperature difference between the electrode recirculation system and the animals' mid-oesophageal temperature (Radiometer Blood Gas Calculator—984300). The latter also permitted calculation of the blood-oxygen saturation from *p*H and P_{O_2}, taking into account base excess and the animals' temperature. Haemoglobin (Hb) and packed-cell volume (P.C.V.) were measured at intervals throughout each experiment. The following derived data were calculated:—

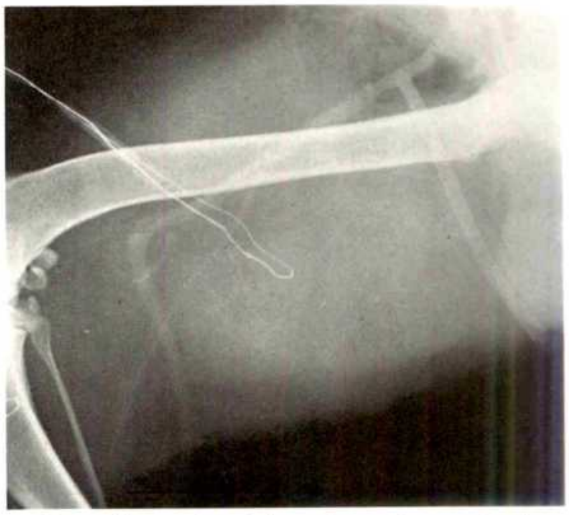

FIG. 2.—Venous phase of the arteriogram demonstrating that the bulk of the radio-opaque medium traversed the femoral venous T-tube.

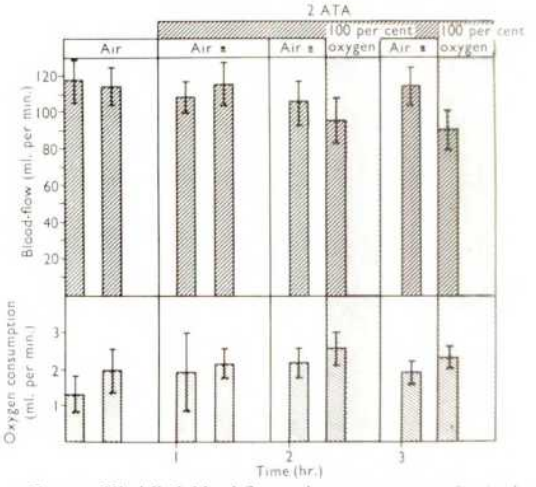

FIG. 3.—Hind-limb blood-flow and oxygen consumption in the contralateral non-ischaemic limb before and during the ischaemia. No significant changes occurred in flow or consumption in the contralateral limb. Oxygen at 2 ATA produced a small but, on the second occasion, significant decrease in limb blood-flow.

1. Blood oxygen content (ml. per 100 ml.) =

$$\text{Hb (g.)} \times 1{\cdot}34 \times \frac{\text{O}_2\ \text{saturation}}{100} + P_{O_2}\ \text{(mm. Hg)} \times 0{\cdot}0031\ \text{(Bunsen coefficient).}$$

Within the range of 7–24 ml. per 100 ml. blood there was a close relationship between this indirect method of measurement of the oxygen content and the direct method of Van Slyke ($y = 0{\cdot}37 + 1{\cdot}06x$; $r = 0{\cdot}983$; Ledingham, McBride, Parratt, and Vance, 1970). Furthermore, in the present study a periodic check was made of the oxygen saturation with the standard haemoreflector (Kipp) and the oxygen content with the Van Slyke apparatus. Comparison of the two methods of measurement of saturation (70 readings) revealed a regression (r) of 0·910 and for the oxygen content (20 readings) of 0·980.

2. Limb oxygen consumption (ml. per min.) =

$$\frac{\text{Femoral vein flow (ml. per min.)} \times \text{femoral arterio-venous oxygen content difference (ml. per 100 ml.)}}{100}$$

3. Limb oxygen availability (ml. per min.) =

$$\frac{\text{Femoral vein flow (ml. per min.)} \times \text{arterial oxygen content (ml. per 100 ml.)}}{100}$$

4. Limb oxygen extraction (per cent) =

$$\frac{\text{Femoral arteriovenous oxygen content difference (ml. per 100 ml.)} \times 100}{\text{Arterial oxygen content (ml. per 100 ml.)}}$$

After the period of stabilization brief periods of ischaemia (15 minutes) were produced, preliminary experiments having shown that the bulk of the changes in flow and oxygen exchange occurred during this time with subsequent complete recovery of the limb. The initial period of ischaemia was established at normal atmospheric pressure, with the inspired gas mixture adjusted to maintain arterial oxygen tension (Pao$_2$) between 95 and 105 mm. Hg. The subsequent stages of each experiment were conducted at 2 atmospheres absolute (ATA), the inspired gas being either 'air-equivalent' (i.e., *circa* 10 per cent O$_2$/90 per cent N$_2$) or 100 per cent O$_2$.

In 5 of the animals of the study, measurements of blood-flow and oxygen exchange were made in the contralateral non-ischaemic limb (the limb vessels were exposed in an identical fashion but were not ligated). The measurements were completed immediately after the comparable measurements in the ischaemic limb.

RESULTS

The experimental protocol and the mean values of limb blood-flow and limb oxygen consumption of all 10 dogs are indicated in *Table I*. After ligation blood-flow fell from 105 ± 7 ml. per minute (mean ± S.E. of the mean) to 39 ± 4 ml. per minute and oxygen consumption rose from 1·06 ± 0·30 ml. per minute to 3·31 ± 0·64 ml. per minute. Release of the arterial snares was associated with a return to normal of both values. Increased atmospheric pressure (with Pao$_2$ unchanged) had no significant effect on blood-flow or on oxygen consumption either during control runs or consequent upon ischaemia. Exposure to 100 per cent oxygen at 2 ATA also failed to produce a significant change in the response of flow or oxygen consumption to ischaemia.

Pao$_2$, femoral venous oxygen tension (Pvo$_2$) and carbon-dioxide tension (Pvco$_2$), femoral arteriovenous oxygen content difference (Δavo$_2$), and oxygen extraction are indicated during the various stages of the experiment in *Table II*. Pvo$_2$ and Pvco$_2$ were 71 and 39 mm. Hg during control runs and 33 and 53 mm. Hg respectively during ischaemia; femoral arteriovenous oxygen content difference rose from 1·1 to 9·5 ml. per minute, and extraction of oxygen correspondingly increased from 5 to 42 per cent. When the arterial oxygen tension was increased to 1226 mm. Hg during ischaemia, Pvo$_2$ fell from 76 to 54 mm. Hg and Pvco$_2$ rose from 42 to 62 mm. Hg. The femoral arteriovenous oxygen content difference rose from 1·1 to 8·0 ml. per minute and the oxygen extraction from 5 to 31 per cent.

Throughout the various stages of the experiment the blood-pressure remained stable. The fall of temperature in the hind-limb during each 15-minute period of ischaemia was minimal.

Table I.—COMPARISON OF LIMB BLOOD-FLOW AND OXYGEN CONSUMPTION IN THE ISCHAEMIC AND THE CONTRALATERAL NON-ISCHAEMIC LIMB

		ISCHAEMIC LIMB (10 dogs; mean ± S.E. of the mean)		CONTRALATERAL NON-ISCHAEMIC LIMB (5 dogs; mean ± S.E. of the mean)	
		Flow (ml. per min.)	O$_2$ Consumption (ml. per min.)	Flow (ml. per min.)	O$_2$ Consumption (ml. per min.)
Air		105 ± 7	1·06 ± 0·30	117 ± 12	1·30 ± 0·46
		$P < 0{\cdot}0005$	$P < 0{\cdot}0025$		
Air + ischaemia		39 ± 4	3·31 ± 0·64	114 ± 10	1·96 ± 0·60
2 ATA	Air equivalent	107 ± 6	0·89 ± 0·18	108 ± 8	1·92 ± 1·06
		$P < 0{\cdot}0005$	$P < 0{\cdot}0025$		
	Air equivalent + ischaemia	40 ± 4	3·36 ± 0·66	115 ± 12	2·14 ± 0·43
	Air equivalent	108 ± 7	0·92 ± 0·27	105 ± 12	2·17 ± 0·42
		$P < 0{\cdot}0005$	$P > 0{\cdot}0005$		
	100 per cent O$_2$ + ischaemia	42 ± 5	3·01 ± 0·34	95 ± 12	2·57 ± 0·45
	Air equivalent	107 ± 7	0·82 ± 0·12	114 ± 11	1·91 ± 0·31
		$P < 0{\cdot}0005$	$P < 0{\cdot}0005$	$P < 0{\cdot}005$	
	100 per cent O$_2$ + ischaemia	37 ± 3	2·65 ± 0·28	90 ± 11	2·33 ± 0·29

In the contralateral non-ischaemic limb of 5 of the animals (*Fig.* 3, *Table III*) blood-flow and oxygen consumption remained essentially stable throughout, although evidence of the vasoconstrictive effect of hyperoxia on the intact circulation (Bird and Telfer, 1966) was noted during both hyperoxic runs, the fall in flow being of statistical significance on the second occasion (114 to 90 ml. per minute, $P < 0\cdot005$).

Table II.—MEAN BLOOD-GAS, BLOOD-FLOW, AND OXYGEN CONSUMPTION IN THE ISCHAEMIC LIMB OF 10 DOGS

		Pao_2 (mm. Hg)	Pvo_2 (mm. Hg)	$Pvco_2$ (mm. Hg)	Δavo_2 (ml. per 100 ml.)	FLOW (ml. per min.)	O_2 EXTRACTION (per cent)	O_2 CONSUMPTION (ml. per min.)
Air		100	71	39	1·1	105	5	1·06
Air + ischaemia		104	33	53	9·5	39	42	3·31
2 ATA	Air equivalent	105	72	42	0·9	107	6	0·89
	Air equivalent + ischaemia	102	35	59	9·3	40	43	3·36
	Air equivalent	106	76	42	1·1	108	5	0·92
	100 per cent O_2 + ischaemia	1226	54	62	8·0	42	31	3·01
	Air equivalent	109	75	42	0·9	107	4	0·82
	100 per cent O_2 + ischaemia	1269	58	61	7·7	37	31	2·65

Table III.—MEAN BLOOD-GAS, BLOOD-FLOW, AND OXYGEN CONSUMPTION IN THE CONTRALATERAL NON-ISCHAEMIC LIMB OF 5 DOGS

		Pao_2 (mm. Hg)	Pvo_2 (mm. Hg)	$Pvco_2$ (mm. Hg)	Δavo_2 (ml. per 100 ml.)	FLOW (ml. per min.)	O_2 EXTRACTION (per cent	O_2 CONSUMPTION (ml. per min.)
Air		97	66	37	1·3	117	6	1·30
Air + ischaemia		103	62	38	2·0	114	5	1·96
2 ATA	Air equivalent	100	62	44	2·0	108	9	1·92
	Air equivalent + ischaemia	99	59	48	2·1	115	10	2·14
	Air equivalent	106	59	49	2·3	105	10	2·17
	100 per cent O_2 + ischaemia	1035	236	53	3·0	95	12	2·57
	Air equivalent	110	63	52	1·8	114	8	1·91
	100 per cent O_2 + ischaemia	1303	403	57	3·0	90	12	2·33

Table IV.—COMPARISON OF OXYGEN AVAILABILITY AND CONSUMPTION IN THE ISCHAEMIC AND THE CONTRALATERAL NON-ISCHAEMIC LIMB

		ISCHAEMIC LIMB (10 dogs; mean ± S.E. of the mean)		CONTRALATERAL NON-ISCHAEMIC LIMB (5 dogs; mean ± S.E. of the mean)	
		O_2 Availability (ml. per min.)	O_2 Consumption (ml. per min.)	O_2 Availability (ml. per min.)	O_2 Consumption (ml. per min.)
Air		21·7 ± 1·8	1·06 ± 0·30	23·9 ± 2·1	1·30 ± 0·46
Air + ischaemia		8·2 ± 0·7	3·31 ± 0·64	24·4 ± 1·7	1·96 ± 0·60
2 ATA	Air equivalent	23·1 ± 1·9	0·89 ± 0·18	23·6 ± 1·6	1·92 ± 1·06
	Air equivalent + ischaemia	8·2 ± 0·7	3·36 ± 0·66	24·3 ± 1·8	2·14 ± 0·43
	Air equivalent	22·6 ± 1·5	0·92 ± 0·27	22·1 ± 2·1	2·17 ± 0·42
	100 per cent O_2 + ischaemia	10·1 ± 1·2	3·01 ± 0·34	23·3 ± 2·9	2·57 ± 0·45
	Air equivalent	21·9 ± 1·2	0·82 ± 0·12	23·6 ± 2·4	1·91 ± 0·31
	100 per cent O_2 + ischaemia	8·8 ± 0·6	2·65 ± 0·28	21·9 ± 3·1	2·33 ± 0·29

The effect of oxygen administration at 2 ATA on oxygen availability and oxygen consumption is indicated in *Table IV* in both the ischaemic and the contralateral non-ischaemic limbs. During ischaemia at 2 ATA, oxygen availability was 8·2 ± 0·7 ml. per minute with air as the inspired gas and 10·1 ± 1·2 ml. per minute during the first exposure to 100 per cent oxygen ($P < 0\cdot05$) with no significant changes in the corresponding value for oxygen consumption. In the contralateral non-ischaemic limb the increase in arterial oxygen tension with 100 per cent oxygen was counterbalanced by a fall in blood-flow. Thus, no significant change in oxygen availability occurred; oxygen consumption also remained unchanged. Excluding the first control run, oxygen consumption in the non-ischaemic limb was consistently higher than in the contralateral ischaemic limb during control runs.

DISCUSSION

Relatively little information is available about the effect of ischaemia on oxygen exchange in peripheral tissues. It has been shown that muscle oxygen tension falls after femoral arterial ligation in the rabbit (Ackerman and Brinkley, 1966), and desaturation of femoral venous blood during ischaemia has been reported (Wang, Reich, Lesko, and Jacobson, 1966). The present experiments have confirmed that a substantial increase in oxygen extraction occurs in the acutely ischaemic limb. A surprising observation, perhaps, was that oxygen extraction was greater than that which could be related solely to the reduction in limb blood-flow with the result that total hind-limb oxygen consumption rose significantly. If this represents a true increase in oxygen consumption per unit of tissue, no conclusion can be drawn as to whether the increase was spread uniformly throughout the limb or affected only a part of the limb. The alternative explanation for the increase in total limb oxygen consumption, namely the diversion through the T-tube of effluent blood from a larger drainage area, seems unlikely during ischaemia and, in any case, could not have accounted for more than a fraction of the calculated increase. Two points are worthy of mention in relation to the observed changes in oxygen consumption. First, the pre-ischaemic femoral venous oxygen tension was higher and the oxygen extraction lower than has been previously reported (Wang and others, 1966). Thus, changes in the femoral venous oxygen tension after ischaemia would inevitably be greater than in experiments in which the initial femoral venous oxygen tension was lower. Secondly, although limb blood-flow was considerably reduced by arterial ligation, the mean flow was 40 ml. per minute during ischaemia which might not have been low enough to produce a reduction in oxygen consumption in the hind-limb tissues, at least for the short duration of ischaemia obtaining in the present study. Pappenheimer (1941) found, in the isolated perfused dog limb, that clamping of the femoral artery was not associated with a fall in the oxygen consumption until the blood-flow had fallen to around 40 ml. per minute, thus confirming earlier work by Freund and Janssen (1923), who reported that there was a critical level of blood-flow below which diminished oxygen consumption occurred in the canine limb (the value was 0·05 ml. per g. per minute). Of interest in relation to the raised oxygen consumption noted in the present study was the observation (von Euler, 1931; Pappenheimer, 1941) that adrenaline injected into the isolated perfused limb produced a fall in the blood-flow of 30 per cent with a concomitant increase in the oxygen consumption, as calculated by the product of blood-flow and arterial venous oxygen content difference. A similar mechanism in the present experiments could have been mediated only at a local level since clamping of the femoral artery produced no significant change in the heart-rate, or the blood-pressure or blood-flow in the contralateral non-ischaemic limb.

The administration of 100 per cent oxygen at 2 ATA was associated with an increase in oxygen availability during ischaemia since the arterial oxygen content rose with no significant further fall in the blood-flow. The mean femoral venous oxygen tension rose by 20 mm. Hg, which could imply improved tissue oxygenation; the absence of any significant alteration in the elevated oxygen consumption, however, complicates the interpretation of the findings in the venous blood. Clearly further studies are necessary to examine in more detail individual variation in response to ischaemia and increased oxygen tension, particularly during periods of more prolonged ischaemia.

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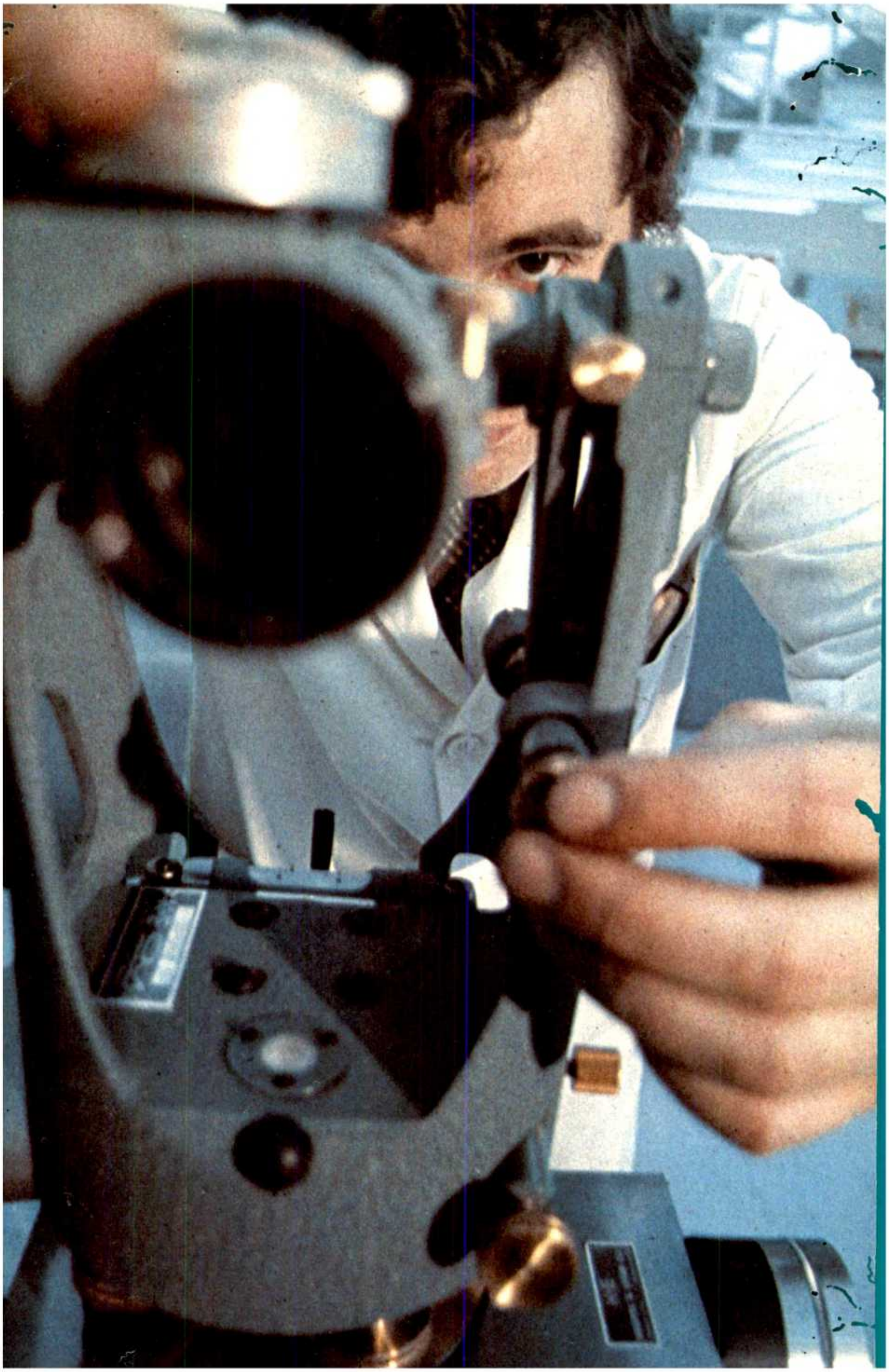

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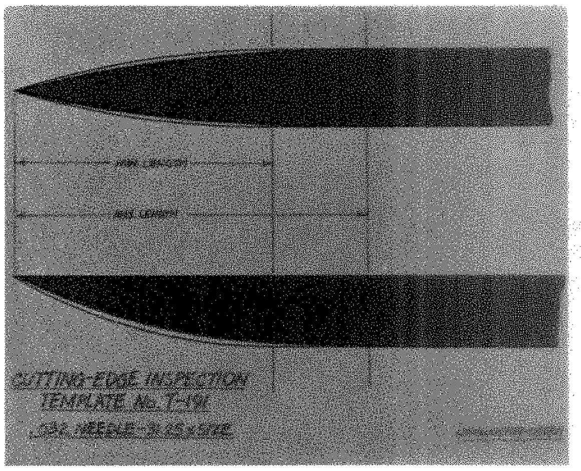

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THE AETIOLOGY AND PREVENTION OF PANCREATITIS FOLLOWING BILIARY-TRACT OPERATIONS

By M. R. B. KEIGHLEY* and N. G. GRAHAM
HUDDERSFIELD ROYAL INFIRMARY

SUMMARY

The incidence of pancreatitis complicating biliary-tract operations is reported from a prospective survey of 75 patients. This study confirms that pancreatitis is much more frequent after choledochotomy than after cholecystectomy alone. Biochemical pancreatitis was demonstrated in over a third of the patients in whom the duct was explored.

The validity of elevated serum amylase in the diagnosis of this complication is established provided that clinical evidence of pancreatitis is also present. The significance of amylasaemia in the immediate postoperative period in the absence of clinical signs is questioned.

Reflux of duodenal contents into the pancreatic duct may be provoked by operative damage to the sphincter of Oddi. In these patients clinical pancreatitis invariably occurred. The avoidance of sphincterotomy in the prevention of this potentially serious postoperative complication is advised. Since pancreatitis was more common after negative exploration of the common bile-duct the value of operative cholangiography in the avoidance of this complication is discussed.

Postoperative pancreatitis is a well-known complication of biliary-tract operations, particularly following supraduodenal exploration of the common bile-duct and transduodenal sphincterotomy (Thomson, Howard, and Vowles, 1957; Partington, 1966). This complication carries a high mortality of the order of 80 per cent (Thomson and others, 1957; Trapnell, 1966) and, although this occurs in a relatively small number of patients following these procedures, it is an event that should be avoided whenever possible.

It is well recognized that the diagnosis of postoperative pancreatitis which frequently occurs in the immediate postoperative period may be difficult (Burton, Eckman, and Haxa, 1957). The importance and validity of serum-amylase estimations in the early detection and diagnosis of this condition have been stressed (Perryman and Hoer, 1954; Mahaffey and Howard, 1955; Keighley, Johnson, and Stevens, 1969).

Until recently postoperative pancreatitis has been thought to be caused by trauma to the gland at operation (Warren, 1951; Blatherwick and Pattison, 1954; Burton and others, 1957). The other factors which have been incriminated include local ischaemia (Burton and others, 1957), ductal obstruction from instrumental oedema or the long-arm T-tube (Diffenbaugh and Strohl, 1956), biliary reflux into the pancreatic duct (Herman and Knowles, 1963), and the reflux of infected bile (Bryne and Joison, 1964). More recently the aetiological importance of duodenal contents entering the pancreatic duct through a damaged or incompetent sphincter has received considerable support (Pfeffer, Stasior, and Hinton, 1957; McCutcheon and Race, 1962; McCutcheon, 1968). It is suggested that this mechanism explains the incidence of pancreatitis following traumatic exploration of the common bile-duct and sphincterotomy (Warren, 1961), and its association with prolonged postoperative ileus and a distended duodenal loop following Polya gastrectomy (Perman, 1935; Wallensten, 1958).

Trapnell (1966) states that postoperative pancreatitis is more common where previous pancreatic inflammation has occurred.

CLINICAL MATERIAL AND METHODS

This communication reports the incidence of pancreatitis following biliary-tract operations. A prospective study of 75 consecutive cases was undertaken during the course of 1 year, from a single surgical unit of one hospital.

The incidence of pancreatitis was assessed by either clinical features or raised serum-amylase results. In the immediate postoperative period when clinical signs were liable to be masked by the effect of recent abdominal surgery, routine serum-amylase estimations were performed. Features of an acute onset of upper abdominal pain, radiating to the back, associated with repeated vomiting and signs of upper abdominal rigidity with absent bowel-sounds were regarded as evidence of pancreatitis. The diagnosis was confirmed by raised enzyme levels, using serum amylase and urinary diastase for this purpose. A control sample was taken on the day prior to operation and a further specimen on the morning following surgery at least 3 hours after the last postoperative sedation had been given. When elevated results were recorded further daily estimations were undertaken until the levels fell to less than 200 units.

Serum-amylase levels greater than 500 units (Somogyi, 1938) were considered to be abnormal. Provided that other conditions associated with elevated amylase had been excluded, figures of over 1000 units were regarded as diagnostic of pancreatitis; this was also supported by a urinary diastase greater than 200 units.

The incidence of pancreatitis following choledochotomy was studied. Supraduodenal exploration of the common bile-duct was performed in 26 (36 per cent) of the patients in this series. In 4 of these, transduodenal sphincterotomy was also undertaken on account of difficulty in the extraction of impacted stones at the lower end of the duct, in cases with chronic pancreatitis, or where exploration from above had been technically inadequate.

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The indications for choledochotomy in this survey included a previous history of jaundice, pancreatitis, or cholangitis; where the duct at operation appeared dilated or contained palpable stones; where small calculi occurred within the gall-bladder. Operative cholangiography had not been undertaken during the course of this survey.

Table I.—POSTOPERATIVE PANCREATITIS IN RELATION TO TIME OF ONSET, SERUM AMYLASE, AND THE PRESENCE OF SYMPTOMS

CASE	OPERATION IN ADDITION TO CHOLECYSTECTOMY	MAXIMUM POSTOPERATIVE AMYLASE	TIME OF ONSET OF PANCREATITIS	SYMPTOMS
	Immediate postoperative pancreatitis			
1	Supraduodenal choledochotomy	640	24 hr. or less	Nil
2	Supraduodenal choledochotomy	799	24 hr. or less	Nil
3	Supraduodenal choledochotomy	1353	24 hr or less	Present
4	Supraduodenal choledochotomy	564	24 hr. or less	Nil
5	Supraduodenal choledochotomy	823	24 hr. or less	Nil
	Early postoperative pancreatitis			
6	Supraduodenal choledochotomy and sphincterotomy	1060	48 hr	Present
7	Supraduodenal choledochotomy and sphincterotomy	1692	72 hr	Present
8	Supraduodenal choledochotomy and sphincterotomy	1277	48 hr.	Present
	Late postoperative pancreatitis			
9	Supraduodenal choledochotomy and sphincterotomy	1200	5 d.	Present
10	Supraduodenal choledochotomy	1028	8 d.	Present
11	Vagotomy and gastro-enterostomy	1217	10 d.	Present

Table II.—POSTOPERATIVE PANCREATITIS FOLLOWING BILIARY-TRACT OPERATIONS

OPERATION	NO. OF CASES	PANCREATITIS		SYMPTOMS PRESENT IN PATIENTS WITH PANCREATITIS	
		No.	Per cent	No.	Per cent
Cholecystectomy alone	49	1	2	1	100
Supraduodenal choledochotomy	26	10	39	6	60
Choledochotomy alone	22	6	27	2	33
With sphincterotomy	4	4	100	4	100

Supraduodenal exploration of the duct was performed using Desjardin's forceps and the patency of the sphincter was confirmed with Bake's dilators. T-tube drainage (of the short-arm variety) was routinely used after choledochotomy.

Specimens of bile collected from the gall-bladder at operation and from the T-tube in the postoperative period were submitted for aerobic and anaerobic culture. The relationship of pancreatitis to the presence of organisms within the biliary tract was analysed, and evidence of previous pancreatitis was noted.

FINDINGS

Postoperative pancreatitis occurred in 11 of the 75 patients undergoing biliary-tract operations, an overall incidence of 15 per cent. In all these patients the serum-amylase level was greater than 500 units (*Table I*).

Five cases developed pancreatitis within 24 hours of operation. Most of these patients had no clinical signs suggestive of pancreatitis and the diagnosis was made on the elevated enzyme levels alone. In the remainder the diagnosis was established betwee the second and tenth postoperative days on the basi of the clinical signs. This was confirmed by a raise urinary diastase and a serum amylase consistentl above 1000 units. Where the diagnosis was mad within 24 hours of operation and no clinical sign occurred, levels between 500 and 1000 units only wer demonstrated. In all these patients the preoperativ amylase level had been less than 200 units.

A high incidence of postoperative pancreatitis (1 cases—39 per cent) occurred in patients undergoin exploration of the common bile-duct, compared wit 1 case (2 per cent) following cholecystectomy alon (*Table II*). Where transduodenal exploration throug the sphincter was also performed in addition t supraduodenal choledochotomy, postoperative pan creatitis invariably occurred. In two-thirds of th patients developing pancreatitis following sup duodenal choledochotomy the diagnosis was m on the raised enzyme levels alone, whereas whe sphincterotomy was also performed signs invariabl accompanied grossly elevated enzyme results.

Prophylactic Trasylol, in a dose of 100,000 unit administered 6-hourly parenterally, was given to 2 of the 26 patients undergoing choledochotomy fo 36 hours immediately after operation. Raised serur amylase occurred in 8 of these cases (36 per cent despite this measure.

The patient developing pancreatitis followin cholecystectomy alone was of interest. A vagotom and pyloroplasty had also been undertaken for concomitant duodenal ulcer and the postoperativ course was complicated by prolonged ileus lastin for 5 days. This patient was readmitted on the tent postoperative day with signs of upper abdomin guarding and rebound tenderness associated wit profuse vomiting, and the serum amylase was raise to a level of 1277 units.

Postoperative pancreatitis was also assessed i relation to the presence of stones in the commo bile-duct. These were found in only 46 per cent c the patients undergoing choledochotomy. Evidenc that stones had not been overlooked was confirme by normal postoperative T-tube cholangiography Postoperative pancreatitis occurred more frequentl in patients in whom no stones were found (70 pe cent; *Table III*). As a result of these findings the value of clinical criteria for exploring the duct was analysed. The only reliable indication for choledochotomy was the finding of palpable stones at operation, although in a third of patients with choledocholithiasis these were impalpable. A previous history of jaundice, cholangitis, and pancreatitis was unreliable evidence of stones within the duct (*Table IV*).

Table III.—POSTOPERATIVE PANCREATITIS FOLLOWING CHOLEDOCHOTOMY IN RELATION TO CHOLEDOCHOLITHIASIS AND PREVIOUS PANCREATITIS

	No. of Cases	Percentage of Cases	Postoperative Pancreatitis	
			No.	Per cent
Choledochotomy	26		10	39
Choledocholithiasis	12	46	3	30
No stones	14	54	7	70
Previous pancreatitis	12	46	4	40
No previous pancreatitis	14	54	6	60

Table IV.—THE VALUE OF CLINICAL INDICATIONS FOR CHOLEDOCHOTOMY IN 26 CASES

Indications	Stones present (12 Cases)		No Stones (14 Cases)	
	No.	Per cent	No.	Per cent
Jaundice	10	84	11	78
Pancreatitis				
Preoperative	5	42	4	28
At operation	6	50	6	43
Cholangitis	4	33	5	35
Dilated common bile-duct	9	75	7	50
Palpable stones	8	67	0	—
Dilated cystic duct and small calculi in gall-bladder	5	42	7	50
Sludge in common bile-duct	6	50	5	35
Biliary colic	9	75	14	100

Table V.—POSTOPERATIVE PANCREATITIS AND ITS RELATIONSHIP TO ORGANISMS WITHIN THE BILIARY TRACT

	No. of Cases	Per cent
Overall incidence of infected gall-bladder bile	27 out of 75	36
Infected gall-bladder bile with pancreatitis	4 out of 11	36
Overall incidence of infected T-tube bile	19 out of 26	73
Infected T-tube bile with pancreatitis	6 out of 10	60

The incidence of postoperative pancreatitis was not related to the occurrence of organisms either in the gall-bladder at operation or in the T-tube in the postoperative period (*Table V*). Postoperative pancreatitis was independent of previous inflammatory episodes within the gland (*Table III*).

In patients developing clinical pancreatitis in the postoperative period the morbidity was increased in terms of prolonged hospital stay, but the overall mortality in this survey was nil. In those patients where a raised serum amylase was the only indication of pancreatitis the length of hospital stay was not extended.

DISCUSSION

The results have demonstrated a high incidence of pancreatitis following choledochotomy. This occurred in over a third of the patients in whom the common bile-duct was explored. Where transduodenal choledochotomy through the sphincter was performed postoperative pancreatitis ensued in every case. There was a high incidence of negative findings when the duct was explored and pancreatitis was more common when the stones were not found.

The validity of serum-amylase levels as a sole criterion for a diagnosis of pancreatitis in the postoperative period was reviewed. As there were no preoperative control figures above the normal range, this would suggest that abnormal results in the postoperative period were probably significant. Where clinical features of pancreatitis were absent within the first 24 hours after operation, serum amylase levels, although elevated, were rarely above 1000 Somogyi units. In these patients the serum-enzyme results returned to normal within 24 hours and the presence of amylasaemia did not appear to influence the overall recovery. It is suggested, therefore, that a raised serum amylase in the immediate postoperative period following supraduodenal choledochotomy does not necessarily signify overt pancreatitis.

This study has investigated some of the factors concerned in the aetiology of pancreatitis following biliary-tract surgery. No importance is attached to the presence of organisms in the biliary tract from the results of this survey. There was no evidence of pancreatic duct filling on postoperative T-tube cholangiography in patients developing pancreatitis in the postoperative period. It is suggested, therefore, that biliary reflux up the pancreatic duct is not an important factor in the pathogenesis of this condition. Direct trauma to the gland has been investigated elsewhere, and it is considered that this is not responsible for pancreatitis following operative procedures, although local trauma to the sphincter alone appears to play an important part in the occurrence of this condition (Keighley and others, 1969).

There has been adequate experimental evidence to suggest that an important cause of pancreatitis in cases with an isolated duodenal loop is duodenal reflux, which can be prevented by tying the pancreatic duct (McCutcheon and Race, 1962; Williams and Bryne, 1967). This would explain the development of this complication in the patient with a prolonged period of ileus following cholecystectomy, thus allowing stagnant duodenal contents to accumulate and to fill the pancreatic duct. Sphincterotomy and extensive exploration of the common bile-duct which rendered the sphincter of Oddi incompetent were invariably followed by clinical pancreatitis. It is suggested from this study that duodenal reflux into the pancreatic duct is an important cause of clinical pancreatitis following these procedures.

In discussing the avoidance of postoperative pancreatitis, these findings have shown that whenever transduodenal sphincterotomy was performed in addition to supraduodenal choledochotomy, clinical pancreatitis with biochemical evidence of pancreatic autodigestion occurred in every case. It would appear that the prophylactic administration of Trasylol in the immediate postoperative period does not protect against this complication. It is argued, therefore, that sphincterotomy should be avoided whenever possible. The value of choledochoduodenostomy in patients with pre-existing pancreatic disease and choledocholithiasis with a dilated common bile-duct has previously been documented (Burgess and Kidd, 1967). Therefore where choledochotomy is indicated the avoidance of trauma to the sphincter might be an important factor in the prevention of this potentially dangerous postoperative complication (Blatherwick and Pattison, 1954).

Since negative exploration of the common bile-duct was associated with a high incidence of postoperative pancreatitis it is argued that this would not have occurred if choledochotomy had been avoided.

The importance of satisfactory operative cholangiography in the definition of stones and the avoidance of unnecessary exploration has been clearly shown (Swedburg, 1952; McEvedy, 1970; Wheeler, Sonpong, and Williams, 1970). Other workers have experienced a similar incidence of negative findings when the common bile-duct is explored on clinical indications alone (Glenn, 1952; Thomson, 1956). It is therefore concluded that pancreatitis could have been avoided in 70 per cent of cases undergoing choledochotomy if operative cholangiography had defined when this was unnecessary. It is suggested that the value of routine operative cholangiography lies not only in the definition of stones but also in the avoidance of unnecessary choledochotomy complicated by a high incidence of postoperative pancreatitis.

Acknowledgements.—We wish to thank Dr. A. M. Barlow, Dr. H. J. Black, and the technicians in the Department of Pathology at Huddersfield Royal Infirmary for their co-operation and help in the biochemical and bacteriological analyses of the present series.

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COMPUTER-ASSISTED STATISTICAL ANALYSIS OF SKELETAL SCINTIGRAMS*

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Summary

Forty-two consecutive skeletal scintigrams of the dorsal and lumbar spine have been statistically analysed using an Elliott 4120 Computer. Each patient had, in addition, anteroposterior and lateral radiographs of the dorsal and lumbar spine taken. All the patients have been followed up for a minimum of 18 months. In each patient the radiological, scintigraphic, and statistically analysed data have been compared and the accuracy of the results determined by the subsequent progress made by the patient. The results indicate that the computer analysis introduced both false positives and false negatives, and it i suggested that, at the moment, the computer assisted statistical analysis of the skeletal scintigran is not sufficiently reliable for clinical use.

During the past few years much work has bee carried out on the analysis of scintigrams obtaine from either a rectilinear scanner or a gamma camera in an attempt to improve the sensitivity of th technique (Tauxe, 1968, 1969; Laughlin, Kenny Weber, Dwyer, Mayer, Greenberg, Dimich, an Hasan, 1969; Winkler, Akhtar, and Knopp, 1969 Hutchinson, St. Clair Neill, and Rimmer, 1971) Unfortunately, these studies have been carried ou on either known phantoms or patients whose follow up has been inadequate.

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* Based on a paper given to the Surgical Research Society in January, 1971.

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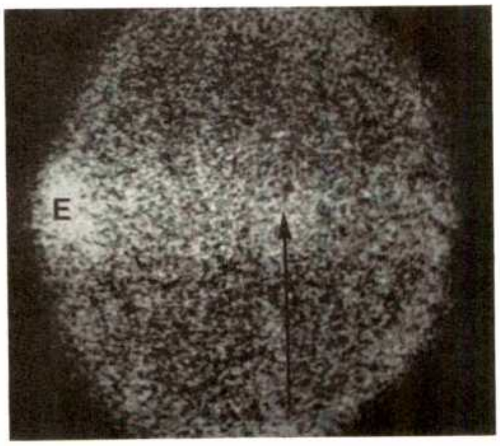
The division of the scintigram into areas must be arbitrary, since any lesion will be an unknown factor as regards its presence, size, depth in the tissues, and uptake of isotope until the scintigram has been obtained and examined. It is possible, therefore, that the analysis of the data may introduce inaccuracies.



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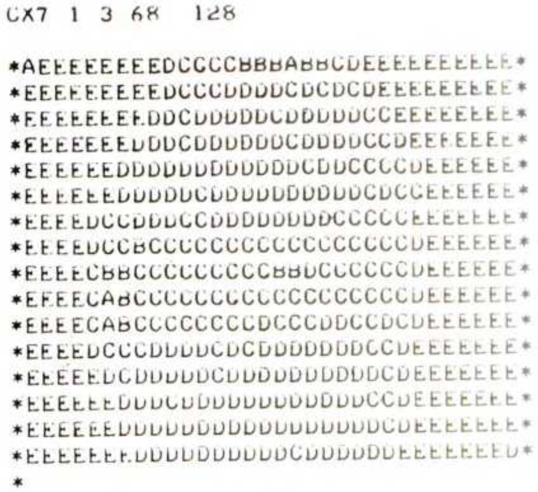

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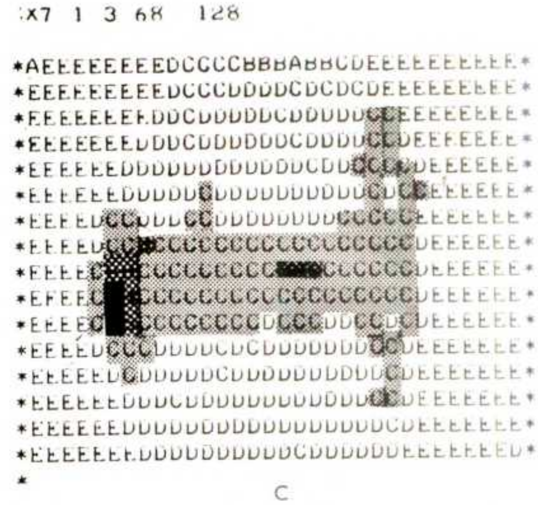

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FIG. 1.—Scintigram of the dorsal spine. A, A lesion (arrowed) can be seen in the centre of the spine. A second area of increased uptake due to the 'edge effect' of the camera (E) can also be seen. B, The computer-assisted statistical analysis of the data. Areas represented by 'A' contain the highest count rate. In the areas 'B' the number of counts is 3 standard deviations less than 'A', and 'C' represents count rates 3 standard deviations less than 'B'. C, Areas 'A', 'B', and 'C' have been marked in. The pattern is similar to the original scintigram.

The present study was carried out to assess the clinical usefulness of computer-assisted statistical analysis of skeletal scintigrams.

MATERIALS AND METHODS

Forty-two consecutive scintigrams of the dorsal and lumbar spine were analysed. Each scintigram was obtained with the gamma camera $1\frac{1}{2}$ hours after the intravenous injection of 1·5 m.c. ^{18}F. The data were fed into a Laben 512-channel multichannel analyser via a specially constructed circuit. The multichannel analyser was used in a bidimensional mode with a 16 × 32-channel matrix so that each scintigram was divided into 512 areas arranged in 16 rows of 32 areas. Each area represented approximately 2 × 2 cm. at the crystal face. The total number of counts accumulated in each square was then printed out and the data were processed in an Elliott 4120 computer.

The computer program was designed so that the area with the highest count rate would be designated by the letter 'A'. Each area containing a total of counts 3 standard deviations less than 'A' would be represented by 'B', each square which was less than 'B' by 3 standard deviations would be represented by 'C', etc.

Standard anteroposterior and lateral radiographs were taken of each region and the radiological, scintigraphic, and statistically analysed findings were compared.

All the patients have been carefully followed up for a minimum of 18 months to assess the accuracy of the findings.

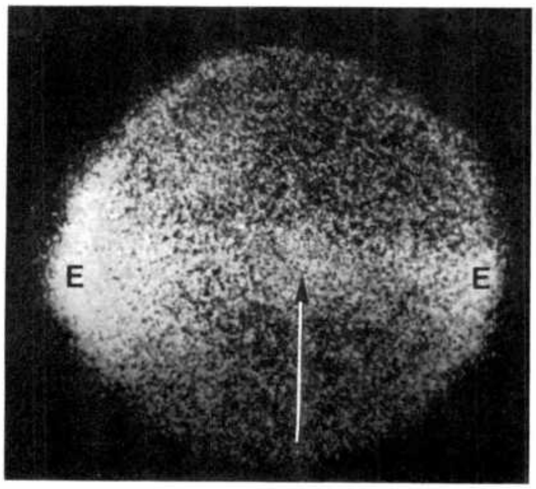
RESULTS

The results are shown in *Tables I–IV*. In 5 of the 42 regions examined skeletal metastases were evident on the radiograph. Three of these lesions were present on both the scintigram and the computer print-out, but in 2 instances the lesions were seen on the scintigram but were not detected by the statistical analysis of the data. These must be considered as 2 false negatives for the computer analysis.

In 9 instances the radiographs were normal, but lesions were seen both on the scintigram and on the analysed print-out (*Fig.* 1). These 9 scintigrams are further analysed in *Table II*. In 7 cases the lesions have subsequently been confirmed either on serial radiographs or at autopsy, and although the remaining 2 lesions have not yet been confirmed, these patients have developed skeletal metastases at other sites. In 2 patients several lesions were seen on the scintigram, although only 1 lesion was apparent on the computer print-out. In both cases all the lesions were subsequently confirmed.

The statistical analysis indicated regions with a significantly increased uptake in 7 instances, although both the scintigrams and the radiographs had been considered normal (*Table III*). As yet none of these 'lesions' has been confirmed, but 1 patient has developed skeletal metastases at other sites. One of the 'lesions' was found in 1 of the control patients in whom there is no sign of malignant disease or of any skeletal abnormality to account for this increased uptake, and this must be regarded as a false positive.

There were 6 instances where the scintigram was abnormal although both the radiographs and the statistical analysis were normal (*Fig. 2*, *Table IV*). In 5 patients the lesions have already been confirmed, indicating that in these 5 instances the statistical analysis was incorrect. The remaining patient in this group has developed metastases at other sites.



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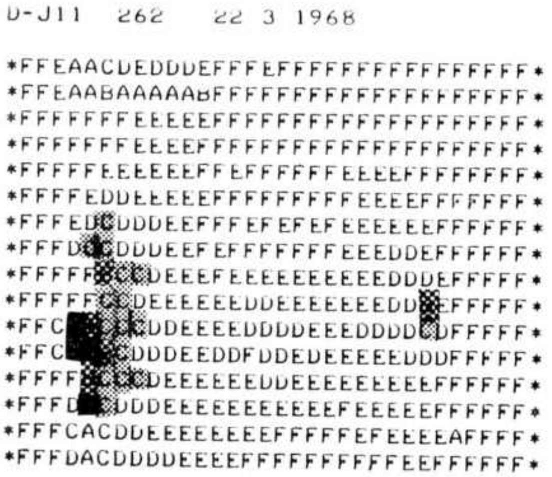

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FIG. 2.—Scintigram of the lumbar spine. A, A lesion (arrowed) can be seen in the third lumbar vertebra. Two areas of increased uptake can be seen in the edge of the picture, due to the 'edge-effect' of the camera (E). B, The computer-assisted statistical analysis of the data obtained from the multichannel analyser. C, Areas 'A', 'B', and 'C' have been marked in. The two areas of 'edge-effect' can be seen but the lesion in L.V.₃ is not apparent.

DISCUSSION

Since this study was commenced there have been many improvements in the computer analysis of scintigrams, particularly in the development of more sophisticated equipment. Unfortunately, the authors of the vast majority of papers have not followed up the patients whom they have examined. If their analysis showed an additional abnormality it was assumed that this was due to a lesion present in the patient. With the lack of adequate follow-up the incidence of false positives or false negatives introduced by the analysis was not known. Much of this work has been carried out by non-clinicians who may not have appreciated the difference that an abnormal scintigram may make to a particular patient's treatment.

In this series each patient has been followed up for a minimum of 18 months. The results obtained

Table I.—COMPARISON OF THE FINDINGS ON THE RADIOGRAPHS, SCINTIGRAPHIC PRINT-OUT, AND COMPUTER-ASSISTED STATISTICAL ANALYSIS OF THE SCINTIGRAPHIC DATA IN 42 CONSECUTIVE SCINTIGRAMS OF THE DORSAL AND LUMBAR SPINE

	RADIOGRAPH POSITIVE		RADIOGRAPH NEGATIVE	
	Computer Positive	Computer Negative	Computer Positive	Computer Negative
Scintigram positive	3	2	9	6
Scintigram negative	0	0	7	15

Table II.—FOLLOW-UP OF THE PATIENTS WITH LESIONS PRESENT ON THE STATISTICAL ANALYSIS AND THE SCINTIGRAPHIC PRINT-OUT BUT WITH NORMAL RADIOGRAPHS

No. of Patients	*Group of Patients*	*Follow-up*
2	Advanced cancer	Metastases at other sites
4	Advanced cancer	Radiograph positive
2	Advanced cancer	Autopsy positive
1	'Early' cancer	Radiograph positive

indicate that, at the present time, the computer-assisted analysis of the skeletal scintigram is not sufficiently reliable for clinical use. Overall there were at least 1 false positive and 5 false negatives in the statistical analysis of the 42 scintigrams, whereas none of the lesions demonstrated on the pictorial scintigram has been shown to be incorrect.

It has been widely accepted that a change in the count rate at the detector head is significant if the change is greater than 3 standard deviations (Vernon, 1968). It is possible that if one accepted only 2 standard deviations as being significant, less false negatives would have occurred with the computer analysis.

Table III.—FOLLOW-UP OF THE PATIENTS WITH NORMAL RADIOGRAPHS AND SCINTIGRAMS BUT WITH 'LESIONS' PRESENT ON THE STATISTICAL ANALYSIS

No. of Patients	*Group of Patients*	*Follow-up*
1	Advanced cancer	Metastases at other sites
5	'Early' cancer	Well
1	Control	Well

Table IV.—FOLLOW-UP OF PATIENTS WITH LESIONS PRESENT ON THEIR SCINTIGRAM BUT WITH RADIOGRAPHS AND STATISTICAL ANALYSIS APPARENTLY NORMAL

No. of Patients	*Group of Patients*	*Follow-up*
2	Advanced cancer	Positive radiograph
3	'Early' cancer	Positive radiograph
1	'Early' cancer	Metastases at other sites

Wherever an area of increased uptake occurs it will be appreciated visually. The areas for the multichannel analysis are defined irrespective of any localized increased uptake of isotope. If a lesion occurs in the middle of one of these defined areas it will probably be seen on the statistical analysis. If the lesion overlaps into three or four areas its increased uptake may be dampened to such a degree by the remaining normal tissue in each area that when the data are analysed the increase may not be statistically significant.

If, as in most instances, the system being examined is an experimental one the preselection of areas to avoid the 'lesion' spilling into several squares may be acceptable, but in the clinical situation it is possible that these manœuvres may introduce false positives and false negatives.

A significant difference between areas is only an indication that a significantly different count rate has been detected at the counting head, and although it is frequently assumed that the eye perceives changes in this manner (Rose, 1948; Dewey and Sinclair, 1961; Matthews, 1964) this may not be the case and the eye may build up images, not by comparing areas but by integrating a series of boundaries to complete a shape (Brownell, 1964). Although it is relatively easy to program a computer to analyse numerical data and to determine the significance of any changes, it is virtually impossible, at the moment, to program for pattern recognition, and it is probable that pattern recognition plays an extremely important role in reading scintigrams. This may also explain why the results obtained from the statistical analysis of the data were inferior to those obtained from the visual interpretation of the scintigrams.

It is hoped that with the introduction of more sophisticated apparatus the computer-assisted analysis of the skeletal scintigram will become more reliable, but it must be stressed that adequate follow-up is essential to determine the incidence of false negatives and false positives. Only if the latter, particularly false positives, can be eliminated will computer-assisted statistical analysis become sufficiently reliable for clinical use.

Acknowledgements.—I am indebted to Mr. P. Vernon, Department of Medical Physics, Royal Postgraduate Medical School, for developing the computer program and for his constant advice, and to Professor J. F. Fowler, Department of Medical Physics, for the facilities provided. I also wish to thank Professor R. B. Welbourn and Mr. J. I. Burn, Department of Surgery, Royal Postgraduate Medical School, for allowing me to investigate their patients and for their constant encouragement.

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SHORT NOTES OF RARE OR OBSCURE CASES

PNEUMOMEDIASTINUM AND SUBCUTANEOUS EMPHYSEMA AFTER PERFORATION OF THE DUODENUM DURING GASTROSCOPY

BY R. N. ALLAN AND C. J. SMALLWOOD
THE GENERAL HOSPITAL, STEELHOUSE LANE, BIRMINGHAM

SUMMARY

The first case of duodenal perforation during gastroscopy is reported. The patient's symptoms were mild in contrast to the dramatic picture of perforated peptic ulcer. He developed a pneumoperitoneum, pneumomediastinum, and, in addition, subcutaneous emphysema of the neck—signs more commonly associated with oesophageal rupture than perforation of the duodenum.

The aetiology of these signs and the prevention of this complication are discussed.

PERFORATION of the upper oesophagus and stomach during gastroscopy is a rare though well-recognized complication using the rigid gastroscope. It is usually caused by direct trauma (Schindler, 1940; Jones, Doll, Fletcher, and Rodgers 1951). The present case is unusual because the duodenum was perforated by insufflation of air during the procedure, and it is interesting that while this patient presented many of the physical signs associated with oesophageal perforation, investigation prior to operation accurately located the site of the leak to the duodenum.

CASE REPORT

In 1962 this man presented with a 5-month history of epigastric discomfort, anorexia, vomiting, weight-loss, and a recent haematemesis. At laparotomy there was a benign gastric ulcer on the lesser curve. A Billroth-I partial gastrectomy was performed and he made an uninterrupted recovery.

In January, 1971, at the age of 73 years, the patient was readmitted with a 2-week history of epigastric pain, anorexia, profuse bile-stained vomiting, weight-loss, and general malaise. There were no abnormal signs on examination and therefore he was treated initially with intravenous fluids and nasogastric suction. A barium-meal examination 5 days after admission showed satisfactory emptying of the stomach with no evidence of recurrent ulceration.

In view of the negative barium-meal examination gastroscopy was performed under local anaesthesia. The gastroscope was passed easily into the stomach. More air than usual was blown in because the gastric remnant proved difficult to dilate. The gastric mucosa and gastroduodenal junction were normal.

Immediately after the examination there were no abnormal signs or symptoms. Within 2 hours, however, the patient complained of slight epigastric pain and the abdomen became distended and firm but there was no rigidity or rebound tenderness. He had a tachycardia (110 per minute) but his blood-pressure remained normal. A few minutes later he developed marked subcutaneous emphysema of the neck and upper chest wall. Straight radiographs of the chest and abdomen showed evidence of a pneumoperitoneum, pneumomediastinum, and extensive subcutaneous emphysema of the chest wall (*Fig.* 1).

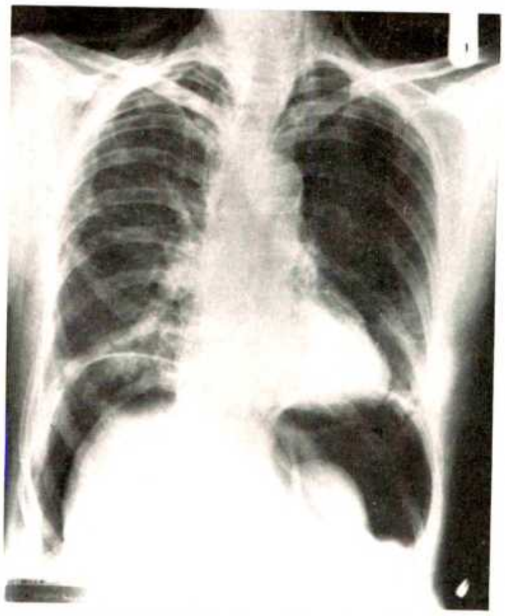

FIG. 1.—Chest radiograph, showing pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema of neck.

A Gastrografin swallow showed the oesophagus to be intact, but there was a perforation in the first part of the duodenum with leakage into the peritoneal cavity (*Fig.* 2).

A laparotomy was performed under general anaesthesia through the old right upper paramedian incision. There was a large volume of free air in the peritoneal cavity, air in the falciform ligament, and numerous adhesions in the upper abdomen. A small quantity of bile-stained fluid flowed from Rutherford-Morrison's pouch. After unpicking the adhesions which bound the duodenum to the undersurface of the liver, a perforation was found in the anterior wall of the duodenum, 1·5 cm. in length. The mucosa appeared normal and the duodenal wall, though thin, had none of the appearances associated with chronic ulceration. The perforation was closed vertically with continuous plain catgut in two layers. Toilet to the peritoneal cavity completed the operation. The patient made an uneventful recovery, the surgical emphysema rapidly regressed, and he was discharged on the tenth postoperative day.

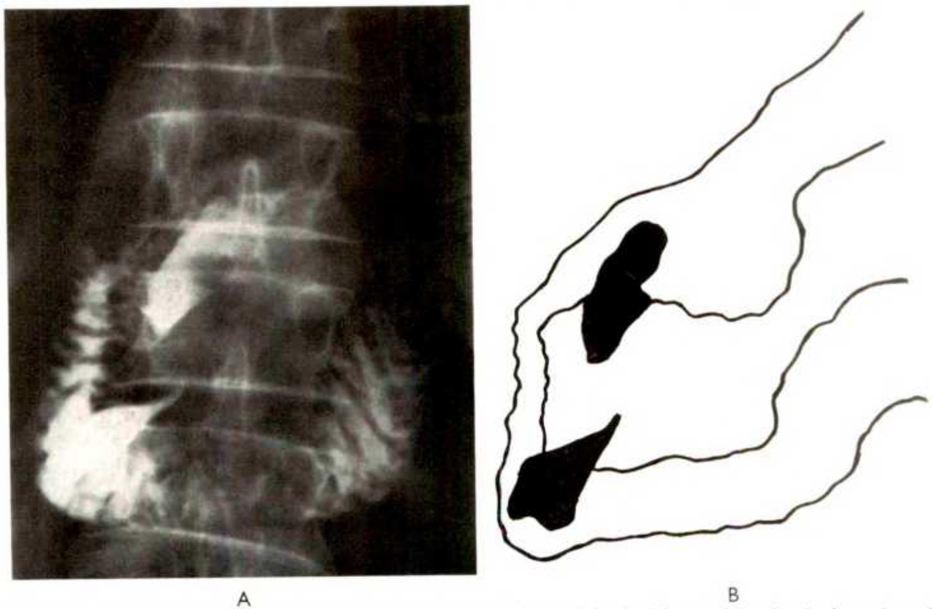

FIG. 2.—A, Barium-meal film, showing Gastrografin leaking from the duodenum (*above*) with some lying free in the peritoneal cavity (*below*). B, Diagrammatic representation of A.

DISCUSSION

Perforation of a viscus during gastroscopy is a rarity. In an extensive survey by English gastroscopists covering 49,000 examinations only 50 perforations of the oesophagus were recorded, an overall rate of 1·2 per 1000 examinations using the rigid gastroscope (Jones and others, 1951). This complication is now less common with the introduction of improved and flexible instruments (Calem, 1962). Perforation of the oesophagus and stomach result from direct trauma; even the jejunum may be perforated if the patient has had a gastro-enterostomy (Rumball, 1939). Duodenal perforation has not been reported before as a complication of either gastroscopy or duodenoscopy (Classen, 1971). There is a single example in the literature of air leaking during gastroscopy from the base of a bleeding gastric ulcer, which at operation appeared to have perforated some time prior to the examination and subsequently had sealed off (Hirschowitz, Balint, and Fulton, 1962).

During the examination of the patient presented here the gastroscope was not passed beyond the gastroduodenal junction, the perforation thus resulting from over-inflation of the duodenum rather than from direct trauma. Air insufflation of the stomach is essential in order to see the gastric mucosa adequately when using a side-viewing instrument. In patients who have had previous gastric resection more air is often used because there is no longer a competent pylorus to retain the air in the gastric remnant. This complication could be prevented by fitting the gastroscope with a pressure-release valve, thus avoiding an excessive rise in intragastric pressure.

The symptoms in this patient, like those described in the literature, are not typical of a spontaneously perforating peptic ulcer because the patient has been heavily sedated, the stomach is empty, and the diaphragms are splinted by the resulting pneumoperitoneum (Boon, 1951).

In this patient a diagnosis of oesophageal perforation was considered initially but the Gastrografin swallow showed the oesophagus to be intact and a perforation to be clearly evident in the first part of the duodenum. This accurate localization of the site of perforation is essential to subsequent surgical management.

The pneumomediastinum probably resulted from old adhesions sealing off the duodenum from the general peritoneal cavity, thus permitting air to track extraperitoneally into the mediastinum and up into the neck. The pneumoperitoneum followed the breakdown of adhesions which had sealed the duodenum and gastroduodenal suture line from the general peritoneal cavity. Though the mucosa of the duodenum appeared normal, both radiologically and at operation, the perforation may have occurred through either the base of an acute ulcer or at the site of a suture-line leak following the original operation which had subsequently sealed off; the latter seems the more likely.

Acknowledgements.—We should like to thank Dr. P. W. Dykes and Mr. G. T. Watts for permission to publish details of this case. Dr. D. K. M. Toye has given us considerable help in preparing this publication.

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ADENOCARCINOMA DEVELOPING IN AN ILEOCYSTOPLASTY

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SUMMARY

Multifocal adenocarcinoma and carcinoma-in-situ arising in the suture line of an ileocystoplasty are reported in a 52-year-old woman who presented with haematuria 15 years after bladder reconstruction for tuberculosis. An origin in the ileal mucosa was established by microscopy. There are similarities with a transitional-cell carcinoma in an ileocystoplasty which has recently been recorded. Both cases are related to tumours associated with ureterosigmoidostomy where the site, tumour types, and latent period are similar. Aetiological factors seem to include a long latent period (15 years or more) and possibly the direct action of urine, recurrent infection, and mucosal ulceration. It is concluded that all patients with gastro-intestinal urothelial anastomoses must be followed up indefinitely.

NEOPLASTIC complications of bladder reconstruction performed for benign inflammatory conditions were unrecorded until recently when a transitional-cell carcinoma arising in an ileocystoplasty was documented (Smith and Hardy, 1971). A second case is now reported in which an adenocarcinoma developed in an ileocystoplasty performed 15 years previously for tuberculosis.

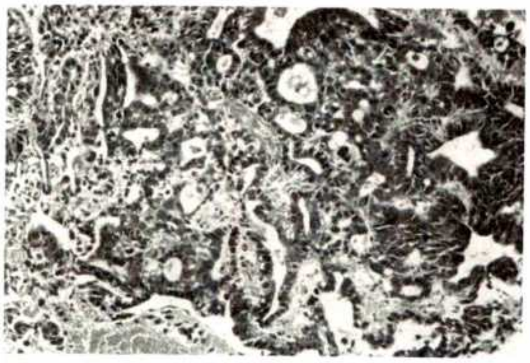

FIG. 1.—Section of the biopsy material, showing a moderately differentiated adenocarcinoma. Normal ileal mucosa is not present. H. and E. (× 96.)

CASE REPORT

A. W., a 34-year-old housewife, was first seen in 1953, when tuberculosis of the renal tract was diagnosed. She was treated with anti-tuberculous drugs but 2 years later a right nephro-ureterectomy was performed, and in early 1956 she had an ileocystoplasty for a contracted bladder. In this operation part of the antimesenteric border of an isolated segment of ileum was anastomosed to the fundus of the bladder.

During the next 5 years the patient developed frequent urinary infections despite adequate antibiotic therapy and complained of an ever-increasing frequency of micturition. *Mycobacterium tuberculosis* was not isolated again. At cystoscopy in 1960 she was shown to have an inflamed bladder with a capacity of only 150 ml. and it was apparent that the ileovesical stoma had contracted to approximately 1 cm. in diameter. One year later a pregnancy was terminated by hysterotomy and she was sterilized by tubal ligation. At the same time the ileovesical stoma of the ileocystoplasty was refashioned and a biopsy of the ileal mucosa near the suture line showed severe acute and chronic inflammation. The number of urinary infections were considerably reduced following this procedure but in 1964 the patient failed to attend for follow-up.

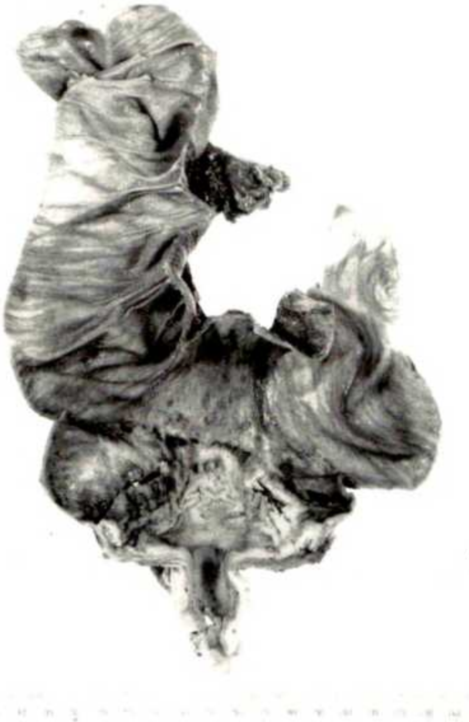

FIG. 2.—Ileocystoplasty specimen opened from behind showing the dilated ileal loop (*above*) anastomosed to the contracted bladder.

She was referred back in March, 1971, complaining of episodes of painless haematuria for a few months. No abnormality was found on clinical examination but microscopic haematuria was detected. Midstream specimens of urine were sterile on culture and the blood-urea and electrolytes were normal. An intravenous pyelogram showed a normal upper urinary tract on the left side and no filling defects were seen in the ileocystoplasty on a cystogram. However, at cystoscopy two red, friable polypoid tumours up to 1 cm. in diameter were seen at the ileovesical junction. No infiltration was felt by bimanual examination but biopsies showed fragments of adenocarcinoma (*Fig.* 1). At the end of April, 1971, the ileal loop, bladder, urethra, ovaries, Fallopian tubes, and uterus were removed and the left ureter was anastomosed to an isolated segment of sigmoid colon by the Leadbetter technique (Leadbetter, 1951). Her postoperative course was uneventful and she has remained asymptomatic.

PATHOLOGY.—The biopsy of the ileal mucosa which was taken in 1961 showed patchy acute mucosal ulceration with epithelial regeneration. There were also areas of severe submucosal chronic inflammation with dense lymphocytic aggregates and fibrosis. There was no evidence of malignant change or tuberculosis.

The uterus, Fallopian tubes, ovaries, and the ileocystoplasty were removed in 1971. The latter consisted of an isolated loop of dilated ileum, 25 cm. long, closed at both ends, and attached along part of its antimesenteric border to the bladder and urethra (*Fig.* 2). The distal 2 cm. of the right ureter was found opening into the vesical part 1·5 cm. above the bladder neck. The orifice of the left ureter was found in a similar position on the other side but the ureter had been cut off flush with the bladder wall. When the ileal loop and bladder were opened, three superficial papillary nodules up to 1 cm. in diameter were found in the region of the ileovesical anastomosis (*Fig.* 3). The vesical mucosa close to the suture line was wrinkled and greyish white (*Fig.* 3) but lower down became smooth and pink. There was slight irregular thickening of the ileum at the ileovesical junction but elsewhere it was thin-walled with a smooth mucosal lining.

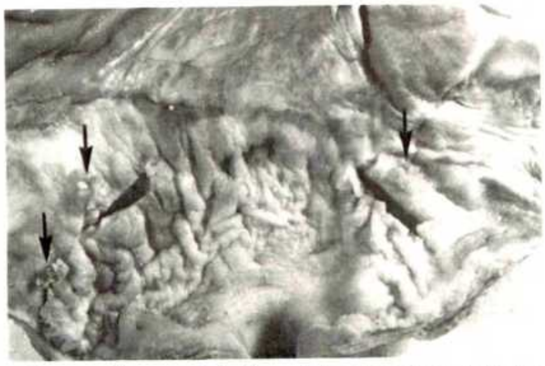

FIG. 3.—Close-up of the ileovesical anastomosis to show the three small adenocarcinomatous polyps (arrows). Below these the mucosa is pale and wrinkled but it is smoother near the bladder neck. (Urgent diagnostic blocks were taken before photography.)

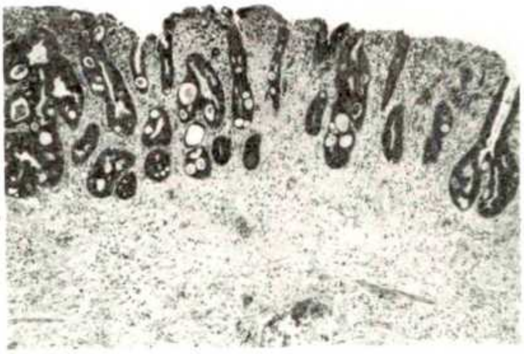

FIG. 5.—Section of the ileal mucosa close to the suture line. There is atypical epithelial proliferation with multilayering of cells within acini and an irregular back-to-back arrangement of the glands. Strands of muscularis mucosae are present in the lower part of the picture. H. and E. (× 39.)

Microscopy of the nodules showed moderately differentiated partly papillary and partly solid adenocarcinoma similar to that seen in the biopsy taken at cystoscopy (*Fig.* 1). The tumours were mainly confined to the mucosal layer with extensive infiltration of the lamina propria (*Fig.* 4) but early invasion through the muscularis mucosa was seen in a few areas. These neoplastic areas were completely separate from one another. However, the ileal epithelium adjacent to the nodules and elsewhere close to the suture line showed atypical epithelial proliferation with irregular multilayering of epithelial cells in glandular acini, numerous mitoses, and an early back-to-back arrangement of glands (*Fig.* 5). These changes were interpreted as a carcinoma-in-situ change of the ileal mucosa. There were also areas of adenomatous hyperplasia (*Fig.* 6). Away from the anastomosis the ileum had a flattened normal epithelium with only occasional villi still present and the muscle coat was atrophic with some increase in fibrous tissue. There was non-keratinizing squamous metaplasia of the mucosa for 1–2 cm. on the vesical side of the suture line, causing the wrinkled greyish appearance described above, but this gradually merged into normal transitional epithelium in the lower part of the bladder. There was no evidence of malignant change in the bladder mucosa.

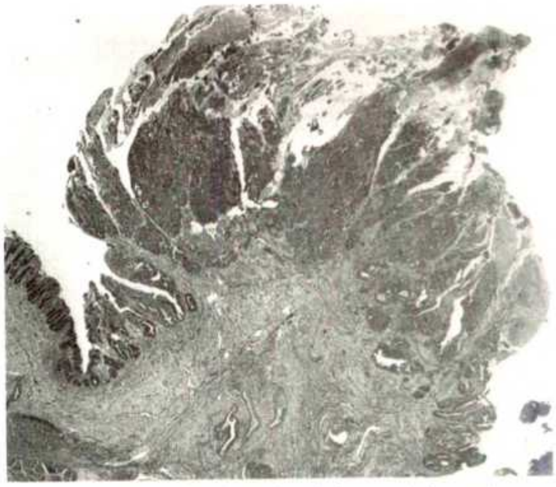

FIG. 4.—Section of a polyp to show dark areas of adenocarcinoma extending towards its base. There is superficial ulceration and more normal glandular epithelium is present on each side. H. and E. (× 12.)

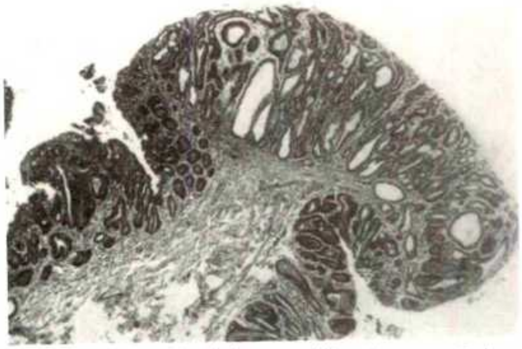

FIG. 6.—Section of the ileal mucosa. There is an area of adenomatous hyperplasia with regular glands each of which is surrounded by stroma and lined by a single layer of cells. There is no evidence of malignant change. H. and E. (× 24.)

Numerous blocks taken perpendicular to the suture line established that both the frank carcinoma and the in situ changes were in the ileal mucosa. Transitional or squamous epithelium was not present proximal to these changes and there were occasional islands of more normal ileal mucosa between these areas and the ileovesical junction. The location of this junction was further established by the presence of muscularis mucosa (*Fig.* 5) and the different arrangement of muscle layers in the ileal wall.

There was chronic inflammation and fibrosis in the subepithelial connective tissue on each side of the anastomosis, but no evidence of tuberculosis was found in any of the tissues. The uterus, ovaries, and Fallopian tubes were normal.

DISCUSSION

The presence of multifocal adenocarcinoma and carcinoma-in-situ close to the suture line in the ileal mucosa of an ileocystoplasty has been established by the microscopic findings in this case. Friable adenocarcinomatous polyps were the source of bleeding with which the patient presented, but because of their superficial nature it is possible that a cure has been effected by radical surgery. It is very unlikely that the neoplastic changes in the ileum are fortuitous and unrelated to its use in reconstruction of the bladder. Primary adenocarcinoma of the ileum is rare (Darling and Welch, 1959; Wood, 1967). There also seems little possibility that this could be a primary adenocarcinoma of the bladder since no connexion was established with the bladder mucosa. Indeed, the latter showed squamous metaplasia and no evidence of glandular metaplasia.

Neoplasia is not recorded in reviews of the complications of ileo- or colocystoplasty (Houtappel and Grundeman, 1960; Maged, 1968; Kuss, Bitker, Camey, Chatelain, and Lassau, 1970). Smith and Hardy (1971) have recorded the only other case which has a strikingly similar clinical history. The ileocystoplasty in their case was also performed for tuberculous contraction of the bladder and there was a long history of recurrent urinary infection following this operation. After a long latent period (17 years) the patient presented with haematuria. However, in their case there was a transitional-cell carcinoma in the ileal loop. Although it is not established how close the tumour was to the ileovesical junction it is possible that it arose in transitional epithelium which had spread across the suture line.

Tumours associated with ureterosigmoidostomy are also rare but have been reported more frequently (Dixon and Weismann, 1948; Urdaneta, Duffell, Creevy, and Aust, 1966), and Whitaker, Pugh, and Dow (1971) have recently reviewed 28 such tumours with some significant observations. In all the cases the tumour was close to the line of the anastomosis, and in 20 cases where there had been a previous benign lesion the mean latent period between ureterosigmoidostomy and the development of the tumour was 19 years. Both adenocarcinomas and transitional-cell carcinomas were recorded as well as adenomatous polyps and undifferentiated carcinomas. The close similarity with the two tumours now recorded in ileocystoplasties cannot be a coincidence and it is likely that the same aetiological factors are responsible.

The carcinogenic agent remains obscure, but the direct action of urine on the gastro-intestinal-urothelial junction over a long period would seem the most likely factor. Deconjugation of ortho-aminophenols, derived from the tryptophan metabolism, to yield active carcinogens in urine has been implicated in the development of carcinoma of the bladder (Boyland, 1959) and the same may apply in this situation. It may also be significant that in both ileal tumours there were long periods of recurrent urinary infection and there is direct histological evidence in the present case of mucosal ulceration and epithelial regeneration before the tumour developed. Recurrent regeneration over a long period of time could lead to neoplastic change as it does in other conditions such as ulcerative colitis. The occurrence of tumours exclusively on either side of the suture line might also be explained by relative ischaemia at this site which would make either the urothelial or the gastro-intestinal mucosa more susceptible to recurrent infection and ulceration.

Whatever the aetiology, the implications of the cases reported to date are obvious. It is apparent that neoplastic changes at the suture line in gastro-intestinal urothelial anastomoses are a rare but real hazard, even when performed for a benign condition. Patients at risk appear to be those who have survived 15 years or more and possibly those who have had a long history of recurrent urinary infections. More cases are likely to occur since these reconstructive procedures have increased in popularity over the past 20 years, particularly following the introduction of ileal loop diversion (Bricker, 1950). The type of tumour recorded here has not yet been reported in this situation, but persistent infection of the urine is a known complication (Kafetsioulis and Swinney, 1968).

It is concluded, therefore, that all patients with gastro-intestinal urothelial anastomoses should be followed up indefinitely so that there may be some chance of detecting neoplastic change as early as possible.

Acknowledgements.—We are grateful to Mr. G. C. Tressider for his encouragement and for allowing us to study one of his cases. Mr. S. Stevens, Mr. R. Hammond, and Miss L. Testa are thanked for technical, photographic, and secretarial assistance respectively.

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A 'CORRUGATED' EXTRAHEPATIC BILE-DUCT: A NEW CHOLANGIOGRAPHIC PICTURE

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SUMMARY

A patient with an operative cholangiogram showing appearances suggestive of multiple diverticula is recorded; these appearances are apparently unique.

In recent years the use of operative cholangiography has become routine in many centres. The cholangiographic picture of the biliary tract in health and disease is now well documented (Le Quesne, 1964). The present paper describes an unexpected operative cholangiogram picture obtained during a routine cholecystectomy.

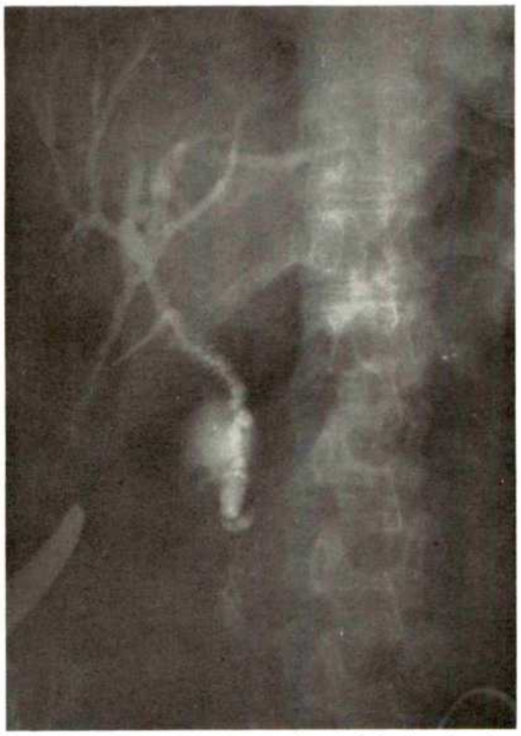

FIG. 1.—Operative cholangiogram after the injection of 6 ml. of contrast material into the cystic duct.

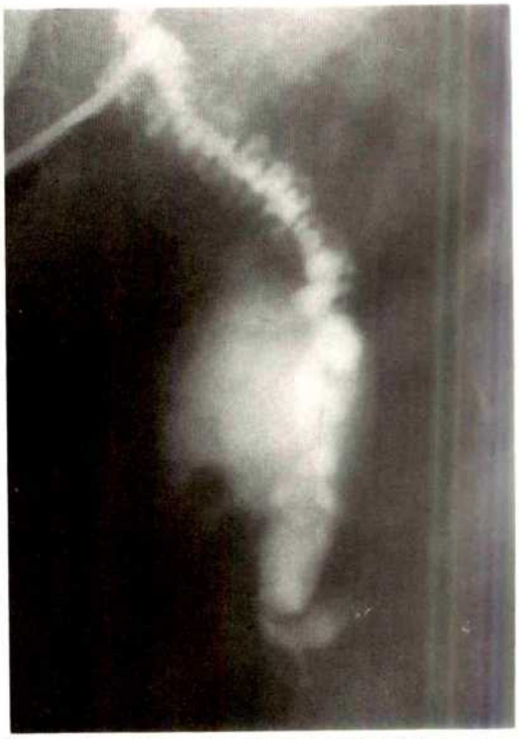

FIG. 2.—Part of *Fig.* 1 (magnified approximately three times), showing the corrugations of the bile-duct.

CASE REPORT

Mrs. L. C., a 59-year-old housewife with 3 children, presented with a 10-year history of dyspepsia which consisted of episodes of pain in the right hypochondrium spreading through to the back and interscapular region. She also complained of upper abdominal distension, flatulence, and fat intolerance. The discomfort did not seem to be related to meals and was not helped by alkalis. At no time had she been jaundiced and she gave no symptoms suggestive of latent jaundice such as a change in colour of her urine or stools. She had experienced no itching and her general health was good. There were no abnormal physical signs.

Single- and double-dose oral cholecystograms showed non-filling of the gall-bladder. An intravenous cholangiogram faintly outlined the common bile-duct which appeared to be normal; the gall-bladder again did not fill. A barium-meal examination and routine liver-function tests were normal.

At laparotomy on 14 Sept., 1970, the only abnormality found involved the biliary tract. The gall-bladder appeared distended and the wall was thickened. The common bile-duct was slightly opaque but was not dilated. During the cholecystectomy the lumen of the cystic duct was found to be obliterated as it entered the gall-bladder. The cystic duct was therefore dissected more centrally and an open lumen was found through which cholangiography was performed. Radiographs were taken after injecting 3, 6, and 9 ml. of contrast medium into the cystic duct. *Figs.* 1 and 2 are photographs of one of these radiographs; the other two radiographs were essentially the same. The walls of the common bile-duct

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(excluding the supra-ampullary portion) and the common hepatic duct were corrugated but not dilated. The intrahepatic ducts seemed to be normal. The terminal portion of the common bile-duct was symmetrically rounded and contrast medium entered both the duodenum and the pancreatic duct. As there appeared to be no dilatation of the common bile-duct and as the dye entered the duodenum with ease it was decided not to open the common bile-duct. The gall-bladder was removed in the usual way and was found to contain clear mucus but no stones or biliary gravel.

The histology of the gall-bladder showed changes consistent with chronic cholecystitis with the occasional Rokitansky-Aschoff's sinus. It is now over 2 years since the operation and the patient has had no further symptoms; liver-function tests which have been repeated recently are normal.

DISCUSSION

The films of this patient have been shown to a large number of surgeons, none of whom could recall having seen anything similar. Examination of the literature also failed to reveal any similar picture. This case would therefore appear to be unique.

If one remembers that the outside of the duct appeared normal at operation the corrugation seen on cholangiography can be interpreted in two ways: first, there may be protrusions of the mucosa outwards into the wall of the duct forming intramural diverticula or saccules; secondly, the mucosa may be being pushed into the lumen of the duct by 'tumours' or 'pseudotumours'. With these suggestions in mind the following scheme for the differential diagnosis has been made.

Intramural Diverticula or Saccules.—Solitary diverticula of the biliary ducts are a well-known entity; intrahepatic and periampullary diverticula have been described (Sterling, 1949; Jackson and Maxwell, 1964; Kune, 1965; Maxwell, Jackson, Davis, Eisen, and Poller, 1967) but the most common variety is the choledochal cyst (Alonso-Lej, Rever, and Pessagno, 1959). A few cases of multiple choledochal cysts have been described (Engle and Salmon, 1964; Esguerra-Gomez and Riveros-Gamboa, 1965). These diverticula involve *all* the layers of the duct wall, thus being unlike the case recorded here.

A true *intramural* sacculation of the gall-bladder exists in adenomyomatosis, a disease for which there are many synonyms including cholecystitis glandularis proliferans and multiple Rokitansky-Aschoff's sinuses. According to Jutras, Longtin, and Lekesque (1960) this disease is an acquired condition of multiple intramural pulsion diverticula probably caused by excessive intraluminal pressure in association with mural inflammation. Adenomyomatosis has not been described outside the gall-bladder and this is thought to be due to the fact that the gall-bladder, unlike the other biliary passages, has a thick muscular wall. It should, however, be noted that the wall of the common bile-duct does contain some muscle-fibres (Burden, 1925; Bloom and Fawcett, 1968).

Recently the author was shown a photograph of a post-mortem specimen demonstrating a dilated and sacculated common bile-duct which was obstructed by a carcinoma of the pancreas. That dilatation occurs in this situation is well known but it is usually uniform and the walls of the duct are smooth. In the present case no obvious obstruction or dilatation was present.

Intraluminal 'Tumours' and 'Pseudotumours'.—Hodes (1965) lists the causes of multiple mural filling defects of the gall-bladder under the above title. Although most of these conditions have not been described as occurring in the common bile-duct their existence is theoretically possible. The tumorous conditions include papillomatosis, adenomatosis, and carcinomatosis. The pseudotumorous conditions include cholesterolosis, adenomyomatosis, neuromatosis, elastosis, lipomatosis, fibromatosis, and hyalinocalcinosis. Biliary gravel and multiple parasites may also produce intraluminal filling defects.

A further condition that has been mentioned in the differential diagnosis is primary sclerosing cholangitis. This condition causes a diffuse irregular narrowing of all the extrahepatic biliary tree and sometimes the intrahepatic ducts are likewise affected (Warren, Athanassiades, and Monge, 1966). This disease does not seem to occur without evidence of obstructive jaundice.

The possible causes of the cholangiogram picture obtained in our patient have been outlined but none of them completely fits the clinical picture. The histology of the gall-bladder was unhelpful; it did, however, show chronic inflammatory changes and it seems possible that the common bile-duct was similarly affected.

Acknowledgements.—I would like to thank Mr. O. D. Morris for allowing me to publish this case. I am grateful to Mr. N. M. Matheson who supplied me with the photograph of the post-mortem specimen described in the text.

I am also grateful to the following who were kind enough to comment on this case: Professor A. J. Harding Rains, Professor W. Hess, Professor L. P. Le Quesne, and Professor S. Sherlock.

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AN UNUSUAL CASE OF SWALLOWED DENTAL PLATE AND PERFORATION OF THE SIGMOID COLON

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SUMMARY

A case of swallowed dental plate is described in which impaction and perforation occurred in the sigmoid colon. This was treated by resection and end-to-end anastomosis combined with transverse colostomy.

CASE REPORT

A 62-YEAR-OLD woman was admitted to the surgical ward at Leith Hospital on Wednesday, 12 Sept., 1968, having swallowed a portion of her upper dental plate while eating fish and chips. This had occurred on the preceding Saturday and later she had dosed herself liberally with castor oil. At first she had had colicky abdominal pain which had become generalized on the day prior to admission. On examination she was found to have a rigid abdomen with peritonism and was maximally tender in the lower abdomen. An erect radiograph of the abdomen revealed a radio-opaque object in the hypogastrium midway between the umbilicus and the pubic symphysis (*Fig.* 1).

Through a low right paramedian incision exploration of the bowel revealed an indurated inflamed area of sigmoid colon approximately 15 cm. long and perforated in its antimesenteric border by a tooth. There was an abscess cavity in relation to the mesentery of the bowel containing a large quantity of foul-smelling pus. Resection of the affected area with end-to-end anastomosis using interrupted silk sutures was carried out and this was supplemented by transverse colostomy. The abdomen was closed in layers leaving a suprapubic drain down to the anastomotic site.

Early postoperative progress was uncomplicated and 3 months later when barium, instilled into the distal colostomy opening, was seen to pass unimpeded to the anus, closure of the colostomy was planned and undertaken. The patient has since returned to normal bowel habit.

PATHOLOGY SPECIMEN.—Macroscopic examination showed the specimen to consist of 10 cm. of pelvic colon which was indurated and thickened by inflammation. A dental plate was impacted at its lumen and a tooth was seen to have perforated the antimesenteric border (*Fig.* 2). The dental plate had also perforated the bowel adjacent to the attachment of the mesocolon and there was an abscess measuring 2×3 cm. in the mesentery (*Fig.* 3). The dental plate was $2{\cdot}5 \times 3$ cm. in size and bore 3 teeth. There was no evidence of diverticular disease or neoplastic process in the specimen.

Microscopic examination revealed a non-specific inflammatory process of the bowel wall and mesentery and confirmed the presence of an abscess wall.

DISCUSSION

The alimentary canal is remarkably resistant to perforation by foreign bodies and, as Turner (1946) pointed out, even dangerous-looking objects usually make an easy passage once they have safely negotiated the gullet. No part of the gastro-intestinal tract is immune to perforation and Macmanus (1941), in a review of 93 cases, found that it occurred most commonly in the ileocaecal region. Foreign-body perforation of the sigmoid colon is not common and only 10 cases are reported in this region in Macmanus's review. Gaur (1967) has described perforation of the sigmoid colon by a cloth, and Goodhead (1965) has reported obstruction and perforation of the sigmoid colon by a garden cane which were treated by Mikulicz exteriorization.

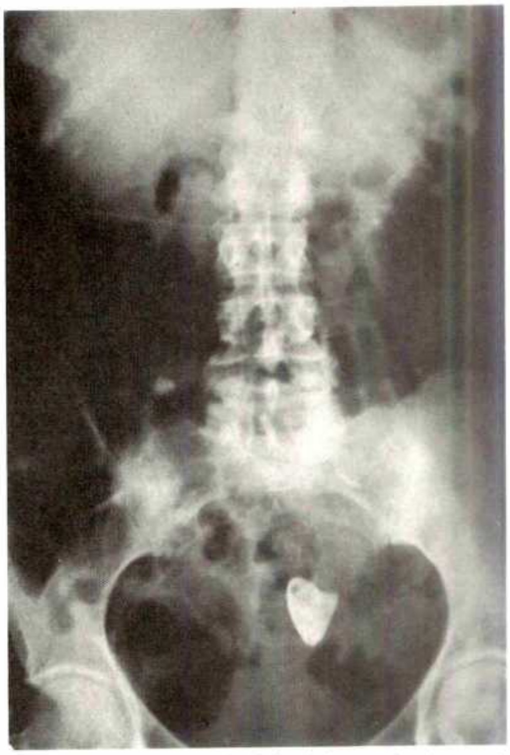

FIG. 1.—An erect radiograph of the abdomen, showing a radio-opaque object in the hypogastrium.

Some cases are recorded in which dental prosthetics have been accidentally swallowed. In the majority of these, impaction occurred in the region of the pharynx or oesophagus. Broken dental plates and partial dentures are more frequently responsible and it is not uncommon for this accident to occur during sleep (Kerr, 1966). Saunsbury (1964) has emphasized that there is a need for modified dental acrylic with greater radio-opacity than is provided by the one such material on the market at present. Barium sulphate is added in the manufacture of acrylic but this has the disadvantage that the acrylic becomes more brittle and less translucent. Metal wires often give precise radiological localization of dental apparatus, and porcelain incorporated in the manufactured teeth can be helpful as this substance shows up well on a radiograph. It was fortunate that in the case which we have described the dental plate was easily identifiable on a straight radiograph owing to its high content of barium sulphate.

It is strange that in the present case the plate passed uneventfully through the oesophagus, the duodenum, and the ileocaecal valve only to become

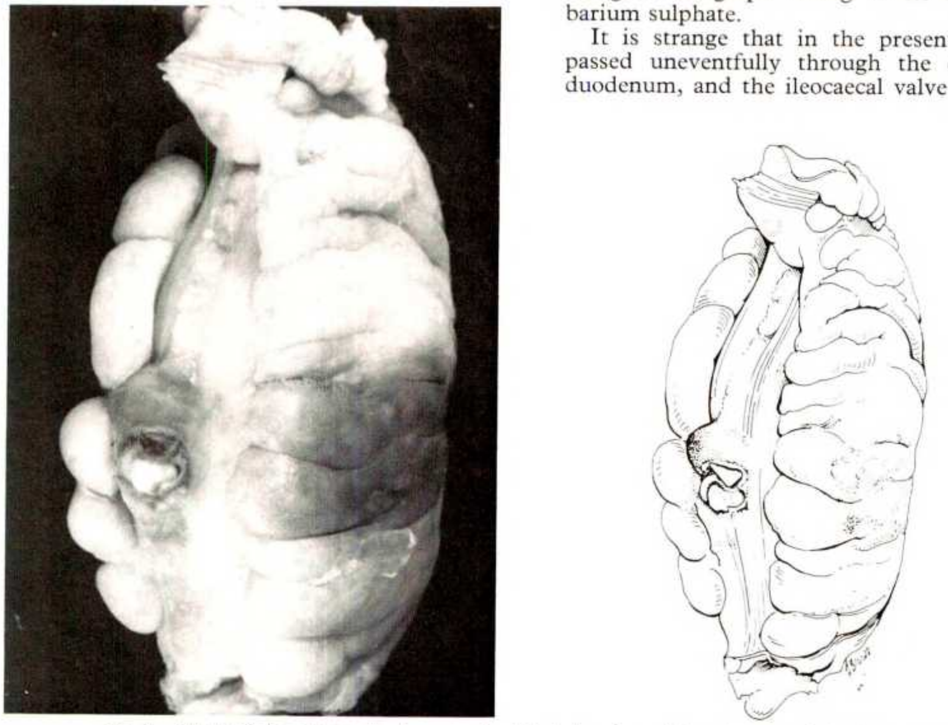

FIG. 2.—Pathological specimen, showing a tooth which had perforated the antimesenteric border of the colon.

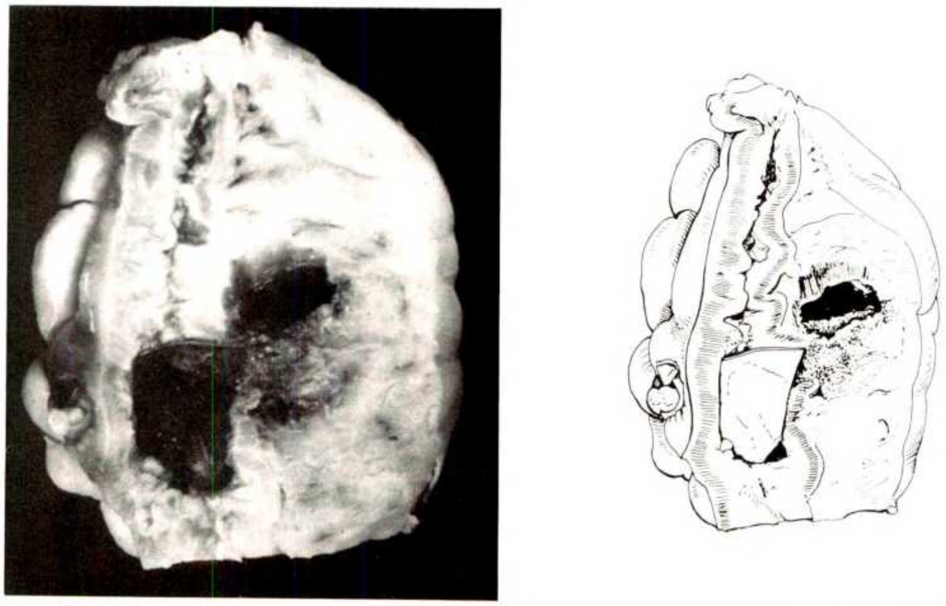

FIG. 3.—Pathological specimen, showing the dental plate which had perforated the bowel adjacent to the attachment of the mesocolon, and also an abscess in the mesentery.

impacted in the sigmoid colon. The resected portion of bowel was carefully examined for evidence of pre-existing disease that might have caused the hold-up, but apart from the extensive damage already noted it appeared to be normal. It may be that the liberal doses of castor oil that the patient had used to assist the passage of the foreign body had caused irritability and spasm of the sigmoid colon and this might account for the situation of impaction.

The particular form of operation used has recently been discussed by Painter (1968) in his paper on perforation of the large bowel due to diverticulitis and this seemed particularly well suited to a situation in which the colon had been extensively damaged by a foreign body. A transverse colostomy was effected to protect the anastomotic site from the passage of faeces, although Painter suggests in his article that such a procedure may be unnecessary in similar cases of resection for perforation of diverticulitis.

Acknowledgement.—We would like to thank the late Mr. A. F. M. Barron for his permission to publish the case.

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REVIEWS AND NOTICES OF BOOKS

The Alcoholic Patient in Surgery. By ALBERT B. LOWENFELS, M.D., New York. 9 × 6 in. Pp. 268 + xii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £6.

IN this well-produced volume the author has tried to review alcoholism in all its aspects—sociological, pharmacological, and pathological. There is an excellent chapter on the pathophysiology of alcohol-induced pancreatitis but in general if the book is really intended as a practical aid to the surgeon too much has been attempted. As a book of reference there is much useful and interesting background reading, but detailed guidance is lacking where it is needed most.

The cautionary instructions in the management of the drunkard with a head injury are welcome and this section should be compulsory reading for all casualty surgeons. The role of solitary or sequential blood-alcohol estimates in this context is not discussed.

Considering the price this book will be a more useful addition to a hospital library than to a personal collection.

Preoperative and Postoperative Care in Neurological Surgery. By BURTON L. WISE, B.A., M.D., F.A.C.S., San Francisco. 9¼ × 6 in. Pp. 128 + xi. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $8.75.

THIS book sets out to provide in an easily readable form sound and practical advice concerning pre- and post-operative management of the neurosurgical patient. It succeeds in this and will be of value to the young doctor entering this speciality.

General topics common to most branches of surgery are discussed, while clear explanations and recommendations are made regarding problems peculiar to neurosurgery, e.g., raised intracranial pressure and internal cerebral herniation.

Professor Wise's particular interest in the metabolic, endocrine, and fluid-balance disturbances encountered in neurosurgery is very evident throughout the three sections into which the book is divided. Section III, comprising about half the text, is exclusively devoted to these aspects.

Some parts of the first two sections on pre- and post-operative management (subdivided into general and neurosurgical) are perhaps a little tenuous in their detail. Bearing in mind the wide variations in established clinical practice this is excusable and is fully compensated for by an extremely comprehensive and useful bibliography appended to each section.

A short but salutary paragraph entitled 'Informed Consent' (to operation in the U.S.A.) in Section I gives one cause to ponder. It emphasizes the need for careful explanation to the patient (and/or his relatives) of the objectives and possible outcome and complications of neurosurgical procedures which may appear to be so straightforward to the uninitiated.

Der Notfall: Gastrointestinalblutung. Edited by HANS-JOACHIM STREICHER and JOACHIM ROLLE, Wuppertal-Elberfeld. 9 × 6 in. Pp. 170 + viii. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.34.

THIS book gives an account of a symposium held at Wuppertal-Elberfeld in March, 1970, at which German surgeons discussed the problems of gastro-intestinal bleeding. The topics covered first aid, resuscitation and transport, diagnostic methods, the causes and pathology of bleeding, and specialized problems such as bleeding in children.

Much of the discussion reflects interesting differences in attitudes in different parts of Germany, and British readers will note differences between German and British experience. There is a lack of controlled clinical trials but the new operation of proximal gastric vagotomy has been routinely performed in Munich for bleeding duodenal ulcer since 1964. The operation is accompanied by pyloroplasty and carries a mortality rate of only 5 per cent.

The Germans have had much more experience of bleeding oesophageal varices than most British surgeons, since every second case of bleeding is reported to be due to oesophageal varices by one author. The favoured operation is an emergency portacaval shunt and there is much discussion about the most effective management.

Human Embryology. Prenatal Development of Form and Function. Fourth edition. By W. J. Hamilton, M.D., D.Sc., F.R.C.S., F.R.C.O.G., F.R.S.E., London, and H. W. Mossman, M.S., Ph.D., Wisconsin. Pp. 646+xii. 1972. Baltimore: Williams & Wilkins Co. £10·50.

Since the termination of the Second World War Hamilton, Boyd, and Mossman's *Human Embryology* has been the standard work throughout the world.

This important work was first published in 1945 and was reprinted seven times in the following 20 years; now the fourth edition makes its appearance under the editorship of Professor Hamilton and Professor Mossman, Professor Boyd having died in 1968. There can be no doubt whatever that the new fourth edition is by far the best that has so far been published. The authors have made this book invaluable, not only to embryologists and anatomists but also to a vast number of surgeons practising plastic surgery, neonatal surgery, urological surgery, ophthalmic surgery, or ear, nose, and throat surgery as their specialty.

The authors have succeeded in dealing with the functional aspects of different organs during development.

An excellent additional chapter has been incorporated in this edition on the development, structure, and functional activities of the placenta. We are full of praise for this extensive work which deals with implantation, determination, differentiation, the organizer mechanism, abnormal development, and twinning.

Quite a feature of this large volume is the excellence of the numerous illustrations. The coloured drawings by A. K. Maxwell are superb. The illustrations of the development of the skeletal system will delight orthopaedic surgeons both at home and abroad.

An excellent production and a great credit to British and American scientific achievement.

Bioceramics—Engineering in Medicine. Edited by C. W. Hall, S. F. Hulbert, S. N. Levine, and F. A. Young, Texas. 9×6 in. Pp. 484+xi. Illustrated. 1972. London: John Wiley & Sons Ltd. £7 10.

This book records the proceedings of a symposium held in New Hampshire in 1970. It contains a wealth of information on implantable devices, and the physiological and pathological problems of prostheses are discussed in some detail. Dental, maxillofacial, and orthopaedic applications gain most consideration, but dissertations on tracheal prostheses and the maintenance of chronic percutaneous electronic leads as well as a discussion of reabsorbable implants are examples of the wide range of topics which are dealt with. The cost is prohibitive except for reference libraries and the specialist reader, for whom some record of the discussion would have been valuable.

Gastrin: Inaktivierung und Abbau. By Hans Peter Seelig, Heidelberg. 9¼×6¼ in. Pp. 110+viii, with 57 illustrations. 1972. Stuttgart: Georg Thieme Verlag. DM.39.

In this monograph the author deals with many aspects of the current knowledge of the antral hormone, gastrin. His personal research provides a large part of the data and attempts to elucidate the fate of gastrin in the body. *In vitro* experiments include work with liver, kidney, gastric antral mucosa, and skeletal muscle homogenates from rats. Human blood-serum has also been studied and all the preparations of this were shown to inactivate gastrin II which the author had purified from hog antra. In high-speed supernatants of kidney and liver homogenates two enzyme systems were found: a specific one (*p*H optimum 6·4) and an apparently non-specific one (*p*H optimum 8·2). Both these enzyme systems inactivated gastrin by deamidation of the C-terminus; sequential hydrolysis of the peptide then occurred.

The author then elaborates his reasons for believing that the liver is a major site of activation of gastrin *in vivo*, which is an interesting view and is not generally held in this country.

Lessons in Surgical Terminology for the Medical Transcriber. By Anne Hadley. 11×8½ in. Pp. 74+ix. 1972. Oxford: Blackwell Scientific Publications. £3·40.

There are far too few medical transcribers both in this country and in America and therefore this book has been published at an opportune time. The various medical vocabularies which are in everyday use are set out in 45 lessons for the 'would-be' medical transcriber.

The use of this book, together with one of the modern medical dictionaries, will greatly aid transcribers of medical lectures, discussions, and debates.

Conference on Shock. Edited by I. McA. Ledingham, M.B., Ch.B. (Glas.), and T. A. McAllister, M.B., Ch.B. (Glas.), Glasgow. 9¼×7 in. Pp. 193+ix. Illustrated. 1972. London: Henry Kimpton. £7.

As our capacity to record and quantify bodily responses becomes greater so it becomes more and more difficult to define the concept of 'shock', and one is tempted to wonder whether, in fact, the term has outlived its usefulness and should quietly disappear. It remains true, however, that patients with very severe acute illness, whatever the cause, have certain patterns of organ failure and system failure in common which demand similar responses on the part of their doctors. With this in mind, the Royal College of Physicians and Surgeons of Glasgow arranged a 2-day symposium on shock in October, 1970, to which experts contributed articles on subjects as diverse as cerebral blood-flow, the sequential assay of whole-blood histamine, crushed-chest syndrome, domiciliary management of myocardial infarction, and bacteriaemia. It is just possible that this is the last such symposium that will ever appear and it can certainly stand comparison with its predecessors. The individual articles are by and large excellent though the book as a whole suffers from a certain vagueness of aim as it is a combination of didactic reviews, personal accounts of research in progress, and speculative hypotheses. Dr. Sykes's article on the factors bringing about tissue hypoxia is an excellent example of the first type and unravels this complicated subject with masterful clarity. The chapters dealing with autoregulation in the renal circulation by Dr. Bell and the sequential assay of plasma catecholamines in early septic shock by John Griffiths are interesting accounts of experimental research, which perhaps should have (and indeed probably already have) been published in specialized journals. By contrast, A. M. Harper's account of the changes occurring in cerebral blood-flow during acute illness appears rather speculative, although it refers to personal work published elsewhere.

There is much more in the book which is individually excellent, and the conference was clearly a success and was enjoyed by its participants. Whether, in fact, this type of reportage is the best means of keeping the clinician abreast of applied physiology nowadays is more doubtful. Owing to the high price this symposium may sell less well than it deserves.

The History of Urology. By LEONARD J. T. MURPHY, M.S., F.R.A.C.S., F.A.C.S., Melbourne. 10 × 7 in. Pp. 531 + xiii. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $32.50.

UROLOGY, oldest of the surgical specialities, badly lacked a good history. There was Desnos's introductory chapter for the *Encyclopédie française d'Urologie* of 1914, and Bransford Lewis's 'History' written for the American Urological Association in 1933, but the one necessitated a long, dusty search and a struggle with the French, and the other, though amusing, nearly always gave the wrong references. Now Mr. Murphy, a practising urologist, has given us a sensible translation of Desnos with the dull bits left out and has added his own lucid contributions to bring the history up to date. The result is elegant and entertaining, full of illustrations, and backed with complete references. It unfolds the story of urology from the earliest days when surgery was urology and little besides, to the last century when the cystoscope and the Roentgen ray made urology the most precise and most accurate of surgical specialities.

Murphy recalls the brilliant heritage of Sylvius, Vesalius, Fallopius, and Eustachius and traces the story through Frère Jacques, Ambroise Paré, Cheselden, Guthrie, Hunter, Lister, and Bigelow. The roll is long and honourable, and even the great William Harvey did not shrink from operating on the testicle. We read again the sorry story of the squabble for recognition of priority in open prostatectomy—Murphy rightly gives credit to Moynihan's ex-house surgeon, McGill of Leeds; we learn of the rise and fall of that non-disease, the floating kidney, which now, alas, has passed the way of tongue-tie and chlorosis. We are told how glow-worms were used to illuminate the bladder and how bougies were generally passed on the upright patient (at St. Peter's they backed them up against a wall). Even that marvellous spoof, the biography of Coudé, is not forgotten.

This book will entertain and fascinate any surgeon, for it is not the story of a minor branch of surgery but of the main trunk, and still the most vigorous shoot, of a grand old tree.

Zahnerhaltungskunde. By ERNST SAUERWEIN, Bonn. 7½ × 4½ in. Pp. 278 + xi, with 76 illustrations. 1972. Stuttgart: Georg Thieme Verlag. DM.12.80.

THIS pocket book on conservative dentistry is mainly aimed at students and practising dentists. The many aspects of conservative dentistry, whether by medical or surgical treatment, are described. The book is well illustrated by line diagrams but the abbreviated text is difficult to read. A good knowledge of German is essential to follow this book but it may be of value to selected dental students.

Renal Transplantation. Theory and Practice. By JEAN HAMBURGER, M.D., JEAN CROSNIER, M.D., JEAN DORMONT, M.D., and JEAN-FRANÇOIS BACH, M.D., Paris. 9 × 6 in. Pp. 326 + xx. Illustrated. 1972. Edinburgh: Churchill Livingstone. £7.

THIS book on renal transplantation by one of the most experienced groups in the world is to be welcomed by all who are interested in the subject. Its presentation is scholarly with an excellent background of the biology of rejection of grafted tissues and a discussion of experimental and theoretical aspects of immunosuppression. Professor Hamburger and his colleagues have worked on both experimental and clinical aspects of transplantation since the early 1950's and one of the first successful non-identical twin transplants was performed by them in 1959. This patient received a kidney from his dizygotic twin, was treated with total body irradiation, and is still alive and well.

As the authors point out, most of the other experience with this method of immunosuppression has been disappointing, and the suggestion by Schwartz and Dameshek in 1959 that the anti-leukaemia drug, 6-mercaptopurine, appeared to make rabbits specifically tolerant to foreign protein and incapable of producing antibodies against that protein led to the use of this and related drugs in animals with kidney grafts. This work was perfomed initially in the United Kingdom and not in Dr. Merrill's laboratory in Boston as stated in the Preface.

The chapters on clinical kidney transplantation, assessment of patients, complications, and results are excellent. The moral and legal aspects are summarized very clearly. I have only one criticism of this book and that is that the main authors do not include a surgeon and since organ transplantation is primarily a surgical subject it is a little unkind to banish the surgeons and the surgery of transplantation to an appendix. The book can, nevertheless, be thoroughly recommended as an up-to-date text on all aspects of renal transplantation. The English translation by Mr. Anthony Walsh is excellent.

Nouveau Traité de Technique Chirurgicale, Volume 4. Edited by JEAN PATEL and LUCIEN LÉGER, Paris. 10 × 7¼ in. Pp. 508, with 476 illustrations. 1972. Paris: Masson & Cie Éditeurs. 390F.

VOLUME 4 of this massive 15-volume treatise on surgical technique deals with cardiac and breast surgery.

The section on cardiac surgery is based essentially on the experience of the cardiovascular surgical centre of the Broussais Hospital in Paris directed successively by F. d'Allaines and C. Dubost. This experience includes over 11,000 cardiac operations of which over 5000 were done by the open-heart technique. The first part of this section deals with general principles of cardiac surgery with special attention to pre- and postoperative management and includes an excellent account of the different approaches to the heart and the great vessels. All the congenital and acquired cardiac lesions are then dealt with, very full technical details and alternative techniques being given. The text is well illustrated by very clear and helpful drawings and each chapter includes many references from the world literature. There follow equally good sections on the coronary arteries, the pericardium, and the great vessels of the chest, with special emphasis on the aorta. A well-balanced chapter on cardiac transplantation and its technique is included in this section. The only criticism which could be levelled at this beautifully produced work is that the volume could have been made smaller by less discussion of the results in what sets out to be an account of surgical techniques.

Unfortunately the second section dealing with surgery of the breast is not of the same quality as the first section and one gets the impression that it was only added as an afterthought and that the authors were given strict instructions about limitation of space available. On the whole the text in this section is very sketchy and several of the illustrations are either unclear or unhelpful. Nevertheless, there is a good description of the cosmetic yet effective approaches for drainage of breast abscesses and excision of benign lesions of the breast, including exploration of the main ducts. The pages dealing with radical mastectomy based on the Halsted operation are badly set out with respect to the relevant illustrations and the authors describe an incision encircling the breast with a transverse extension across the axilla which looks difficult to close and probably results in swelling of the arm postoperatively. Simple mastectomy is dealt with very sketchily and the accompanying photographs are useless. A short account is given of 'conservative' radical mastectomy and there are brief accounts of extended radical mastectomies including, rather surprisingly, interscapulothoracic amputation which must be very rarely carried out nowadays. The Editors' deliberate policy is to include paediatric surgery and plastic surgery under the relevant systems, and this results in a chapter on several operations for plastic reconstruction of the breast which are well illustrated but not critically analysed. This whole section on breast surgery contains no references at all.

The essential and best part of this volume is that dealing with surgery of the heart and great vessels. This in itself makes it an excellent reference work which includes a wealth of information justifying its price of £32.

Gastroenterology: An Integrated Course. Edited by IAIN E. GILLESPIE, M.D., F.R.C.S., Manchester, and T. J. THOMSON, M.B., Ch.B., F.R.C.P., Glasgow. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 270+ix. Illustrated. 1972. Edinburgh: Churchill Livingstone. £1·50.

THIS book comes as a very welcome companion in a rapidly expanding field of medicine and surgery. It provides the postgraduate with a rapid synopsis of current advances, and the interested undergraduate with an entrée into a specialized field.

One outstanding advantage of this book is that it deals with the medical and surgical aspects of gastro-enterology concurrently, evaluates the different forms of treatment, and helps both the surgeon and the physician to see the other's point of view.

It is written in an interesting and attractive form, and at its current price will enjoy considerable popularity.

Nouveau Traité de Technique Chirurgicale, Volume 6. Edited by JEAN PATEL and LUCIEN LEGER, Paris. $9\frac{3}{4} \times 7\frac{1}{4}$ in. Pp. 1223. Illustrated. 1972. Paris: Masson et Cie Editeurs. 390F.

THIS volume is one of a multi-volume textbook of operative surgery of which five volumes have previously been published.

This excellent work on head and neck surgery is up to the high standard of the others with beautifully clear line drawings illustrating the minutiae of surgical technique and a clear concise text which is easily followed without any deep knowledge of French explaining the indications for operation, the possible complications, and the post-operative care. Each chapter is preceded by a short description of the surgical anatomy involved.

For a textbook on head and neck surgery this volume covers many surgical disciplines. For example, there are aspects of surgery which would normally be considered the province of the ear, nose, and throat surgeon. There is a chapter on the vascular lesions affecting the major vessels of the neck. The surgery of the vocal cords and of the thyroid is covered as well as the surgery of the tongue and larynx. There is also a section which is devoted to plastic surgery as it affects the head and neck with reference to such general problems as scalp injuries and the excision of rodent ulcers, and also rhinoplasty and face-lifting, together with plastic surgery of the eyelids.

Such diversity makes this volume essentially a book of reference. It is not likely that any surgeon would wish to buy this volume as his individual interest would only be catered for in a relatively small part of the book.

Osteosynthese Praxis. By F. SCHAUWECKER, Tübingen. $9\frac{1}{2} \times 7$ in. Pp. 236+viii, with 517 illustrations. 1972. Stuttgart: Georg Thieme Verlag. DM.98.

THIS is an atlas of internal fixation of fractures by screws, plates, wires, and intramedullary nails. The 236-page book has no less than 517 illustrations which are excellent black-and-white line drawings. The text is limited to a description of the diagrams but at the same time stresses the important technical points in any particular method of internal fixation. The line diagrams are so clear and self-explanatory that a knowledge of German is not essential. In spite of its high cost it should be of considerable interest to orthopaedic surgeons involved in the surgery of trauma.

The Scientific Basis of Medicine. Annual Reviews 1972. Edited by IAN GILLILAND, M.D., F.R.C.P., and JILL FRANCIS. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 400+ix. Illustrated. 1972. London: The Athlone Press. £4.

IN this volume the British Postgraduate Medical Federation has once again published a selection from the series of lectures on the scientific basis of medicine delivered in the winter of 1970–1. The 19 lectures, all by experts in their fields, cover a wide range of topics illustrating the diversity of modern clinical science. Although many of the subjects covered are outside the range of ordinary surgical practice the book constitutes a fascinating review of the scope of present-day medical research, and all surgeons should find something to stimulate and fascinate them in the variety of subjects discussed. Of particular interest to surgeons are the lectures on transplantation immunology and the haemostatic functions of platelets. The opening lecture, 'Clinical Research: Its Contribution to Biological Thought' by Sir Harold Himsworth is, as would be expected, a masterly dissertation which cannot fail to be of interest to all concerned in this field of activity. The Postgraduate Medical Federation is to be congratulated on an admirable publication, which well merits a place in all medical libraries.

Aktuelle Orthopädie. By P. HINZ, Heidelberg, and R. PLAUE, Heidelberg. $9\frac{1}{2} \times 6\frac{1}{2}$ in. Pp. 60. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.39.80.

THIS is a monograph about club-hand deformity associated with aplasia of the radius. The writer reviews over 100 patients with this deformity most of whom were thalidomide victims. The mechanical problems are presented and the many different types of surgical treatment that have been used are discussed.

This book provides an extensive list of references on this highly specialized subject and, in spite of its relatively high price, should be of great interest to orthopaedic surgeons involved in treating patients with this deformity.

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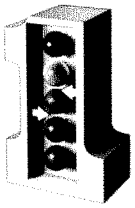

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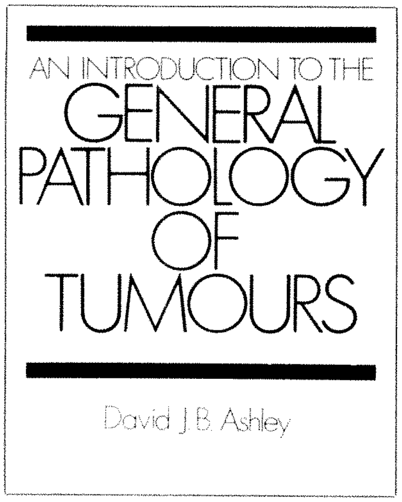

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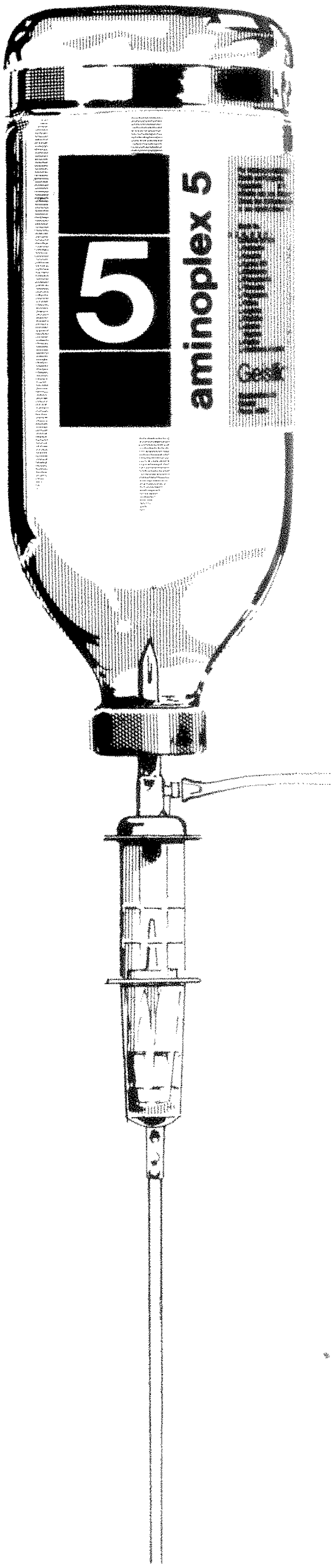

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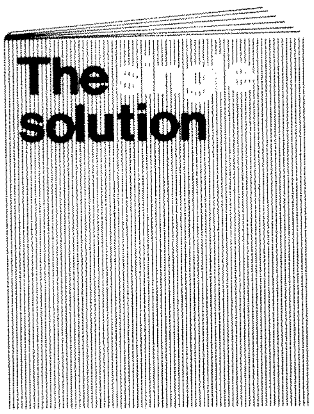

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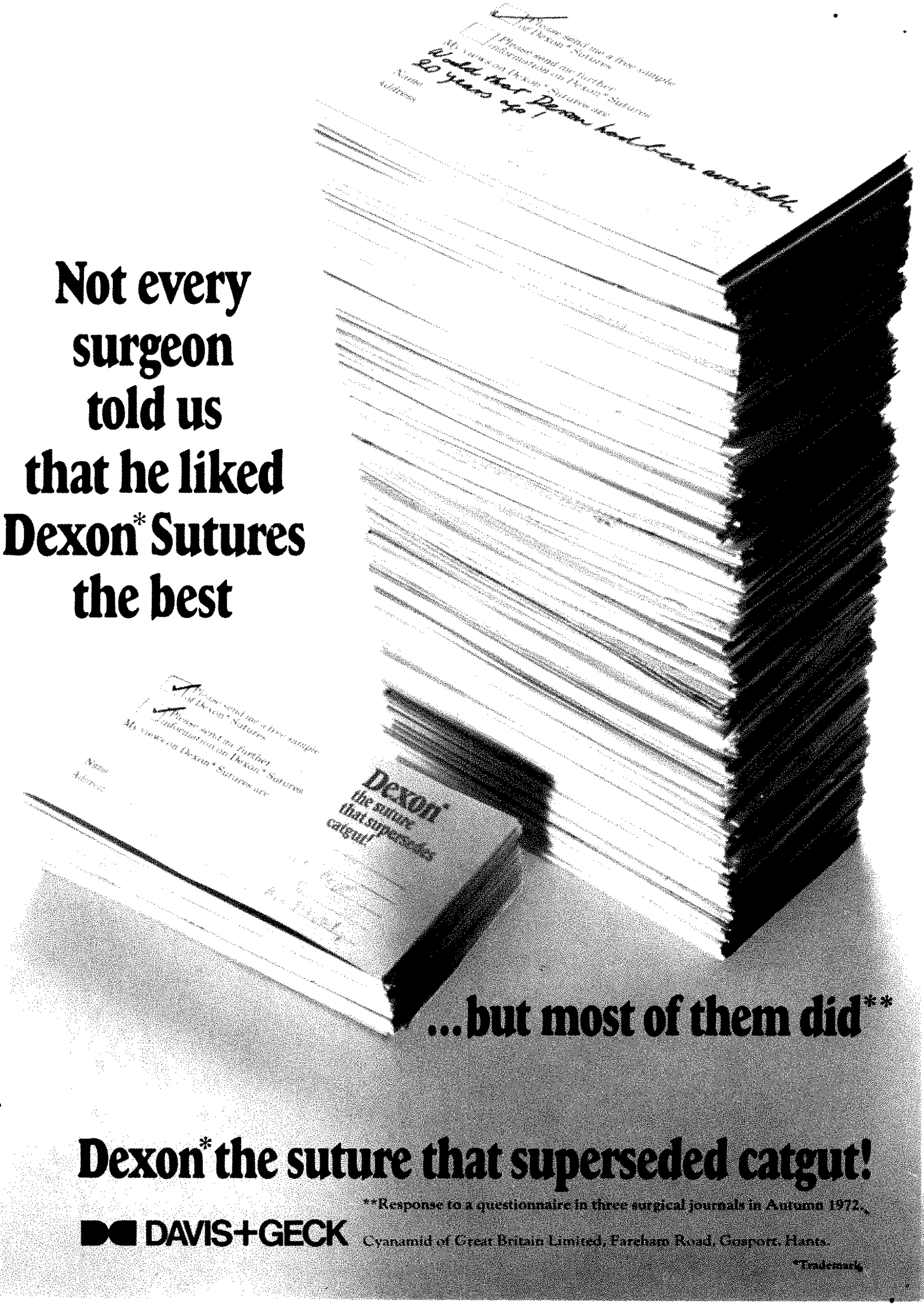
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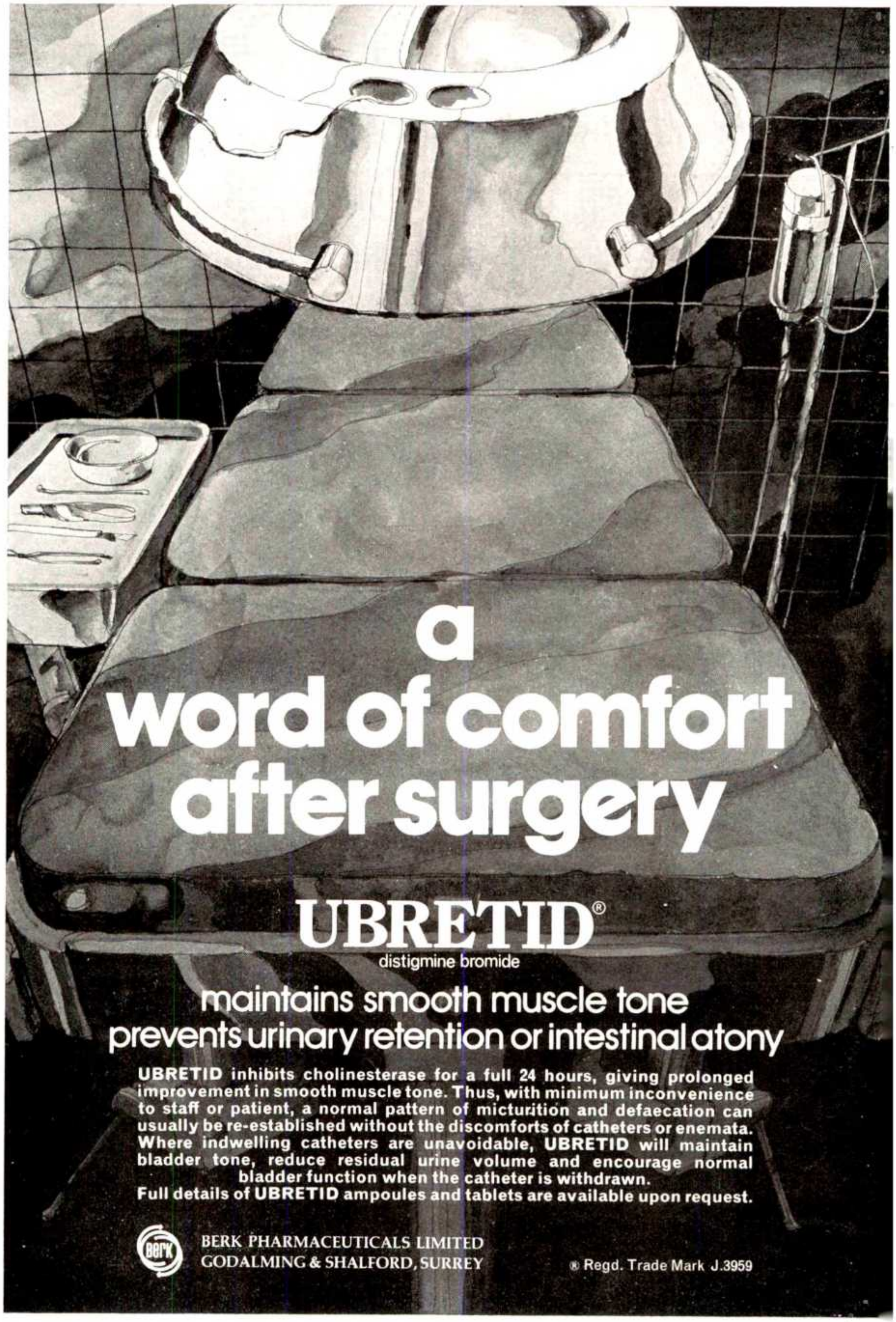

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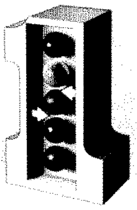

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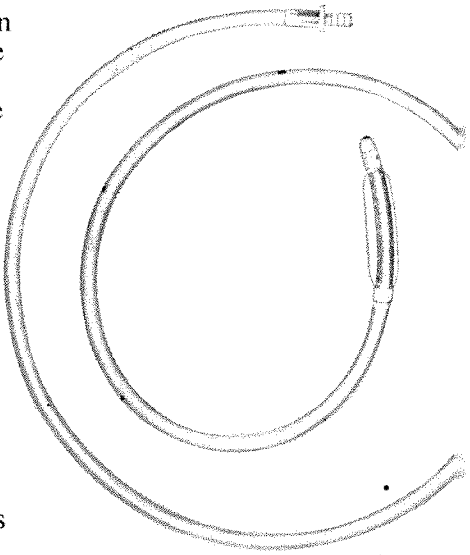

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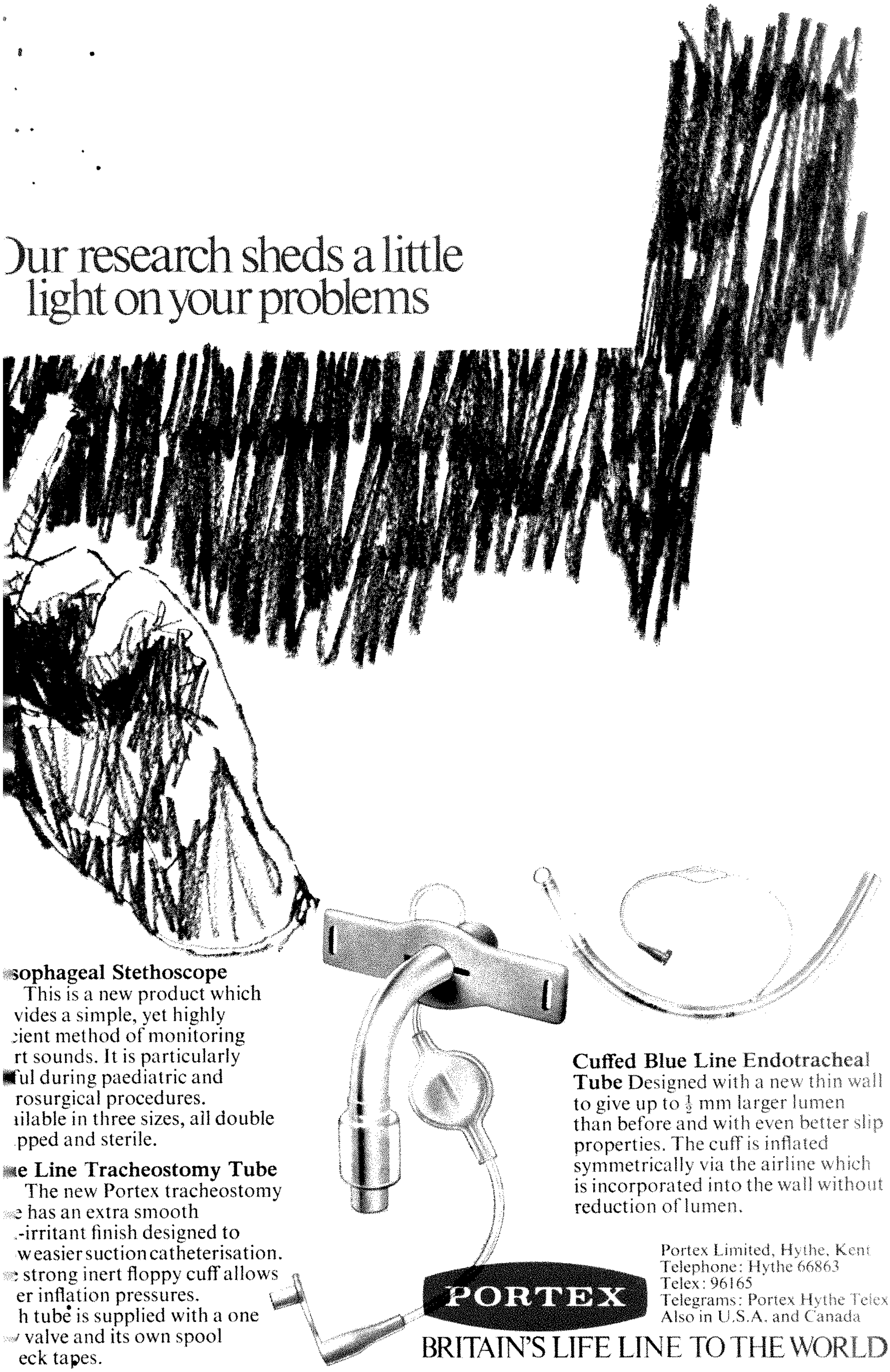

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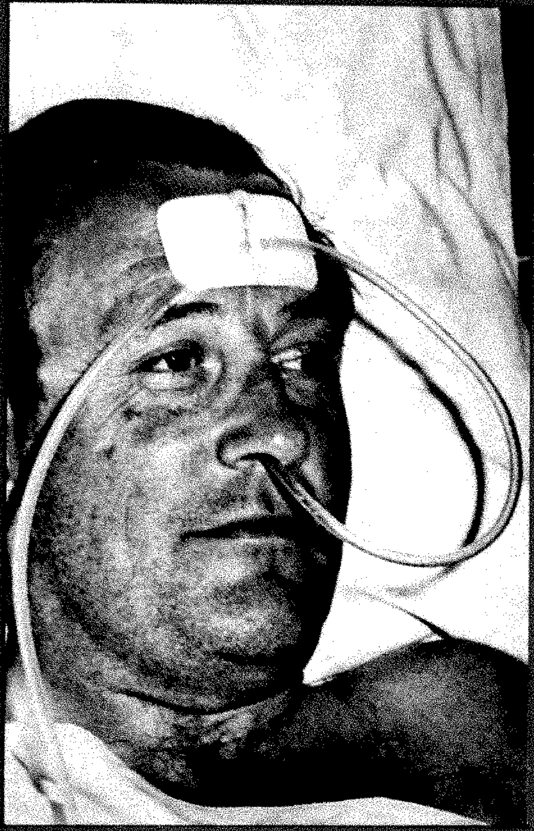

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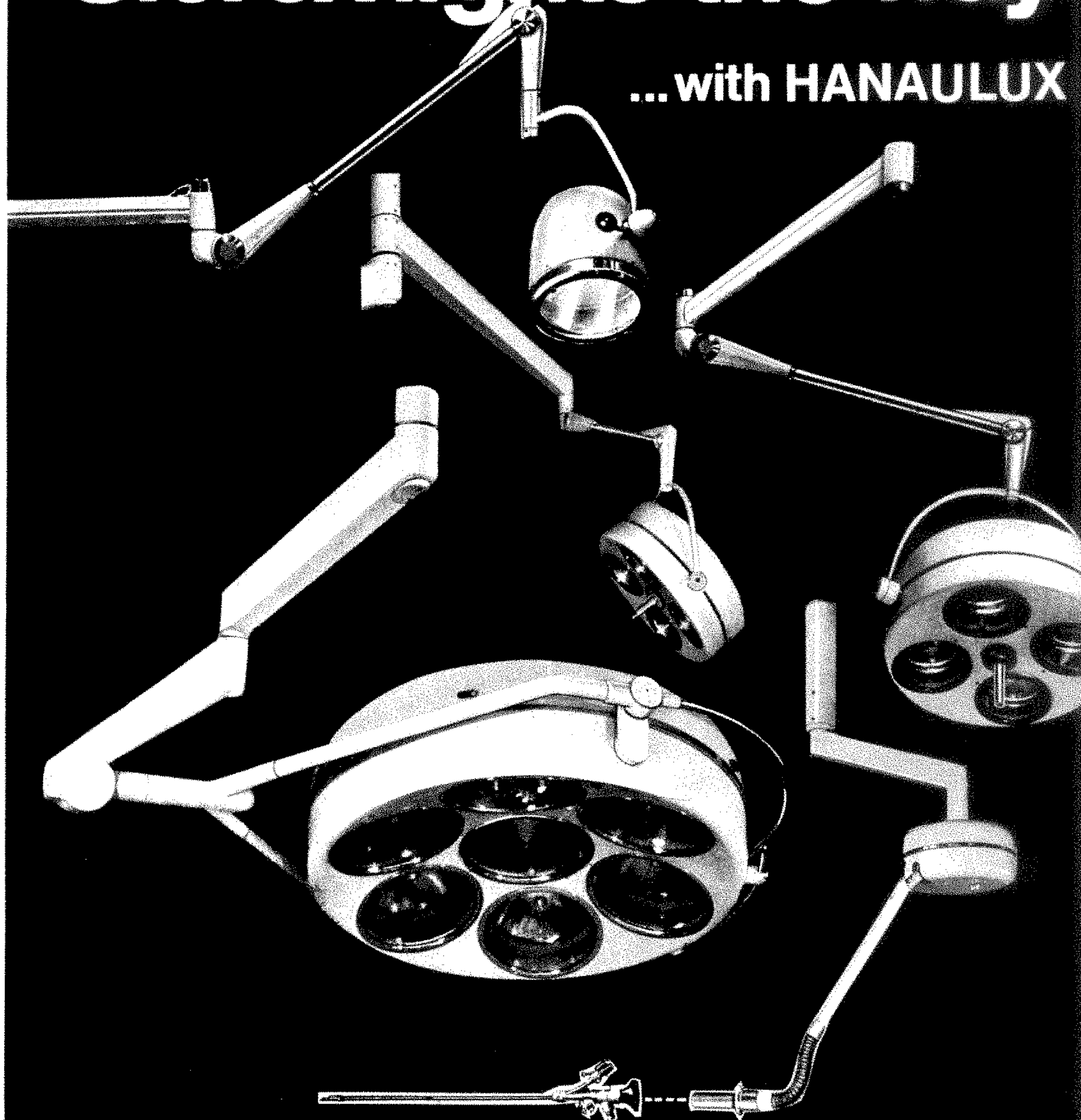

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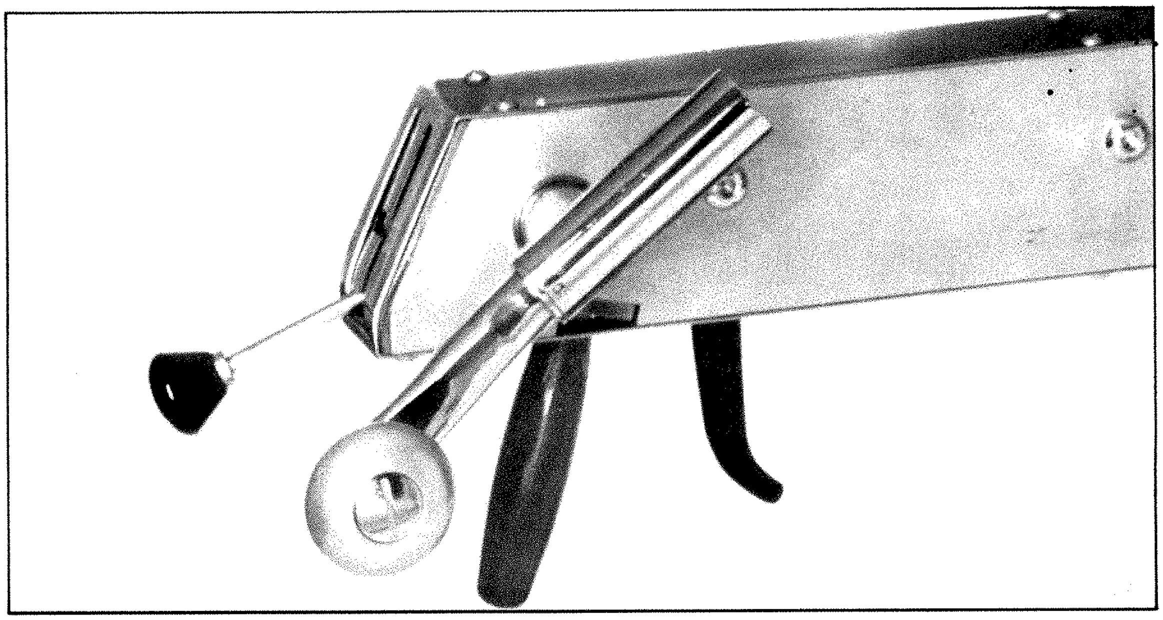

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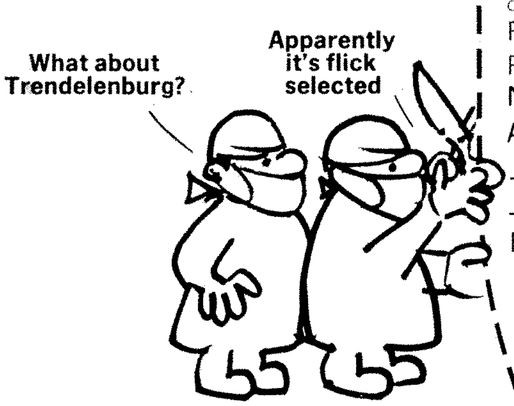

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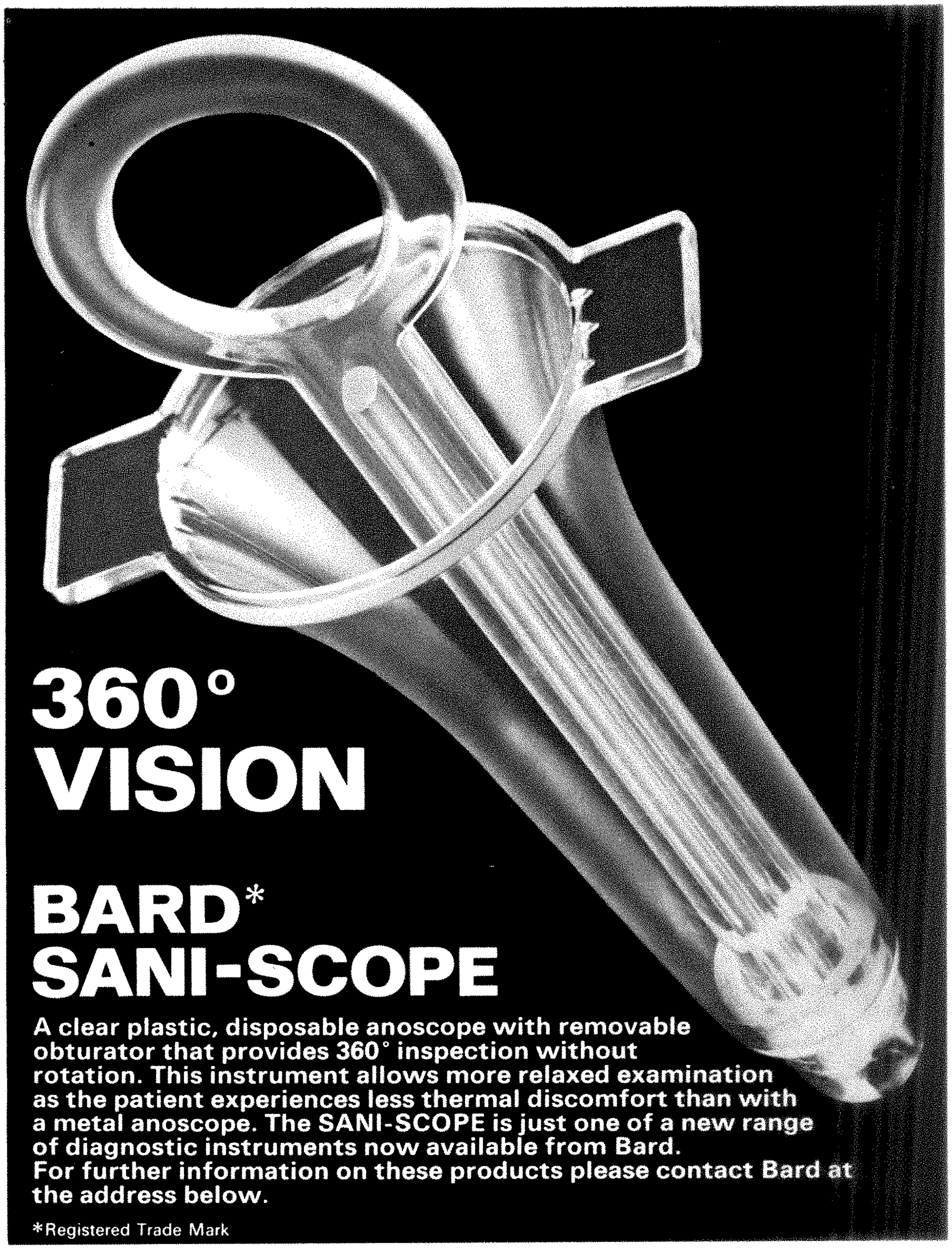

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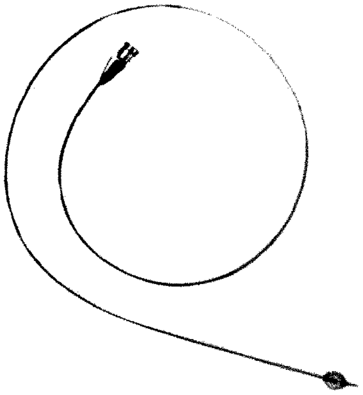

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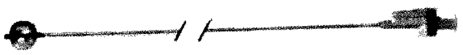

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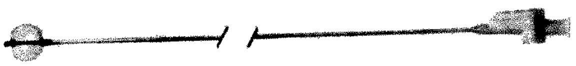

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	41	*Biliary Balloon Probe (Short Tip)*
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	A	*Revision Number*
	080	*Length in Centimeters*
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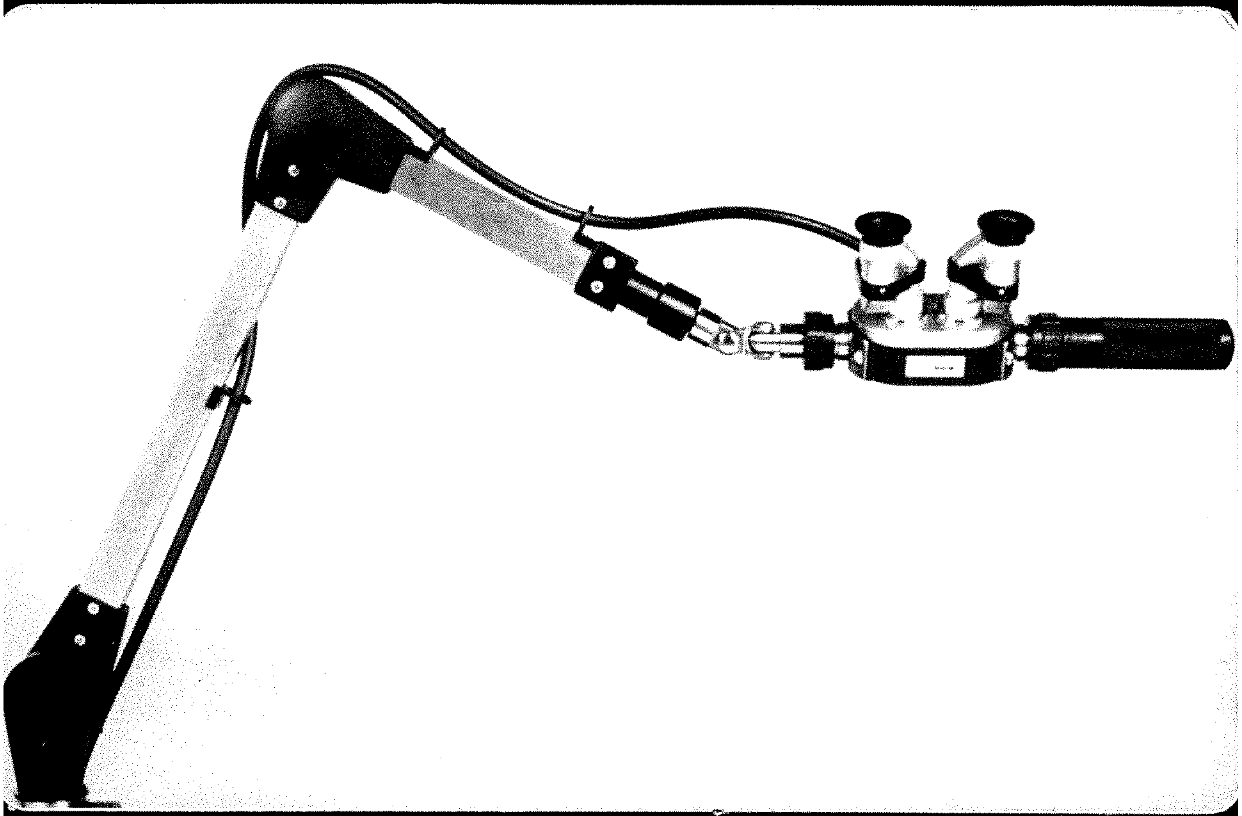

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THE
BRITISH JOURNAL OF SURGERY

Vol. 60 MARCH, 1973 No. 3

ORIGINAL PAPERS

ADENOCARCINOMA AND CROHN'S DISEASE

A REPORT OF 2 CASES AND ANALYSIS OF THE LITERATURE

By S. G. DARKE, A. G. PARKS, J. L. GROGONO, and D. J. POLLOCK
THE LONDON HOSPITAL

SUMMARY

Two cases of carcinoma developing in a segment of Crohn's disease are described, one in the large intestine and one in the small intestine. From an analysis of the literature, evidence is advanced with regard to age at the time of developing carcinoma, duration of symptoms attributable to Crohn's disease, anatomical distribution, and observed incidence compared with chance incidence. It is concluded that there is a small but significant risk of carcinoma developing, both in the small and large intestines, in Crohn's disease.

In view of the known predisposition for carcinomatous change in chronic ulcerative colitis it is desirable to know if a similar situation exists for Crohn's disease. This problem was reviewed recently in relation to both the small intestine (Wyatt, 1969) and the large intestine (Hywel Jones, 1969). For the small intestine, where the spontaneous occurrence of carcinoma is rare, it was concluded that there might be a predisposition to carcinomatous change. For the large intestine, however, it was suggested that no significant relationship existed.

Two further cases of carcinoma developing in a segment of Crohn's disease which have recently been seen at the London Hospital are reported in this communication; one in the large intestine and one in the small intestine. Six further cases from the literature are added to those previously reviewed, and further evidence is advanced concerning the relationship between the two conditions.

CLINICAL MATERIAL

All the cases of Crohn's disease seen at the London Hospital since 1948 have been reviewed. *Table I* shows the site of the disease in this series of 167 patients, and indicates the type and distribution of the various malignant tumours found. In 3 cases carcinoma and Crohn's disease occurred at the same site; in 2 this was in the large intestine, while the other was in the small intestine.

Table I.—ANALYSIS OF 167 CASES OF CROHN'S DISEASE PRESENTING AT THE LONDON HOSPITAL BETWEEN 1948 AND 1970

Site of Disease	*No. of Cases*
Total number of cases of Crohn's disease	167
Crohn's disease involving small intestine only	98
Crohn's disease involving small and large intestines	48
Crohn's disease involving large intestine only	21
Carcinoma and Crohn's disease at the same site	3
Carcinoma of colon at different site	2
Lymphosarcoma of small intestine	1
Leukaemia	1
Myeloma	1
Carcinoma of lung	1

CASE REPORTS

Case 1.—Mr. A. K., a 60-year-old clerk, was admitted to the London Hospital in November, 1970, with a 45-year history of attacks of partial small-bowel obstruction. Over the previous 2 years the attacks had become more severe and he had had watery diarrhoea but no rectal bleeding. On examination, he was thin but otherwise fit. There was tenderness in the right iliac fossa and there was a scar from an appendicectomy performed when he was aged 6. Sigmoidoscopy was normal. Haemoglobin estimation showed a mild iron-deficiency anaemia. Although barium-meal, follow-through, and barium-enema examinations were normal a straight radiograph of the abdomen taken during an attack showed several small-bowel fluid levels.

At operation Crohn's disease was found to involve the terminal 38 cm. of ileum. A large faecalith lay immediately proximal to the diseased bowel. There was no macroscopic evidence of malignant disease. An extended right hemicolectomy was performed. The patient's postoperative course was uneventful and when seen 4 months later he was well.

PATHOLOGY.—The right hemicolectomy specimen consisted of 64 cm. of terminal ileum, the caecum, and 13 cm. of ascending colon. The distal 30 cm. of ileum were thickened and matted together by dense adhesions. Two of the loops were connected by a fistula. The colon appeared normal apart from a polyp, 0·7 cm. in diameter, 5 cm. above the ileocaecal valve. The limits of excision were clear of disease. No enlarged lymph-nodes were present.

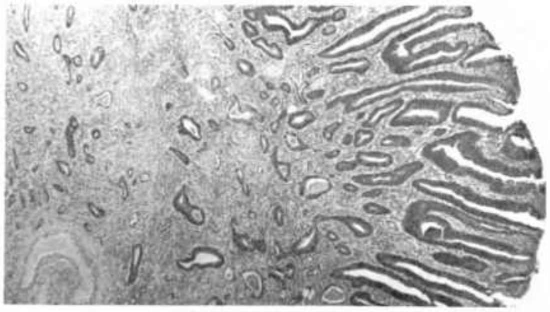

FIG. 1.—*Case* 1. Section of rectal nodule, showing invasion by a well-differentiated adenocarcinoma. H. and E. (× 25.)

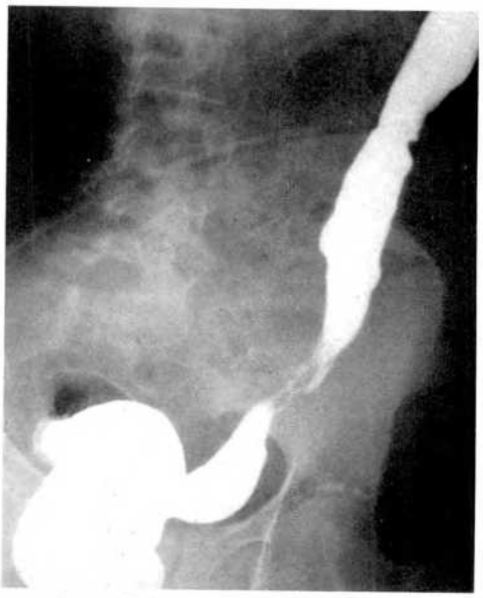

FIG. 3.—*Case* 2. Barium-enema film, showing a smooth filling defect in the sigmoid colon.

Sections showed thickening of the ileum, which was partly due to submucosal fibrosis and partly to muscular hypertrophy. The mucosa was ulcerated with an underlying infiltrate of polymorphs and plasma cells which extended through the muscle coats. Foci of pyloric metaplasia were present. In the submucosa collections of lymphoid tissue were seen. No granulomata were present. A fissure extended through the muscle coat of the bowel at one point. Immediately above this lesion the full thickness of the ileum was infiltrated by a well-differentiated adenocarcinoma (*Fig*. 1). The adjacent bowel showed in situ carcinoma which extended to the opening of the fissure. Lymph-nodes showed reactive hyperplasia only. The appearances were those of Crohn's disease of the terminal ileum with an adenocarcinoma. The colon was normal apart from a benign adenomatous polyp.

Case 2.—A 67-year-old housewife was admitted in November, 1969, with a 2-month history of diarrhoea, rectal bleeding, and weight-loss (13 kg.). She also complained of recent anal pain, and examination revealed a large perianal ulcer approximately 5 cm. in diameter (*Fig*. 2).

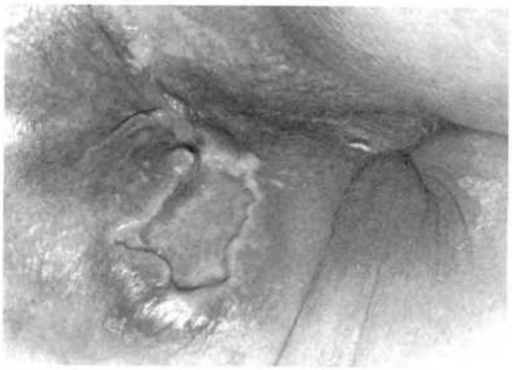

FIG. 2.—*Case* 2. Large perianal ulcer.

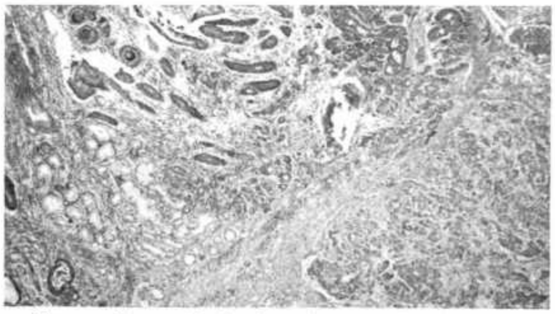

FIG. 4.—*Case* 2. Section from the terminal ileum showing invasion by a quite well-differentiated adenocarcinoma. An area of pyloric metaplasia is present on the left-hand side. H. and E. (× 21.)

At this time her haemoglobin was 8·9 g. A barium-enema examination showed a smooth stricture in the upper sigmoid colon which was consistent with a diagnosis of Crohn's disease (*Fig*. 3).

Laparotomy showed the changes of Crohn's disease from the mid-transverse colon to the rectum. The diseased colon was defunctioned by establishing an end-transverse colostomy. The patient made a good postoperative recovery and her perianal ulcer healed. However, when seen as an out-patient in October, 1970, she complained of dark-red rectal bleeding. On sigmoidoscopy a hard, nodular area was seen at 8 cm. from the anus and biopsy confirmed the presence of invasive adenocarcinoma. An abdominoperineal resection of the rectum and colon distal to the colostomy was therefore performed, from which she made an uneventful recovery.

PATHOLOGY.—Macroscopic examination of the specimen showed four raised irregular nodules 13 cm. from the anus, the largest being 0·6 cm. in diameter. The mucosa around the nodules had a faintly granular appearance. The mucosa 4 cm. above these lesions was irregular. There were mucosal nodules up to 2 cm. diameter with fissures and submucosal fibrosis. The anus was normal.

Sections from the nodules at 13 cm. from the anus showed invasion of the rectum by a well-differentiated adenocarcinoma. The tumour extended through the submucosa to invade the inner muscle coat for a short distance. The surface of the tumour had a villous pattern. The mucosa close to the tumour was mildly atrophic with small areas of ulceration. Sections from the region immediately above the tumour showed extensive ulceration with fissures extending through thickened submucosa into the muscle coat. There was a transmural infiltrate of lymphocytes and plasma cells. Foci of lymphocytes, sometimes with germinal centres, were present at all levels including the serosa. No granulomata were present. Occasional crypt abscesses were seen near areas of ulceration only. Sections of lymph-nodes showed reactive changes only with no granulomata or tumour cells. There were no premalignant epithelial changes. The presence of transmural inflammation and fissures strongly supported the clinical diagnosis of Crohn's disease of the colon with adenocarcinoma in the same segment (*Fig.* 4).

Table II.—DETAILS OF CASES OF CROHN'S DISEASE AND CARCINOMA INVOLVING THE SAME SEGMENT OF SMALL INTESTINE WHICH HAVE BEEN REPORTED IN THE LITERATURE

AUTHOR	AGE AND SEX	CLINICAL PRESENTATION PRECIPITATING SURGERY	DURATION OF SYMPTOMS ATTRIBUTABLE TO CROHN'S DISEASE	SITE OF CROHN'S DISEASE	SITE OF CARCINOMA	PROGNOSIS
Ginzberg, Schneider, Dreizin, and Levinson (1956)	30 M.	Intestinal obstruction	19 yr.	Jejunum	Jejunum	Hepatic metastases
Kornfield, Ginzberg, and Aldersberg (1957)	36 F.	Intestinal obstruction	8 yr.	Jejunum, ileum, colon	Jejunum	Carcinomatosis
Bersack, Howe, and Rehak (1958)	34 M.	Diarrhoea and malaise	9 yr.	Duodenum, jejunum, ileum	Duodenum, ileum	Carcinomatosis
Crohn and Yarmis (1958)	—	—	—	Jejunum, ileum	Jejunum	—
Lear (1958)	—	—	—	Ileum	Ileum	—
Buchanan, Huebner, Woolvin, North, and Novack (1959)	47 M.	Intestinal obstruction	28 yr.	Ileum	Ileum	Lymph-node metastases
Weingarten, Parker, Chazen, and Jacobson (1959)	44 F.	Intestinal obstruction	21 yr.	Jejunum, ileum	Jejunum	Peritoneal metastases
Weingarten and Weiss (1960)	28 F.	Abdominal fistula	5 yr.	'Small intestine'	'Small intestine'	Carcinomatosis
Zisk, Shore, Rosoff, and Friedman (1960)	61 F. 62 F.	Intestinal obstruction Abdominal mass	1 wk. 23 yr.	Terminal ileum Ileum, colon	Terminal ileum Ileum	Lymph-node metastases No apparent recurrence
Steele and McNeely (1960)	38 M.	Abdominal mass. No operation. Post-mortem diagnosis	14 yr	Jejunum, ileum	Distal ileum	Carcinomatosis
Almond, Neal, and Moedl (1960)	48 F.	Intestinal obstruction	2½ yr.	Ileum	Ileum	—
Hoffert, Weigarten, Friedman, and Morecki (1963)	40 M.	Peritonitis	3 mth.	Ileum	Ileum	Carcinomatosis
Berman and Prior (1964)	51 M.	Intestinal obstruction	25 yr.	Ileum	Ileum	—
Sheil, Clark, and Goligher (1968)	40 F.	Diarrhoea; weight-loss	5 yr.	Ileum	Ileum	Peritoneal metastases
Cantwell, Ketting, Carney, and Ludwig (1968)	60 M.	Intestinal obstruction	31 yr.	Ileum	Ileum	Peritoneal metastases
Morowitz, Block, and Kinsner (1968)	41 M.	Intestinal obstruction	22 yr.	Whole small bowel	Ileum	Metastatic carcinoma
Tyers, Steiger, and Dudrick (1969)	37 M.	Intestinal haemorrhage	15 yr.	Whole small bowel	Jejunum	No evidence of spread but died of haemorrhage
Wyatt (1969)	33 M.	'Ileo'-rectal fistula	7 yr.	Ileum	Ileum	No evidence of spread but died postoperatively
Magnes and De Bell (1969)	71 M.	Intestinal obstruction	12 yr.	Ileum	Ileum	Lymph-node metastases
Farmer, Hawk, and Turnbull (1970)	43 M. 61 F.	Intestinal obstruction Intestinal obstruction	4 yr. 7 yr.	Jejunum, ileum Jejunum	Jejunum Jejunum	Carcinomatosis Carcinomatosis
Brown, Weinstein, and Janowitz (1970)	55 F.	Intestinal obstruction	—	Ileum	Ileum	Died postoperatively ? cause
Schuman (1970)	34 M.	Intestinal obstruction	7 yr.	Ileum	Ileum	Lymph-node metastases
Present series (1973)	60 M.	Intestinal obstruction	45 yr.	Ileum, caecum, ascending colon	Ileum	No apparent recurrence

The third case in which carcinoma and Crohn's disease occurred in the same segment of intestine was in the rectum of a 47-year-old man who has been separately reported (Hardy and Youngs, 1972).

Table III.—DETAILS OF CASES OF CROHN'S DISEASE AND CARCINOMA INVOLVING THE SAME SEGMENT OF LARGE INTESTINE WHICH HAVE BEEN REPORTED IN THE LITERATURE

AUTHOR	AGE AND SEX	CLINICAL PRESENTATION PRECIPITATING SURGERY	DURATION OF SYMPTOMS ATTRIBUTABLE TO CROHN'S DISEASE	SITE OF CROHN'S DISEASE	SITE OF CARCINOMA	PROGNOSIS
Warren and Sommers (1948)	—	—	—	Ascending colon	Ascending colon	—
Van Patter, Bargen, Dockerty, Feldman, Mayo, and Waugh (1954)	—	—	—	—	—	—
Martinelli and Belluci (1959)	56 F	Intestinal obstruction	3 mth.	Ileum, caecum, ascending colon	Ascending colon	No sign of spread
Wein and Spector (1964)	48 M	For fistula	20 yr	Caecum, ileum, ascending colon	Caecum	No apparent recurrence
Atwell, Duthie, and Goligher (1965) (*see* Sheil and others (1968) for details)	50 F	Biopsy rectal bleeding showed incidental carcinoma	21 yr	Rectum	Rectum	No apparent recurrence
	—	No details	—	—	—	—
	—	No details	—	—	—	—
Crohn and Yarmis (1966)	—	—	—	?	Distal transverse colon	—
	—	—	—	?	Distal transverse colon	—
Parrish, Kansten, McRae, and Moretz (1968)	65 F.	Routine right hemicolectomy for mass in right iliac fossa	4 mth	Ascending and transverse colon	Caecum and ascending colon	No apparent recurrence
Perrett, Truelove, and Massarella (1968)	34 F.	Right hemicolectomy for mass in right iliac fossa	9 mth	Caecum and terminal ileum	Caecum	Apparent cure
	61 F.	Total colectomy following incomplete excision	3 wk.	Whole colon	Sigmoid, transverse colon, caecum	Died 4 years later; cause unknown
	72 F.	Hemicolectomy for mass in right iliac fossa	3 wk.	Caecum and ascending colon	Caecum	No apparent recurrence
Hywel Jones (1969)	37 F	Rectovaginal fistula	13 yr.	Colon and caecum	Rectum	Carcinomatosis
	61 F	Diarrhoea and malaise Barium-enema examination, suspicious change	2 mth	Sigmoid	Sigmoid	No apparent recurrence
	60 M.	Stricture at 12 cm	2 mth	Sigmoid	Sigmoid	
	70 M.	Growth seen on sigmoidoscopy	6 wk.	Rectum	Rectum	
Kipping (1970)	27 M.	Colectomy for umbilical fistula	7 yr.	Whole colon	Rectum	Died 2 years later, carcinomatosis
Hardy and Youngs (1972)	58 M.	Positive rectal biopsy	18 yr.	Ileum, colon, rectum	Rectum	Died; carcinomatosis
Present series (1973)	67 F.	Positive rectal biopsy	12 mth.	Transverse colon and distally	Rectum	No apparent recurrence

REVIEW AND ANALYSIS OF THE LITERATURE

The literature on Crohn's disease and carcinoma involving the same segment of intestine is shown in *Table II* for the small intestine (25 cases) and *Table III* for the large intestine (20 cases). The analysis of data relating Crohn's disease and carcinoma is considered separately for the small and large intestine.

Small Intestine.—

Age Incidence.—The average age at the time of diagnosis of carcinoma in a segment of Crohn's disease ('Crohn's carcinoma') is 46 years. This contrasts with an average age of 61 in a group of 119 cases of small-bowel carcinoma unassociated with Crohn's disease (carcinoma *de novo*) from the Birmingham Cancer Registry (Wyatt, 1969, from Brookes, Waterhouse, and Powell, 1968). This is shown in histogram form in *Fig.* 5 and the difference between the two groups is statistically significant ($P < 0{\cdot}01$).

Duration of Symptoms.—The duration of symptoms in the patients with 'Crohn's carcinoma' prior to surgery tended to be longer than that in patients coming to surgery for simple Crohn's disease in a series of 86 cases described by Cornes and Stetcher (1961); this is shown in *Table IV*. However, there is no statistical difference ($P > 0{\cdot}2$). It is unlikely that the carcinomas were responsible for long-standing symptoms; of 45 cases of unassociated small-bowel carcinoma described by Brookes and others (1968), 43 cases had symptoms of less than 2 years' duration.

Distribution through the Intestine.—The anatomical distribution of 'Crohn's carcinoma' through the intestine is shown in *Table V*. This is compared with a series of 321 small-bowel carcinomas collected between 1920 and 1960 from the world literature (Rocklin and Longmire, 1961). The 'Crohn's carcinoma' cases occurred mainly in the terminal ileum, and the carcinoma *de novo* cases were evenly distributed through the intestine. There is a statistically significant difference between this distribution ($P < 0{\cdot}01$).

Table IV.—DURATION OF SYMPTOMS PRIOR TO SURGERY IN PATIENTS WITH 'CROHN'S CARCINOMA' COMPARED WITH THOSE WITH SIMPLE CROHN'S DISEASE OF THE SMALL INTESTINE

DURATION OF SYMPTOMS (yr.)	SMALL-BOWEL CROHN'S DISEASE (Cornes and Stetcher, 1961)		'CROHN'S CARCINOMA' (Present series)	
	No. of Cases	Percentage of Total	No. of Cases	Percentage of Total
0– 5	42	49	6	27
6–10	21	73	5	50
11–15	11	87	3	64
16–20	7	95	1	68
21–25	3	98	4	86
26–30	—	98	1	91
30+	2	100	2	100
Total	86	100	22	100

Table V.—RELATIVE ANATOMICAL DISTRIBUTION THROUGH THE BOWEL OF 'CROHN'S CARCINOMA' AND CARCINOMA *de novo* OF THE SMALL INTESTINE

	DUODENUM		JEJUNUM		ILEUM	
	No.	Per cent	No.	Per cent	No.	Per cent
'Crohn's carcinoma' (Present series)	1	4	7	28	17	68
Carcinoma of the small bowel *de novo* (Rocklin and Longmire (1961)	113	37	108	34	98	29

Table VI.—REPORTED INCIDENCE OF 'CROHN'S CARCINOMA' OF THE SMALL INTESTINE

Author and Centre	*Reported Incidence*
Sheil, Clark, and Goligher (1968). Leeds General Infirmary	1 : 240
Crohn and Yarmis (1966). Mount Sinai Hospital	1 : 676
Present series (1973). London Hospital	1 : 146
Average	1 : 354 (0·3 per cent)
Estimated chance incidence	$1 : 10^9$

Incidence.—The incidence of adenocarcinoma of the small intestine may be estimated from two sources (Ackerman and del Regato, 1962; Haffner and Semb, 1969). A comparable figure of approximately 0·3 per 100,000 population per year is obtained from both sources after correction for survival rates and intercurrent deaths. The prevalence of Crohn's disease at all sites is 9 per 100,000 (Evans and Acheson, 1965). The chance of the diseases occurring together is therefore more than 1 in a thousand million. The chance is smaller still if allowance is made for both diseases affecting the same segment of intestine. *Table VI* shows the observed incidence in various reported series and the average for these is 0·3 per cent.

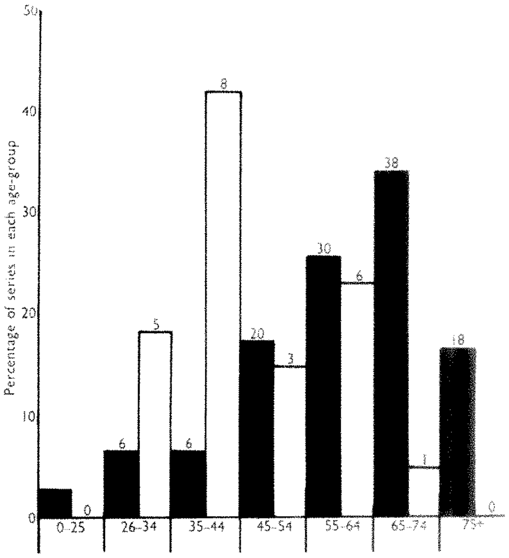

FIG. 5.—Age distribution of patients with 'Crohn's carcinoma' (white) compared with that for patients with carcinoma *de novo* (black) of the small intestine. Figures at the top of each column are the actual number of cases in each age-group.

Large Intestine.—

Age Incidence.—The age at diagnosis of 'Crohn's carcinoma' of the large bowel was compared with a series of 1171 cases of carcinoma of the large bowel occurring *de novo* (Goligher, 1941). There was no statistical difference.

Duration of Symptoms.—The duration of symptoms at the time of diagnosis fell into two groups. Nine patients had a history of under 1 year and an average age of 59 years. Five patients had a much longer history, averaging 18 years, but in spite of this their average age was only 44.

Distribution through the Intestine.—The anatomical distribution of 'Crohn's carcinoma' in the colon is shown in *Table VII* and compared with a large series of cases of carcinoma *de novo* from Leeds (Smiddy and Goligher, 1957). There is a statistically significant difference in the distribution ($P < 0{\cdot}01$), carcinoma *de novo* occurring mainly distally and 'Crohn's carcinoma' more proximally. The sex incidence in these two groups is comparable.

Incidence.—The prevalence of large intestinal Crohn's disease, including the caecum, can be estimated from the fact that the large intestine is involved to some extent in 55 per cent of cases of Crohn's disease (Avery Jones, Gummer, and Lennard Jones, 1968). The prevalence is therefore 6 per 100,000 population (Evans and Acheson, 1965). The average age of the present series of 'Crohn's carcinoma' is 53 years. For a population of this age the death-rate from carcinoma of the colon and rectum is 36 per 100,000 (Registrar General, 1969). However, the corrected 5-year survival is 42 per cent (Cutler and Lourie, 1964), suggesting an incidence of approximately 60 per 100,000. An estimate of a chance association is therefore greater than 1 in ten million. The chances of the two diseases occurring at the same site is smaller still. In the present series there are 2 cases of large intestinal carcinomas anatomically discrete from a coexistent segment of Crohn's disease. Two similar cases are reported in the literature (Davis and Caley, 1960; Hawk and Turnbull, 1966). *Table VIII* shows the observed incidence in various reported series and the average of these is 1·8 per cent.

Table VII.—RELATIVE ANATOMICAL DISTRIBUTION THROUGH THE BOWEL OF 'CROHN'S CARCINOMA' AND CARCINOMA *de novo* OF THE LARGE INTESTINE

SITE OF DISEASE	CARCINOMA *de novo* (Smiddy and Goligher, 1957)		'CROHN'S CARCINOMA'	
	No. of Cases	Per cent	No. of Cases	Per cent
Rectum	944	57	6	30
Sigmoid	350	22	3	15
Caecum and ascending colon	149	9	7	35
Transverse colon	77	5	4	20
Hepatic	29	1·5	—	—
Splenic	50	3	—	—
Descending colon	45	3	—	—
Total	1644		20	

Table VIII.—REPORTED INCIDENCE OF 'CROHN'S CARCINOMA' OF THE LARGE INTESTINE

Author and Centre	*Incidence*
Van Patter, Bargen, Dockerty, Feldman, Mayo, and Waugh (1954). Mayo Clinic	1 : 22
Crohn and Yarmis (1966). Mount Sinai Hospital	2 : 291
Atwell, Duthie, and Goligher (1965). Leeds General Infirmary	3 : 106
Perrett, Truelove, and Massarella (1968). Oxford	3 : 82
Hywel Jones (1969). St. Marks Hospital	2 : 189
Present series (1973). London Hospital	2 : 69
Average	1 : 58 or 1·8 per cent
Estimated chance incidence	1 : 10^7

DISCUSSION

The evidence that Crohn's disease predisposes to carcinoma is based on three points:—

1. The age of the patient at the time of diagnosis of 'Crohn's carcinoma' compared with that for carcinoma *de novo*.
2. A comparison of the anatomical distribution between these two groups.
3. A comparison of the estimated chance incidence and observed incidence.

'Crohn's carcinoma' of the small intestine occurs in a younger age-group and more frequently in the ileum than carcinoma *de novo*. These two findings are statistically significant. That this age difference and distribution simply reflect the group sampled is unlikely. A comparable incidence of other small-bowel malignant tumours would be expected, but only 3 cases have been reported—a lymphosarcoma in this series and 2 cases of reticulum-cell sarcoma (Hughes, 1955; Wyburn-Mason, 1968). There is also a sparsity of tumours in other sites; in this series only 6 other malignant conditions were found, and in a series from King's College Hospital, London, there were 6 cases out of 302, none of which was in the bowel (Murray, 1968).

For the large intestine a statistically significant difference has been shown between the anatomical distribution of 'Crohn's carcinoma' and carcinoma *de novo*. Again this may simply reflect the group sampled. However, although carcinoma of the large intestine is common, only 4 cases of coexistence with Crohn's disease have been reported (*vide supra*).

No difference in age in the two groups exists for the large intestine, but large intestinal Crohn's disease tends to occur later in life and requires surgical treatment at an earlier stage (Cornes and Stetcher, 1961). It is interesting to note, however, that the 'Crohn's carcinomas' in the large intestine fall into two subgroups: one having a long history at a younger age, and the other a short history at an older age. A long history of inflammatory disease preceding the development of carcinoma, as found in ulcerative colitis, is suggestive of a predisposition. However, as in the small intestine, the figures relating to duration of symptoms are too small to reach statistical significance.

On considering the pathological features of Crohn's disease, it would seem unlikely to predispose to carcinoma. It is predominantly a submucosal disease involving short segments of intestine and, unlike ulcerative colitis, premalignant changes are not a feature (Dawson and Pryse-Davies, 1959; Morson and Pang, 1967; Lee, 1971). Steiger and Dudrick (1970) draw attention to Schuman's (1970) case, which is the seventh report of carcinoma occurring in a defunctioned loop of Crohn's disease, and Lennard Jones and Morson (1969) wondered if bacterial stasis might have a carcinogenic effect on the bowel. On the other hand, these might represent the conditions under which Crohn's disease could continue chronically active yet not actually precipitating further surgery. An individual predisposition to both diseases could be invoked, perhaps based on an immunological abnormality common to both diseases, and this would explain coexistent carcinomas.

It is important to have some assessment of the risk of malignant change in Crohn's disease. For ulcerative colitis the practical risk in an Oxford Survey was 3·5 per cent (Edwards and Truelove, 1964), but under certain circumstances it may reach 25 per cent (De Dombal, Watts, Watkinson, and Goligher, 1966). For Crohn's disease the observed risk of adenocarcinoma is 0·3 per cent for the small intestine and 1·8 per cent for the large intestiine. Although the risk is less for the small intestine, the evidence for a causal relationship, as previously described, is greater.

The development of carcinoma in the presence of Crohn's disease presents difficult problems in diagnosis and management. Both diseases frequently present with altered bowel habit, symptoms of obstruction, and anaemia. Preoperative diagnosis of the carcinoma is most unlikely in the small intestine, and improbable in the large intestine, except when within sigmoidoscopic or colonoscopic range (e.g., *Case* 2 in the present series). In the small intestine the carcinoma is most commonly found by the pathologist; of 14 cases operated for intestinal obstructions, in only 4 was the carcinoma itself causing the obstruction. The tumour had frequently spread, 14 out of the 18 small-intestine cases in which data are available having lymph-node metastases, and in a previously defunctioned loop the danger of spread before surgery is even greater.

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THE USE OF IMMUNIZED PIG LYMPH-NODE CELLS IN THE TREATMENT OF PATIENTS WITH ADVANCED MALIGNANT DISEASE

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SUMMARY

The treatment of 14 patients with advanced malignant disease by the infusion of pig lymph-node cells pre-immunized against the appropriate tumour is described.

Marked tumour necrosis was seen in 7 cases and 4 of the patients obtained definite clinical benefit.

It is suggested that the therapy may be of most value when used in conjunction with other forms of treatment.

MITCHISON (1954) demonstrated that it was possible to transfer immunity against a mouse lymphoma by injecting cells from the lymph-nodes draining an allogenic tumour transplant into a second mouse which was isogenic with the first. Subsequently Mitchison (1955) repeated this observation using a mouse sarcoma. He found that the optimal time for cell transfer was at 5–10 days after immunization against the tumour.

This evidence for the importance of cell-mediated immunity in resistance to tumour growth led Woodruff and Symes (1962) to treat A-strain mouse mammary carcinomata, transplanted subcutaneously to isogenic hosts, by sublethal whole-body irradiation and intravenous injection of CBA spleen or lymph-node cells from animals pre-immunized against the appropriate tumour. Marked tumour necrosis was produced, but apparently complete tumour destruction was invariably associated with the induction of fatal graft versus host (G v H) disease. However, it was subsequently found that marked tumour regression could be produced, without accompanying G v H disease, by treating intraperitoneal tumour transplants by intraperitoneal injection of immunized spleen cells. It was suggested that early intimate contact between lymphoid and tumour cells contributed to the selective anti-tumour effect.

Another means of focusing the attack of immunized immunologically competent cells on the tumour rather than on the host was suggested by the work of Symes (1967). He found that in splenectomized mice there was a positive correlation between tumour size and the degree of anti-tumour effect produced by a given number of immunized spleen cells.

At a clinical level Woodruff and Nolan (1963) treated 8 patients by intravenous or intraperitoneal injection of normal lymphoid cells from other patients and in every case they noted some evidence of tumour necrosis. Nadler and Moore (1965) cross-immunized pairs of patients against the tumour of the other and then transfused immunized lymphocytes in the opposite direction. Tumour regression was observed in 3 out of 14 patients.

The *in vivo* immunization of a patient against the tumour of another patient raises difficult ethical problems. Therefore in order to potentiate the anti-tumour effect Symes, Riddell, Immelman, and Terblanche (1968) and Symes, Immelman, Peacock, Riddell, and Rhys Davies (1970) investigated the use of mesenteric lymph-node cells, from pigs immunized by the implantation of multiple fragments from the appropriate tumour into the mesentery, in the treatment of 5 patients with advanced malignant disease. Four of these patients showed definite, though temporary, regression of the tumour which was most marked in 2 of the 3 cases where the pig cells were infused into the arterial blood-supply of the tumour.

The present paper describes further experience in the treatment of advanced malignant disease with immunized pig cells.

MATERIALS AND METHODS

Selection of Patients.—In all 14 cases treated the patient had symptoms due to incurable malignant disease. Furthermore, the patients had either not responded, or seemed unlikely to respond, to the other methods of therapy currently available.

Immunization of the Pigs.—In each case several pieces of the tumour to be treated (of approximately 3 ml. total volume) were obtained. Multiple fragments of viable tumour were then prepared (each about 0·1 ml.) and implanted singly into separate pockets made in the small-bowel mesentery of the pig. Where the tumour had been obtained from a site liable to be infected the pig was treated systemically with an appropriate antibiotic.

For the retreatment of 1 patient a bull calf was immunized in a similar manner.

Preparation of Lymph-node Cell Suspensions.—Aseptic precautions were used throughout. The hyperplastic lymph-node chain was removed *in toto* 7 days after the implantation of the appropriate tumour fragments. The capsule was removed from the nodes. They were then cut into small pieces with fine scissors and the pieces were further reduced to a cell suspension in Medium 199 (Wellcome) using a hand-operated glass-piston blender. The cells were strained by gravity through a stainless-steel mesh of reducing pore size (30, 100, and 200 mesh). Finally, the cell suspension was centrifuged in an M.R.C. blood-transfusion bottle at 580 *g* for 5 minutes and resuspended in 100 ml. of fresh Medium 199. Total and in some cases 'viable' (using 0·165 per cent trypan blue exclusion) cell counts were performed on the cell suspension. The percentage cell viability in *Cases* 6, 7, 8, 10, 11, 12, 13, and 14 was 78, 86, 76, 87, 60, 56, 87, and 91 per cent respectively. The viability of the bull-calf lymph-node suspension used in *Case* 11 was 69 per cent.

Administration of Pig Lymph-node Cells.—In order to minimize the risk of a hypersensitivity reaction to pig protein each patient received 25 mg. of Phenergan i.m. 30 minutes before cell infusion, which was carried out over a period of 15 minutes under general anaesthesia. Two patients (*Cases* 4 and 10) experienced mild reactions (*see* Symes and others, 1970, and the Results for details). Otherwise the infusion of cells was uneventful.

RESULTS

A synopsis of the 14 patients treated is presented in *Table I*.

Table I.—Synopsis of Patients with Advanced Malignant Disease treated by Infusion of Pig Lymph-node Cells immunized against the Appropriate Tumour

Case No.	Age and Sex	Diagnosis	Treatment given	Survival after Treatment (d.)
1*	40 M.	Malignant melanoma	Day −7: Splenectomy Day −2: Melphalan, 30 mg. i.v. Day 0: Pig cells, 3·5 × 10⁹ i.v.	15
2	43 F.	Malignant melanoma	Day −7: Splenectomy Day −2: Melphalan, 30 mg. i.v. Day 0: Pig cells, 7·86 × 10⁹ i.v. Day 12: Autoplastic stored spleen cells, 2 × 10⁹ i.v.	56
3*	64 F.	Adenocarcinoma of ovary with hepatic secondaries	Day −2: Melphalan, 18 mg. i.v. Day 0: Pig cells, 6·50 × 10⁹ via aorta	12
4†	40 M.	Adenocarcinoma of colon with hepatic secondaries	Day 0: Pig cells, 12·4 × 10⁹ via hepatic artery	151
5‡	56 F.	Adenocarcinoma of pancreas with hepatic secondaries	Day 0: Pig cells, 22·4 × 10⁹ via coeliac axis	63
6	48 M.	Adenocarcinoma of bladder with hepatic secondaries	Day 0: Pig cells, 5·2 × 10⁹ via hepatic artery	1
7†	49 M.	Adenocarcinoma of rectum	Day 0: Pig cells, 4·6 × 10⁹ via internal artery	42
8	51 M.	Adenocarcinoma of colon with hepatic secondaries	Day 0: Pig cells, 5·06 × 10⁹ via hepatic artery Day 22: 5-F.U. via hepatic artery	35
9*	58 F.	Adenocarcinoma of colon with hepatic secondaries	Day 0: Pig cells, 8·75 × 10⁹ via hepatic artery	5
10‡	62 F.	Adenocarcinoma of breast with multiple metastases	Day 0: Pig cells, 1·67 × 10⁹ i.v.	32
11†	62 M.	Transitional-cell carcinoma of bladder	Day 0: Pig cells, 2·5 × 10⁹ via aorta Day 181: Bull-calf cells, 7·52 × 10⁹ via aorta	322
12‡	64 M.	Adenocarcinoma of bladder	Day 0: Pig cells, 5·75 × 10⁹ via aorta Day 30: Total cystectomy	52
13†	74 M.	Transitional-cell carcinoma of bladder	Day 0: Pig cells, 4·80 × 10⁹ via aorta	100
14‡	62 M.	Adenocarcinoma of bladder	Day 0: Pig cells, 5·05 × 10⁹ via aorta	86

* Patients showing massive tumour necrosis which may have contributed to early death.
† These patients obtained definite clinical benefit.
‡ No evidence of tumour regression was seen.

The patients may be divided into three groups according to the outcome of treatment:—

1. Cases in which definite clinical benefit was obtained (*Cases* 4, 7, 11, and 13).
2. Patients showing massive tumour necrosis in which clinical and pathological evidence suggested that this had occurred following treatment and which probably contributed to early death (*Cases* 1, 3, and 9).
3. Patients in whom there was no evidence of tumour regression, as judged clinically and pathologically (*Cases* 5, 10, 12, and 14).

In 3 patients (*Case* 6, who died on the day following treatment, and *Cases* 2 and 8) it was not possible to evaluate the outcome. Autopsy on *Case* 6 suggested that death was due to tumour progression and was not related to the injection of foreign cells.

Illustrative cases in each group are presented below.

CASE REPORTS

Group 1.—

Case 4.—This patient has been reported previously (Symes and others, 1970) and therefore will be mentioned in outline only. He presented with a carcinoma of the sigmoid colon and hepatic enlargement due to secondary tumour deposits. Following excision of the primary tumour, part of which was used to immunize the pig, the lymphocytes were infused over a period of 30 minutes into a catheter placed in the hepatic artery. During the next 70 days the patient's general condition improved, his liver decreased markedly in size as shown by clinical examination and a technetium scan (*see* Symes and others, 1970), and he returned for a time to light activity. By day 110, however, tumour growth had recommenced and was associated with inferior vena caval obstruction. He died on day 151 and at autopsy large areas of the hepatic secondaries were found to be calcified.

Case 7.—This man had an inoperable carcinoma of the rectum which had not responded to radiotherapy. Tumour tissue for the immunization of the pig was obtained through a proctoscope. On day 13 following cell infusion, examination under anaesthesia was carried out independently by two surgeons, who both reported the tumour to be approximately half its pretreatment size. At this time it was felt that the tumour was on the borderline of being resectable and the patient was therefore discharged in the hope that some further regression would permit surgical excision. The patient was reported to be well for the next 6 weeks, during which time he took a holiday. However, when he was re-examined on day 53 the tumour showed evidence of massive regrowth. It was now filling the pelvis and a fistula was present opening on to the anterior abdominal wall. The patient died on day 67.

Case 11.—This patient had a 9-month history of transitional-cell carcinoma of the bladder, which had failed to respond to a course of radiotherapy given 4 months previously.

Cytoscopy in April, 1971, showed a large tumour occupying the left wall of the bladder, and rectal examination revealed a left-sided pelvic mass fixed to the pelvic wall. At this time an intravenous pyelogram (*Fig.* 1) confirmed the presence of a filling defect in the left half of the bladder and showed a non-functioning left kidney.

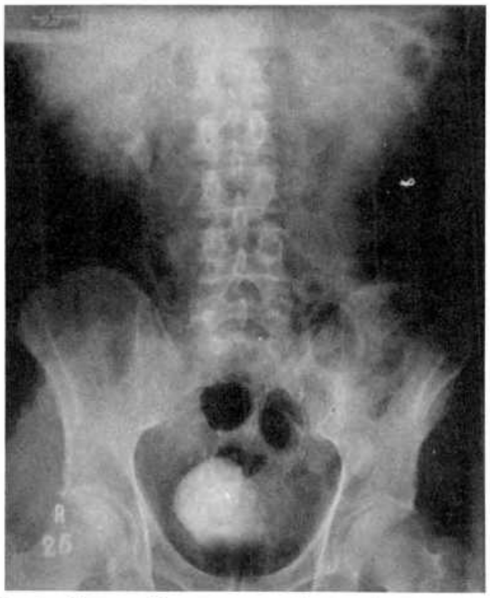

FIG. 1.—*Case* 11. Pretreatment pyelogram, showing a large filling defect in the bladder and a non-functioning left kidney.

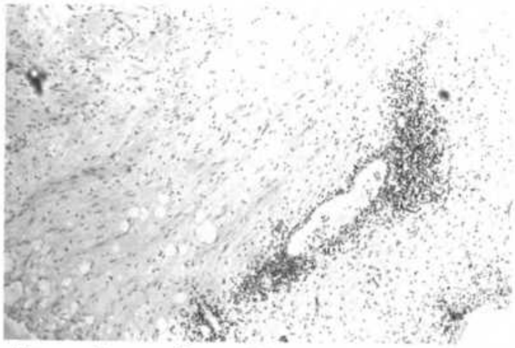

FIG. 3.—*Case* 11. Tumour biopsy 14 days after treatment. There is extensive tumour necrosis and marked lymphocytic infiltration. H. and E. (× 35.)

On day 14 after the infusion of pig cells a biopsy of the tumour showed marked necrosis and lymphoid-cell infiltration (*Figs.* 2 and 3), whilst no filling defect in the bladder was seen on the intravenous pyelogram. The pelvic mass was also smaller. At cystoscopy on day 48 the tumour appeared as a flat ulcer and radiological evidence of left kidney function was obtained (*Fig.* 4). On day 83 a small recurrence of the tumour in the bladder was resected; otherwise the patient remained well.

However, by day 154 there had been a massive recurrence of the tumour and this was treated by a second infusion of immunized lymphocytes obtained from a bull calf to avoid the risk of sensitivity to pig antigens. There was again evidence of marked tumour necrosis following therapy at cystoscopy on day 195. Following this the patient remained well until the end of 1971, but thereafter his condition deteriorated and he died on day 322.

At autopsy the primary tumour was seen to be almost totally necrotic, but there was evidence of massive recent involvement of the liver by secondary tumour.

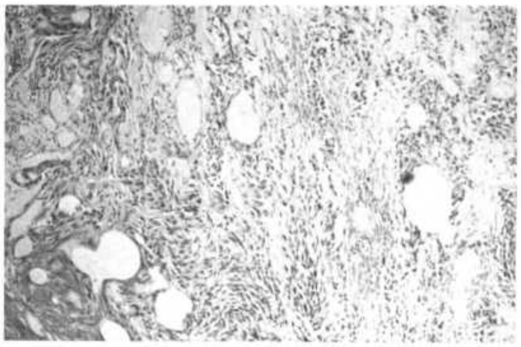

FIG. 2.—*Case* 11. Pretreatment biopsy of the transitional-cell carcinoma of the bladder. H. and E. (× 35.)

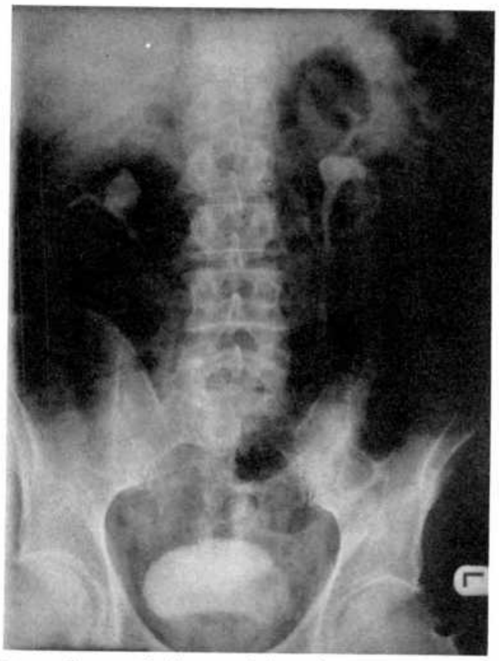

FIG. 4.—*Case* 11. Pyelogram 48 days after treatment, showing return of left kidney function.

Case 13.—This man presented in August, 1969, with haematuria due to an invasive transitional-cell carcinoma of the bladder. Radiotherapy given between October, 1969, and May, 1970, was associated with regression of the tumour. However, haematuria recurred in October, 1970, and the tumour grew steadily for the next 15 months.

At cystoscopy in January, 1972, the patient had a large left-sided bladder tumour and there was also a hard extravesicular mass fixed to the left pelvic wall. An intravenous pyelogram showed a non-functioning left kidney. On day 14 following the infusion of pig lymphocytes cystoscopy revealed massive haemorrhagic tumour necrosis which was confirmed histologically. The patient has remained well since, being active at a home, and has had only a single episode of haematuria. Cystoscopy on day 84 showed oedematous necrotic tumour on the left bladder wall (confirmed histologically) and pelvic examination at that time revealed some thickening on the left pelvic wall but no mass.

GROUP 2.—

Case 9.—This woman had a carcinoma of the sigmoid colon removed by anterior resection in June, 1969. In October, 1970, she was readmitted with liver secondaries. At laparotomy the diagnosis was confirmed and a catheter was inserted into the hepatic artery. A portion of the tumour was removed from the liver and used to immunize a pig. Histology confirmed that the tumour in this biopsy was a viable mucus-secreting adenocarcinoma.

On day 2 following the infusion of immunized lymphocytes into the hepatic artery the patient developed abdominal distension and marked ankle oedema. On day 5 the patient inhaled vomit and died, following the onset of rapidly progressive weakness. At autopsy the liver, which weighed 3480 g., was found to contain multiple deposits of tumour most of which had a necrotic appearance and some of which were surrounded by areas of hyperaemia. Histology confirmed the presence of large areas of tumour necrosis.

Cases 1 *and* 3.—These patients have previously been reported (Symes and others, 1970). Seven days before the infusion of pig lymphocytes both patients were subjected to splenectomy. They were given Melphalan intravenously 2 days before infusion as an immunosuppressant to promote the survival of the pig cells. Over approximately the next fortnight both patients showed massive tumour necrosis. In *Case* 1 this affected multiple subcutaneous melanoma deposits, some of which became cystic. In *Case* 3 the pelvic mass comprising the primary ovarian tumour and the liver, colonic, lung, and subcutaneous secondaries became almost totally necrotic. Both patients died at the height of this necrosis.

GROUP 3—

Case 10.—This woman presented with an 18-year history of carcinoma of the breast. Previous treatment had been radical mastectomy, radiotherapy, and hyposectomy.

In February, 1971, she was admitted with multiple subcutaneous tumour deposits, one of which was excised to immunize the pig. A total of 88 ml. of a suspension containing immunized pig cells was infused intravenously over a period of 15 minutes. At the end of the infusion the patient appeared flushed and complained of headache, which reaction began to subside after 10 minutes.

Following treatment there was no detectable regression in the tumour deposits and she died on day 32 from progression of her disease. Autopsy confirmed that there was no abnormal tumour necrosis.

DISCUSSION

It has been widely contended that to attempt immunotherapy for advanced malignant disease is probably a waste of time (*see* Alexander, 1970, for example). This is certainly true where the object of the therapy is to increase the patient's resistance to his tumour. However, in the present study an attempt has been made to 'import' an immunological response, induced in a pig, by the adoptive transfer of lymph-node cells. In theory the lymph-node cells may attack the patient (graft versus host, G v H) or the tumour (graft versus tumour, G v T) or both. The problem is to obtain the maximum G v T and the minimum G v H effects. We have sought to do this by administering pig lymphocytes into the arterial blood-supply of the tumour, thus facilitating contact between the lymphocytes and the tumour cells. In addition, the magnitude of the immunological response by the pig cells to a particular antigen may depend on the amount of the antigen present. Thus, the presence of a large tumour may accentuate the G v T effect and protect the patient from G v H reaction. Experimental evidence to support this idea has been provided by Symes (1967).

An alternative approach to eliminating the G v H effect would be to extract nucleic acids from the immunized pig cells and to administer these to the patient (Alexander, Delorme, Hamilton, and Hall, 1967). However, this method depends on there being tumour-specific antigens present against which the foreign lymphocytes could be specifically immunized. Such a condition may not obtain in advanced tumours.

From the present series of patients there would seem to be satisfactory evidence that the infusion of immune pig lymphocytes can result in tumour necrosis. This was observed in a number of different tumour types. By contrast in no case was there any evidence that tumour growth was enhanced.

The importance of direct lymphocyte–tumour-cell contact is emphasized by the superior results from intra-arterial as compared with intravenous infusion of pig cells (*Table I*).

The administration of an immunosuppressant before infusing the pig cells resulted in massive necrosis and early death in 2 cases (*Cases* 1 and 3) of the 3 so treated and the practice was therefore discontinued.

An important but perhaps obvious conclusion is that the greatest benefit to the patient is likely to result from the treatment of a tumour at a site where extensive necrosis will not produce a catastrophic effect on body function, for example, *Cases* 7, 11, and 13.

Owing to the presence of one or more clones of resistant tumour cells (*see*, for example, *Cases* 7 and 11) it is probable that this therapy will not in itself ever prove curative except in a tiny percentage of cases. Its place is, therefore, as an adjunct to other types of treatment. For example, following the infusion of pig cells an inoperable tumour may for a short time become resectable (*Case* 7). Also the possibility of giving radiotherapy or a cytotoxic drug after cell infusion might be considered. In *Case* 14 the tumour showed increased vascularity and lymphoid infiltration in spite of its high viability. This patient is therefore to receive radiotherapy.

Acknowledgements.—We should like to thank Miss Teresa Lai and Dr. Jennifer Rees for their assistance in this project. We are grateful to Mr. D. C. Bodenham, Dr. H. Eckert, Mr. R. C. L. Feneley, and Professor J. H. Peacock for referring cases to us.

The advice of Mr. G. W. Sweetnam and his staff in matters of animal welfare is gratefully acknowledged.

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THE EFFECT OF INNERVATION, DENERVATION, AND MUSCLE TYPE ON THE REUNION OF SKELETAL MUSCLE

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SUMMARY

The left plantaris and soleus and the right and left sternohyoid muscles of rats were transected surgically and cross-repaired to form conjoined muscle bellies composed of two innervated muscles, two denervated muscles, and one denervated and one innervated muscle.

Subsequent maceration of the conjoined muscle belly showed that regeneration had taken place by inoculation of the growing tips of the regenerating fibres in the doubly denervated muscle belly and in the innervated–denervated muscle belly but not in the case of the doubly innervated muscle belly.

Muscle type was not found to influence this process.

The significance of these findings is discussed.

THE ability of mammalian skeletal muscle to recover following damage has been known since 1865 (Waldeyer, 1865). A variety of techniques have been used to induce damage including chemical toxins (Walton and Adams, 1956), ischaemia (Clark, 1946), direct percussion (Allbrook, Baker, and Kirkaldy-Willis, 1966), crush lesions (Clark, 1946; Saunders and Sissons, 1953; Hall-Craggs, 1971), and surgical division of muscle bellies (Clark, 1946; Jones, 1949; Gay and Hunt, 1954). Saunders and Sissons (1953) and Hall-Craggs (1971) examined the effect of denervation on the process of regeneration. In both these studies damage was induced by crushing the muscle bellies transversely between the blades of a haemostat.

Surgical exposures, however, often involve the complete division of muscle bellies at right-angles to the direction of the fibres. This procedure thus isolates a portion of the muscle from its parent innervated muscle belly. The fate of the isolated portion following such a procedure is of interest surgically. The present study was undertaken (1) to confirm previous reports of end-to-end anastomosis of severed muscle-fibres (Gay and Hunt, 1954) and to explore its nature; (2) to examine the effects of innervation and denervation on this process (Saunders and Sissons 1953, Hall-Craggs, 1971), and (3) to find out whether the processes of repair are comparable when reunion is attempted between muscles of different physiological types.

METHODS

Surgical Procedures.—Wistar rats of both sexes weighing between 150 and 275 g. were used. Two series of operations were performed under general anaesthesia, which was induced and maintained by 4 per cent chloral hydrate (1 ml. per 100 g) introduced intraperitoneally. A prophylactic dose of 0·3 ml. of Intramycetin was administered intramuscularly to each rat postoperatively.

In the first series of operations a vertical dorsal incision was made between the bellies of the left gastrocnemius exposing the plantaris and soleus. The proximal half of the soleus and the distal half of the plantaris were excised and the cut surfaces of the remaining muscle bellies were then joined with three 000000 silk sutures.

Of the 18 rats which were subjected to this procedure, both the plantaris and soleus were denervated in 6 by the removal of a 1·5-cm. segment of the tibial nerve. In a further 6 animals the soleus alone was denervated by the division of its motor nerve, which was then buried in the lateral head of the gastrocnemius. In the final 6 rats the nerve-supply of both the soleus and plantaris was preserved.

In the second series of operations a vertical median incision was made in the neck to expose the sternohyoid muscles. The muscle bellies were divided surgically; on the right just caudal to the superior motor end-plate. The cranial portion of the right muscle and the caudal portion of the left were then cross-repaired. The remaining muscle on the right was allowed to retract into the neck and that on the left was excised. Eighteen rats were subjected to this procedure. In 6 rats both the right and left sternohyoid muscles were denervated by division of the superior motor nerve at its point of entry into the muscle belly. The nerve was then buried in the subjacent omohyoid to prevent reinnervation. In 6 rats the right muscle alone was denervated, and in the final 6 rats the nerve-supply of both the right and left sternohyoid muscles was retained.

The conjoined muscle bellies of both series of operations were removed and examined after 3 weeks by maceration, histochemical, and histological techniques. For each technique 12 rats were used (2 from each of the three groups of the two series).

Maceration.—The muscle bellies were fixed in 10 per cent formol–saline and macerated in 20 per cent nitric acid at room temperature for up to 56 hours. Individual fibres or bundles of fibres were then teased out under a dissecting microscope, mounted in glycerin, and examined using phase microscopy. This technique represents a modification of that used by Gay and Hunt (1954).

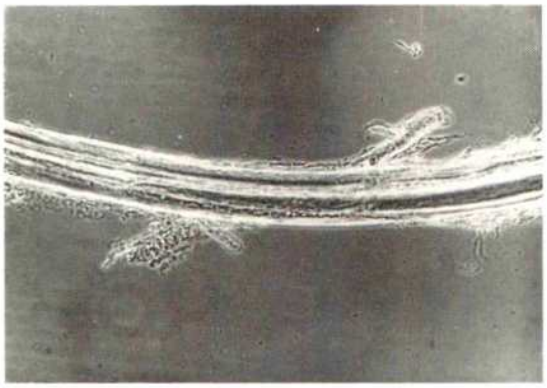

FIG. 1.—Junctional zone of three macerated fibres from a conjoined muscle belly composed of innervated plantaris and denervated soleus. (× 60.)

Histochemistry.—The excised muscle bellies were plunged into *n*-hexane cooled to -70° C. by a mixture of solid CO_2 in acetone. Blocks were prepared of the experimental muscle and of the control muscle from the contralateral leg in the first series and the adjacent sternomastoid in the second. Transverse sections were cut at 10 μm. at sites away from the site of reunion and stained for diphosphopyridine nucleotide-tetrazolium reductase (DPNH-TR) (Engel and Brooke, 1966).

Histology.—The muscle bellies were fixed in 10 per cent formol-saline and embedded in paraffin wax. Longitudinal sections were cut at 15 μm. and stained using Weigert's hematoxylin and Van Geison's picric acid.

RESULTS

In both series the conjoined muscle bellies appeared to have joined when examined macroscopically after 3 weeks. After maceration a variable number of fibre bundles could be followed across the join.

It was observed that when the conjoined muscle belly was composed of two denervated muscles or of an innervated and a denervated muscle the majority of fibre bundles could be so traced. Individual fibres were teased from a bundle and mounted on a slide so that the observed junctional zone was opposite a diamond scratch mark on the surface of the slide. Under the phase microscope the junctional zone (*Fig.* 1) was seen to be composed of mature fibre which was practically indistinguishable from the fibre away from the join. However, some of the fibres ended by bifurcating into one or two collateral 'buds' (*Fig.* 2) which appeared to join with similar buds from the other side of the join. Longitudinal splitting (Hall-Craggs, 1970) was observed in several of the mounted fibres.

When the conjoined muscle belly was composed of two innervated muscles only a few individual fibres could be traced across the join. The majority ended by dividing into several collaterals which were long and thin and which interwove in a complex manner with similar buds from the other side (*Fig.* 3). It was not possible to identify with certainty the anastomosis of fibres.

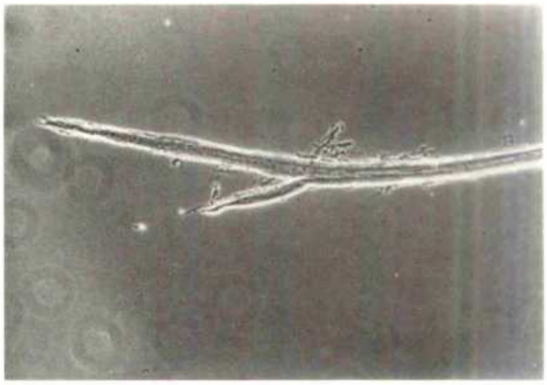

FIG. 2.—Isolated end of an innervated sternohyoid muscle-fibre macerated from a doubly innervated conjoined muscle belly, showing a collateral sprout. (× 60.)

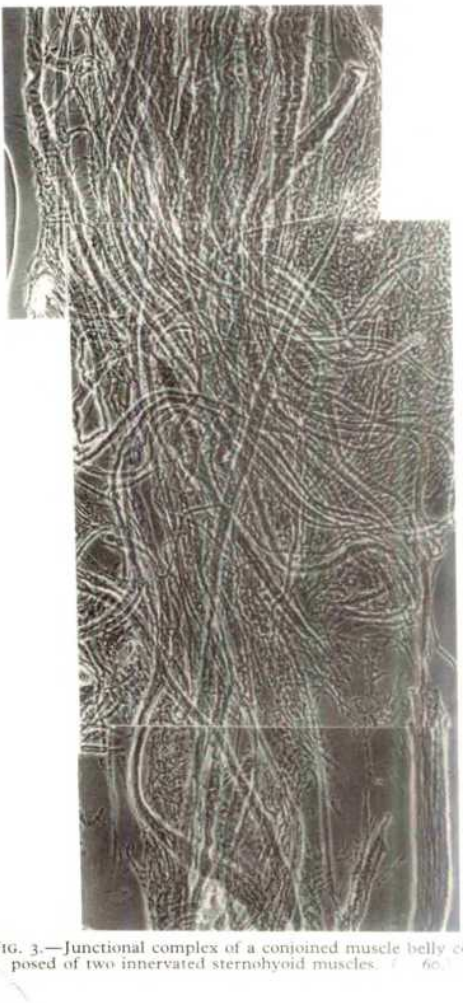

FIG. 3.—Junctional complex of a conjoined muscle belly composed of two innervated sternohyoid muscles. (× 60.)

Longitudinal sections revealed a variable amount of connective tissue. More was present in the doubly innervated muscle belly. Transverse sections cut cranial and caudal to the join were examined to check the effectiveness of the denervation procedure and the completeness of innervation. Sections cut through a denervated muscle belly showed almost uniformly decreased fibre diameter and enzyme staining. Sections through the innervated muscle bellies showed occasional areas of decreased fibre diameter, indicating that some fibres had been denervated during the operative procedure.

DISCUSSION

Regeneration of striated muscle through or across a region of damage has been investigated by several authors. One of the difficulties of interpretation of the findings has been the non-uniformity of the damage produced. Saunders and Sissons (1953) claimed complete destruction of the muscle-fibres but stated that the degree of damage to the sarcolemmal tubes was not the same in all parts of the crushed areas. In some areas the tubes remained more or less intact while in others they were completely destroyed. For this reason it was decided to transect the muscle bellies surgically. The plantaris and soleus and the right and left sternohyoids were chosen for the experiment because in both situations the muscles are of similar size, adjacent to each other, and have an accessible motor nerve, thus facilitating the approximation of the transected muscle bellies and allowing denervation to be achieved readily. The plantaris and soleus are physiologically fast and slow muscles respectively while the sternohyoid is a fast muscle.

The present study confirms the earlier reports that regeneration of striated muscle across a surgical division is possible and not interfered with by simultaneous denervation. Individual fibres of two conjoined denervated muscles and conjoined innervated and denervated muscles were traced from one side through the junctional zone to the other side and in some cases individual fibres were traced from tendon to tendon of the conjoined muscle belly. Collateral buds at the tips of regenerating fibres from both denervated and innervated muscle were seen. Clark (1946) claimed that regenerating tips are capable of a growth maximum of 1–1·5 mm. per day, which raises the possibility that regeneration could take place by the growing buds replacing the isolated portion of the muscle by substitution down the existing sacrolemmal tubes in a manner reminiscent of peripheral nerve repair. However, in the present study growing tips were only seen at the junctional zone and arising from fibres on both sides of the join and on several occasions the growing tips of one muscle were seen in the process of anastomosing with those of the opposite muscle, when the conjoined muscle belly was composed of at least one denervated muscle, thus confirming the previous report (Gay and Hunt, 1954) that regeneration is achieved by the reunion of the damaged ends of the muscle-fibre.

There was a quantitative difference in the number of growing tips seen. When the conjoined muscle belly was composed of at least one denervated muscle the majority of fibre bundles were composed of mature fibres, only a few of the fibres ending in growing tips with collateral sprouts. When the muscle belly was composed of two innervated muscles the majority of the fibres on both sides of the join ended in growing tips interweaving with each other without making contact. The fact that they did interweave suggests that contraction of the muscle had not interfered with the possibility of contact. It is thought that the few fibres that did cross the join were regenerated fibres formed by union between an innervated fibre and a fibre denervated accidentally during operation.

It is suggested that the production of growing tips with collateral sprouts is a general response of the striated muscle-fibre to injury and that when the potential for anatomical union has been achieved by inosculation between the opposing growing tips, which occurs when at least one of the fibres is denervated, the sprouting of collaterals is inhibited. Thus, in the present series when innervated muscle was confronted by innervated muscle there was profuse sprouting of collaterals but anastomoses were not observed. Whether this is because contraction of muscle-fibres on both sides of the join was sufficiently disrupting to prevent the earlier delicate changes of union taking place or whether there was some more profound influence of the nerve is not yet understood. Hall-Craggs (1971), using rat sternohyoid muscle, demonstrated that the altered fibre pattern produced by crushing the motor nerve 3 weeks before crush transection of the muscle belly was in due course transferred to isolated fibres on their recovery. It seems, therefore, that innervated muscle will adopt an uncommitted portion of another muscle, whether of the same physiological type or not, and incorporate it into a functional unit under the control of one motor nerve, but that when two functional units are confronted the processes of regeneration are impeded and continuity of the muscle belly is restored by the fibrous tissue repair.

Acknowledgements.—My thanks are due to Dr. E. C. B. Hall-Craggs for his constant help and advice with all stages of the experiment, to Mr. J. Sheppard for the preparation of histological material, and to Mr. D. Gunn for the photographic work.

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THE ARTERIAL COMPLICATIONS OF POLYCYTHAEMIA VERA

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SUMMARY

Of 200 patients referred for management of polycythaemia vera, 98 (49 per cent) had presented with vascular complications and 68 (34 per cent) of these involved arteries. Transient but recurrent cerebrovascular accidents and digital artery occlusions were the typical arterial complications. If polycythaemia was not promptly treated there was a risk of permanent hemiplegia, monocular blindness, and severe ischaemia of the leg.

Embolism may have accounted for some of the arterial complications. A possible source for emboli —a proximal mural thrombus—was demonstrated in all 5 patients who were examined with femoral arteriography and in 2 patients who underwent surgery. In selected cases thrombectomy may be indicated to prevent further embolism.

In 1903 William Osler first drew attention to the vascular complications of polycythaemia. Brown and Giffin in 1930 and Norman and Allen in 1937 reported a total of 198 patients with polycythaemia from the Mayo Clinic, a third of whom had vascular complications. In 250 autopsies of patients dying with polycythaemia Chievitz and Thiede (1962) found vascular catastrophes to be the commonest cause of death.

In the present paper the vascular complications in 200 patients with polycythaemia vera are reported and the arteriographic and microscopic appearances of the arterial lesions in the limbs are described. Arterial embolism is suggested as a possible cause of some of the complications.

CASE MATERIAL

The case records of 200 in-patients of Hammersmith Hospital who were treated between the years 1952 and 1972 were studied. All were referred to the Radiotherapy Department of Hammersmith Hospital for the management of polycythaemia vera. The diagnosis of polycythaemia vera was made on the peripheral blood-picture and in doubtful cases confirmed by the estimation of the red-cell volume and bone-marrow puncture. All received radioactive phosphorus treatment.

VASCULAR COMPLICATIONS

Of the 200 patients, 98 (49 per cent) presented with vascular complications; these were arterial in 68 cases (34 per cent), venous in 57 (28 per cent), and both arterial and venous in 27 (13 per cent). In all, therefore, there were 144 different vascular complications in 98 patients (*Table I*).

Comparison between the 98 patients who presented with vascular complications and the 102 patients without such complications revealed no significant difference in age; the average age for the patients with complications was 61 years, while that for those without complications was 59 years. The sex distribution was also comparable in the two groups; the incidence of males in the group with complications was 60 per cent, while that in the group without complications was 56 per cent.

Table I.—Vascular Complications at the Time of Diagnosis of Polycythaemia Vera in 200 Cases

Type of Complication	No. of Patients Affected	
Cerebrovascular accident	39*	78 different arterial complications in 68 patients†
Coronary artery disease	10*	
Peripheral artery disease	25	
Monocular blindness	4	
Superficial thrombophlebitis	30	66 different venous complications in 57 patients†
Deep-vein thrombosis	25	
Pulmonary embolization	4*	
Portal-mesenteric thrombosis	5*	
Subclavian vein thrombosis	1	
Priapism	1	

* One fatal incidence occurred in each group.
† 27 patients had both arterial and venous complications.

Cerebrovascular Accidents. — Thirty-nine patients had cerebrovascular accidents; 9 of these were hypertensive, while the remainder had a diastolic blood-pressure of below 100 mm. Hg. Twenty-six of the 39 patients had suffered symptoms and signs consistent with temporary cerebral ischaemia, such as transient hemiplegia, facial weakness, or aphasia, lasting from half an hour up to 2 weeks, and in some cases recurring. Thirteen patients had permanent neurological loss, 6 of these having suffered one or more transient attacks before these permanent signs had developed. One patient died of a further cerebrovascular accident soon after admission and before treatment of the polycythaemia could be started.

Monocular Blindness.—Four patients had suffered attacks of transient blindness (amaurosis fugax). After several episodes 1 of these patients had become permanently blind in one eye because of retinal artery occlusion.

Coronary Artery Disease.—This was present in 10 patients.

Peripheral Artery Disease.—Twenty-five patients had symptoms of arterial disease affecting the limbs. In 15 of these the digital arteries only were involved, causing sudden ischaemia of a single finger or toe. By the time that the diagnosis of polycythaemia was confirmed, 10 patients had already undergone amputations of one or more digits. These local amputations healed well as the main arteries were patent and all the peripheral pulses were present (*Fig.* 1). Three further patients had had toes amputated in the past but presented with femoral artery occlusion, 2 of whom required a through-knee amputation. In the remaining 7 patients femoral artery occlusion occurred without preceding ischaemia of the toes. None of these required amputation or arterial surgery.

Mortality.—Four deaths—all the result of vascular complications—occurred during investigations and treatment, the cause of death being cerebrovascular accident in 1, myocardial infarction in 1, pulmonary embolism in 1, and mesenteric vein thrombosis in 1.

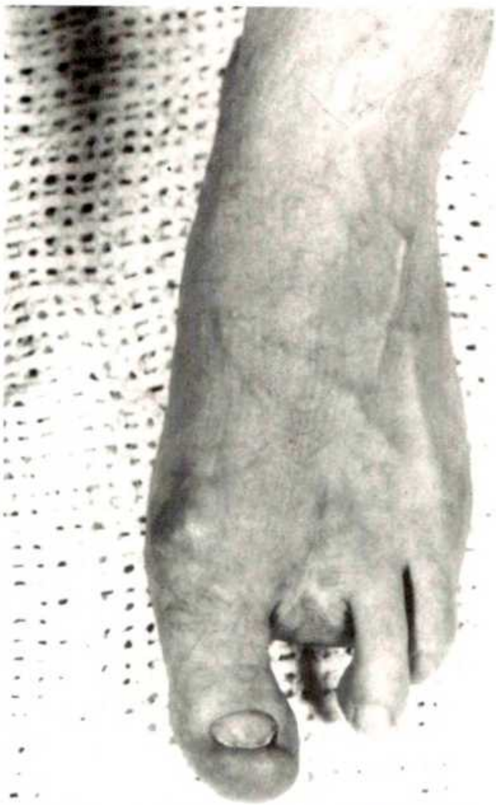

FIG. 1.—*Case* 2. Left foot with the second and third toes amputated.

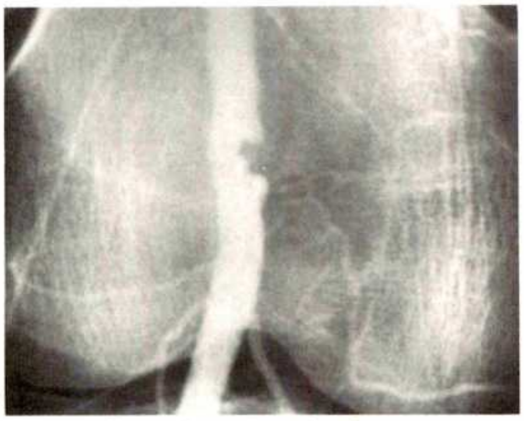

FIG. 3.—*Case* 2. Femoral arteriogram.

ARTERIOGRAPHIC FINDINGS

In 5 of the 15 patients with digital ischaemia but with palpable pulses at the ankle, femoral arteriograms were done. In all cases short localized segments of narrowing were found in the femoral or popliteal arteries. Apart from these narrowed segments, the main arteries appeared free from disease (*Figs.* 2, 3). The digital arteries were not sufficiently visualized on the radiographs for comment. Arterial surgery was carried out in 2 of the 5 patients who had had femoral arteriograms done and in both the narrowed segments were found to be due to mural thrombus.

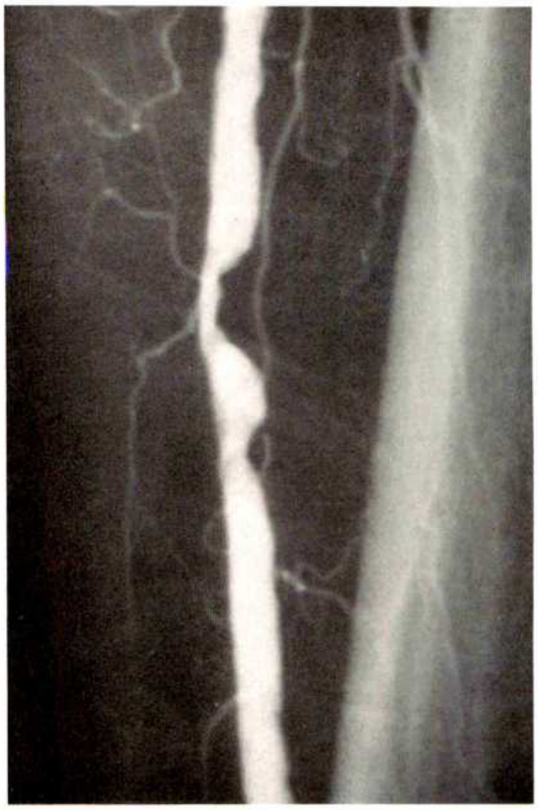

FIG. 2.—*Case* 1. Femoral arteriogram.

CASE REPORTS

Case 1.—A 66-year-old female was discovered to have polycythaemia when she presented with a painful ulcer on the sole of the left foot (*Fig.* 4). She also complained of tiredness, a burning sensation of her face and feet, and headaches.

On examination her face was flushed, and she had a palpable spleen and a blood-pressure of 180/80. All peripheral pulses, including those of left foot, were easily palpable. Blood investigations revealed the following: haemoglobin, 16·7 mg. per 100 ml. (114 per cent); packed-cell volume, 57·1 per cent; white-blood count, 11,000; platelets, 602,000 per c.mm. Her red-cell volume was 39 ml. per kg. and the bone-marrow showed generalized cellularity.

An intravenous pyelogram and other investigations were unremarkable. Two pints of blood were withdrawn and 5 m.c. of radioactive phosphorus were given intravenously. During the following 6 weeks her general health improved but she continued to complain of continuous pain in the left foot and developed ischaemia of the tip of the second and fourth toes. At this time her blood-count was normal: haemoglobin, 13·6 g. per 100 ml., platelets, 150,000 per c.mm. A femoral arteriogram showed no general arterial disease, but near the adductor opening there were two well-demonstrated narrowings (*Fig.* 2). On exploration these lesions proved to be focal mural thrombi with firm pale edges. The central portions had the appearance and consistency of red-currant jelly. Microscopy of the endarterectomy specimen (*Figs.* 5, 6) showed only a moderate amount of atheroma in the vessel wall. Much of the mural thrombus was organized. Seven well-defined elastic laminae indicated separate episodes of thrombosis. The central portion of the thrombus (*Fig.* 6) was recent and unorganized.

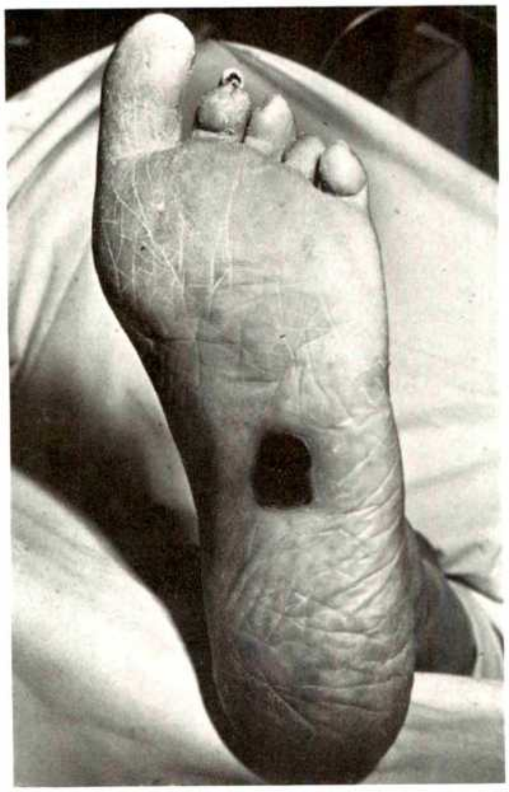

FIG. 4.—*Case* 1. Ischaemic ulcer on the sole of the foot. Note the loss of the tip of the second toe.

After discharge the patient developed no further vascular complications over a period of 2 years.

Case 2.—A 56-year-old male had had the second and then the third toe of his left foot amputated because of the sudden onset of ischaemia $2\frac{1}{2}$ years before the diagnosis of polycythaemia was made (*Fig.* 1). On these occasions his haemoglobin had been 16·1 and 16·5 g. per 100 ml., respectively, but no further investigation had been carried out at that time. Two years later after the sudden onset of left hemiplegia he was referred to the Hammersmith Hospital. Blood investigations on this occasion revealed the following: haemoglobin, 19 g. per 100 ml.; white-blood count, 12,000; platelets, 640,000 per c.mm. His blood-volume was increased and the bone-marrow was hypercellular but other investigations were unremarkable. Two pints of blood were withdrawn and radioactive phosphorus was given. His blood-count returned to normal, but while receiving intensive physiotherapy when he was making good recovery from his hemiplegia he complained of continuous pain in his left foot and was referred to the peripheral vascular clinic.

On examination the blood-pressure was 180/110 and all the peripheral pulses including those of the left foot were

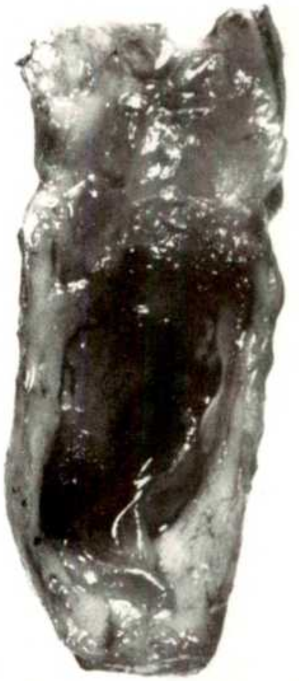

FIG. 5.—*Case* 1. Cross-section of the endarterectomy specimen. Note the multiple laminations of organized mural thrombus on the left, with an area of unorganized thrombus on the right.

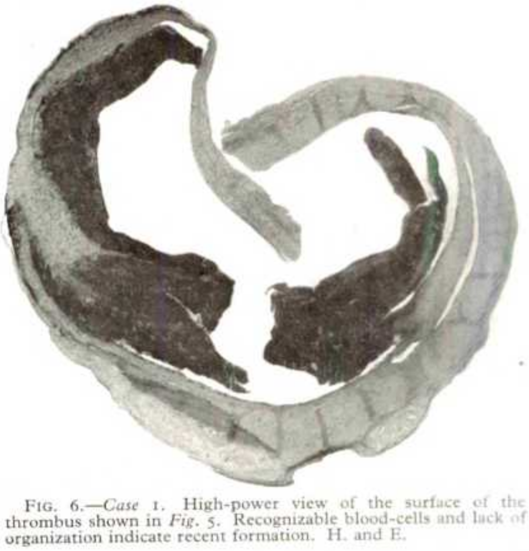

FIG. 6.—*Case* 1. High-power view of the surface of the thrombus shown in *Fig.* 5. Recognizable blood-cells and lack of organization indicate recent formation. H. and E.

palpable. The amputation sites of the second and third left toes were well healed, but the left big toe was cold and ischaemic. A left femoral arteriogram showed narrowing of the popliteal artery (*Fig.* 3). He was placed on the waiting list and admitted later for endarterectomy. By this time his haemoglobin had risen again to 16 g. per 100 ml. and platelets to 400,000 per c.mm. During surgery, therefore, blood-loss was not replaced, allowing a deficit of about 2 pints to occur. The arteries showed moderate atheroma and the narrowed segment proved to be due to focal, organized, laminated mural thrombus. On the third and twentieth days after surgery he had two haemorrhages from the site of the arteriotomies. There was no infection in the wound. At the time of the second haemorrhage the popliteal artery was found to be thrombosed and a Fogarty catheter was used to clear it. Foot pulses did not return but there was no clinical increase of the ischaemia in the foot for about a year, when severe claudication and rest pain developed and despite a further attempt to clear the popliteal artery a Gritti-Stokes amputation became necessary.

DISCUSSION

Untreated polycythaemia vera carries a high risk of intravascular thrombosis. Brown and Giffin (1930) and Norman and Allen (1937) reported an incidence of vascular thrombosis of about 30 per cent. In our 200 cases there was a higher rate of almost 50 per cent. This may be explained by the higher average age in the present series (60 years) as opposed to that in the two series reported above which was 52 and 57 years, respectively.

The initial vascular symptom may be relatively trivial: superficial thrombophlebitis, ischaemia of one toe or finger, minor and transient cerebral or visual disturbances. Nevertheless, the recognition of the underlying polycythaemia is important because, if left untreated, more severe complications may follow. This was shown in 13 patients with permanent hemiplegia about half of whom had suffered minor transient 'strokes'; also 2 patients who required amputation of the leg had had ischaemic toes amputated without diagnosis of the underlying polycythaemia, and 1 patient became blind in one eye after attacks of transient blindness.

The diagnosis of polycythaemia may be difficult on clinical signs, as not all patients have plethora, injected conjunctivae, and a palpable spleen. Also routine haemoglobin estimation may show only a relatively minor increase—no more than 17 g. per 100 ml.—which may be because in polycythaemia occult blood-loss sometimes occurs from the gastro-intestinal tract, and, paradoxically, may even lead to anaemia (Szur, 1971).

The treatment of polycythaemia vera, namely the suppression of bone-marrow with radioactive phosphorus (Szur, Lewis, and Goolden, 1959), may take up to 8 weeks to become fully effective. In a patient with vascular complications, therefore, urgent reduction of blood-volume and red-cell mass is important. Cranley, Fogarty, Krause, Strasser, and Hafner (1963) reported improvement in ischaemic symptoms in polycythaemia after phlebotomy. This improvement is only temporary so that elective, as opposed to emergency, surgery should always await long-term radio-isotope control. Wasserman and Gilbert (1963) found an increase in haemorrhagic and thrombotic complications in patients undergoing surgery with untreated, or insufficiently controlled, polycythaemia. Our experience with *Cases* 1 and 2 seems to support this conclusion as no complications occurred in *Case* 1 with well-controlled polycythaemia, but in *Case* 2, whose polycythaemia was insufficiently controlled, both bleeding and clotting complications occurred.

Although the diagnosis and treatment of polycythaemia are well established, the pathogenesis of its arterial complications is uncertain. The earliest hypothesis to explain arterial occlusions was put forward by Oppenheimer in 1929. He wrote: 'The great viscosity of blood causes increased wear and tear on the vessels, thus favouring the development of arteriosclerosis in much the same way as high blood-pressure does in hypertensive patients.' There is no pathological evidence to support Oppenheimer's hypothesis. Also we found the pattern of arterial involvement to be different from that in arteriosclerosis: in polycythaemia cerebrovascular accidents were four times (39 cases) more common than in coronary artery disease (10 cases), while in patients with arteriosclerosis the reverse is true (Taylor and Calo, 1962); in polycythaemia ischaemia of the toes and fingers commonly occurs before claudications (18 out of 25 cases), while in arteriosclerosis proximal artery occlusion usually precedes ischaemia of digits. In polycythaemia women and men are almost equally affected, while in arteriosclerosis males predominate (*Table II*).

Table II.—COMPARISON OF ARTERIAL COMPLICATIONS IN ARTERIOSCLEROSIS AND POLYCYTHAEMIA VERA

	POLYCYTHAEMIC ARTERIAL LESIONS*	ARTERIOSCLEROTIC ARTERIAL LESIONS†
Coronary artery disease : cerebrovascular accident	1 : 4	4 : 1
Distal peripheral artery disease : proximal peripheral artery disease	3 : 1	1 : 4
Sex ratio:— Male : female	3 : 2	9 : 1

* In the present 98 cases.
† In the 450 cases of Taylor and Calo (1962).

The sudden occlusion of small distal vessels in polycythaemia is generally thought to be due to local thrombosis (Millikan, Siekert, and Whisnant, 1960). We believe that at least in some, if not in all, embolism is the cause. First, in 18 of our patients sudden ischaemia occurred in a single digit, and although other digits of the same limb became ischaemic at later dates, in no case were several digits simultaneously involved. This episodic and asymmetrical course suggests embolism rather than local thrombosis. Secondly, in all 5 patients examined with arteriography a possible source of emboli—a proximal mural thrombus—was found. Thirdly, the surgical removal of the fragile thrombus of red-currant jelly texture prevented further distal ischaemia in *Case* 1.

In the lower limb, therefore, we believe that there is radiological and histological support for embolism being the cause of ischaemia. This evidence is not available as yet for patients with attacks of cerebral ischaemia. However, transient cerebral symptoms have been shown to be caused by micro-emboli in the non-polycythaemic patient (Pickering, 1964) and there may well be a similar mechanism in polycythaemia.

Embolism from mural thrombus would imply the possibility of prevention by thrombectomy. In cases where polycythaemia was well controlled this was successful, but in *Case* 2, who in retrospect would seem ill suited for surgery, it led to complications.

In conclusion, patients with distal arterial lesions should be examined for evidence of polycythaemia, and if this is found, for a possible source of emboli, but surgery should only be undertaken after full medical control of the underlying polycythaemia.

Acknowledgements.—We wish to thank Dr. L. Szur and Mr. Peter Martin for allowing us to study their patients and for their help in the preparation of this paper. We are also grateful to Mrs. Margaret Buttery of the Medical Records Department, Hammersmith Hospital, and to Mr. W. Hinks and Mr. A. M. Moreman for their help with the photography.

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HIGH BLOOD VISCOSITY: AN AETIOLOGICAL FACTOR IN VENOUS THROMBOSIS

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SUMMARY

This is a preliminary report on a prospective study of 52 general surgical and gynaecological patients designed to investigate a possible relationship between a high blood viscosity and the development of deep venous, thrombosis (D.V.T.). The blood viscosity of the patients was measured immediately before operation and the development of venous thrombosis was monitored with the radioactive fibrinogen technique. The 11 patients who developed a D.V.T. had a blood viscosity, prior to operation, 21 per cent higher than the patients who did not develop venous thrombosis. The difference was 29 per cent if correction was made for variation in the haematocrit. It was found that a general surgical patient, over 40 years of age, with a preoperative blood viscosity above 4·3 cP (corrected to a haematocrit of 45 per cent) will have a 73 per cent chance of developing a D.V.T. after operation.

VIRCHOW (1846) first described the relationship between pulmonary 'thrombi' and deep venous thrombosis (D.V.T.), and its importance has been appreciated, the thrombi now being termed 'emboli', and confirmed since then. The problem of pulmonary embolism and clinically silent thrombosis has been recognized for many years. Recently, with the introduction and widespread use of ^{125}I-labelled fibrinogen for the detection of D.V.T., it has been shown to be particularly common in postoperative patients, where an incidence of D.V.T. of 30–35 per cent has been found (Hobbs and Davies, 1960; Atkins and Hawkins, 1965; Kakkar and Flanc, 1968; Flanc, Kakkar, and Clarke, 1968; Negus, Le Quesne, Brown, and Chapman, 1968; Kakkar, 1969; Howe, 1970).

Knowing this high incidence of D.V.T., attempts have been made, using the new diagnostic methods, to reinvestigate the aetiology of this condition. In addition, a search has been made to find a screening test which may delineate the group of patients at particular risk of developing D.V.T., so that special preventive measures may be concentrated on this group.

According to Virchow's (1846) triad, the factors predisposing to thrombosis are stasis, increased coagulability of the blood, and changes in the vessel wall. Damage to the intima of the vein in situations other than direct trauma is unlikely and therefore can be discounted as a frequent cause of the deep venous thrombosis. There has, however, been considerable emphasis in the past on changes in the constituents of the blood, particularly the platelets, at the time of surgery. It has been shown that increased platelet adhesiveness occurs in the postoperative period, in the puerperium (Wright, 1942), in recurrent venous thrombosis, as well as in thromboembolic pulmonary hypertension (Hirsh and McBride, 1965). However, in a prospective study no correlation was observed between changes in platelet adhesiveness and the development of D.V.T. (Negus, Pinto, and Brown, 1969). Changes in platelet adhesiveness were of no value in the prediction of postoperative venous thrombosis.

There is much more circumstantial evidence relating postoperative D.V.T. to perioperative venous stasis. McLachlin, McLachlin, Jory, and Rawling (1960) demonstrated that reduced flow occurs in patients in the horizontal supine position, and Clark and Cotton (1968) showed that during general anaesthesia popliteal and external iliac vein flow is reduced by at least 50 per cent. This has led to the trial of a number of techniques designed to reduce perioperative stasis, and thus thrombosis. There has, however, been no indication why in a group of patients subjected to similar conditions of reduced venous flow some develop D.V.T. but not others. An abnormal increase in blood viscosity may give rise to a situation of relative stasis. Blood viscosity, which has long been recognized as one of the primary determinants of blood-flow, has been studied very little in a clinical context, although there have been isolated reports of abnormal blood viscosity in a number of conditions associated with poor blood-flow (Dormandy, 1970; Dintenfass, 1971).

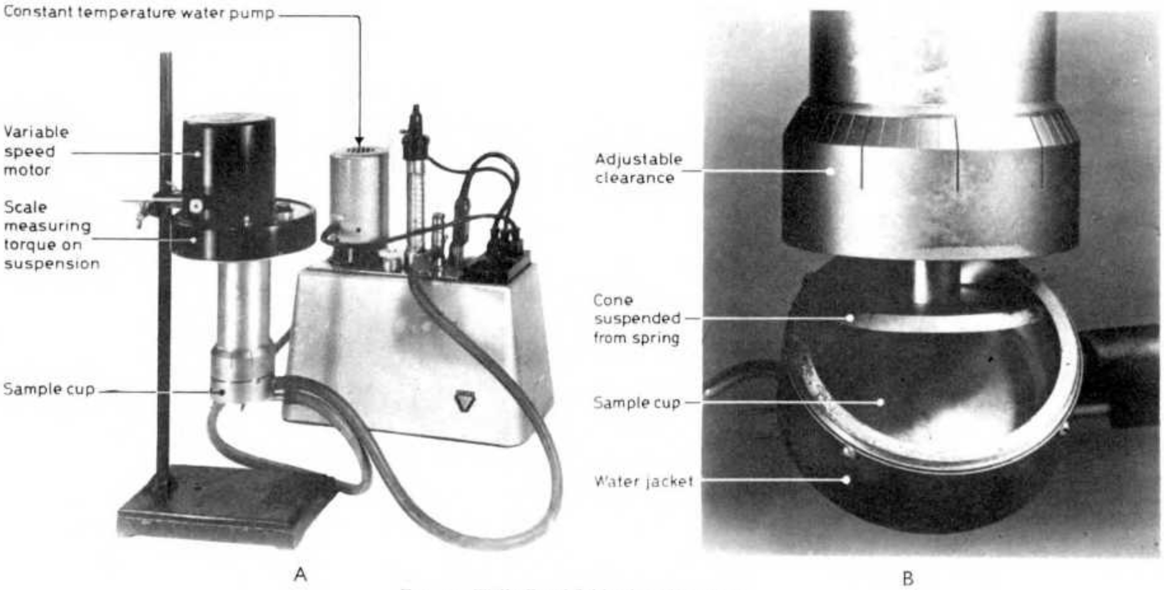
Constant temperature water pump
Variable speed motor
Scale measuring torque on suspension
Sample cup
A
Adjustable clearance
Cone suspended from spring
Sample cup
Water jacket
B

FIG. 1.—Wells-Brookfield microviscometer.

The present authors have studied patients with established D.V.T. confirmed by ^{125}I-fibrinogen studies and phlebography, and found them to have a higher blood viscosity than normal control subjects (Dormandy and Edelman, 1971). It was decided, therefore, to carry out a prospective study of patients undergoing operation, with reference to their blood viscosity and the subsequent development of venous thrombosis.

MATERIALS AND METHODS

Fifty-two patients admitted for elective general surgical or gynaecological operations were studied. Their ages ranged from 20 to 82 years. Patients were excluded if the operation was to be on the legs, groin, or thyroid gland, or if they had a history of a recent thrombotic episode. The thyroid was blocked with sodium iodide and 100 μc. of ^{125}I-labelled human fibrinogen were given intravenously preoperatively. The legs were scanned pre- and postoperatively on the day of operation and on the first, third, fifth, seventh, and ninth postoperative days. In most cases with positive scans confirmatory phlebography was performed.

Blood viscosity was measured with a Wells-Brookfield microviscometer (*Fig.* 1) which is an adaptation of an industrial machine and has previously been used extensively for studying blood (Dormandy, 1970). A conical disk is rotated in the small rhodium cup containing the blood sample by a variable-speed motor, through a beryllium-copper spring connexion. The drag on the rotating cone which is due to the viscosity of the sample can then be measured by the torque on the spring suspension. Although the difference in velocity between the rotating cone and the cup increases towards the periphery the distance between the two surfaces also increases. Therefore, with a cone of the correct angle the velocity gradient or shear rate will be kept constant throughout the sample. Thus, viscosity in centipoises (cP) can then be calculated from the dimensions of the chamber, the rotational speed of the cone, and the torque in the spring suspension. The cup is surrounded by a water-jacket to keep the sample at 37° C. because viscosity is critically dependent on temperature.

The viscometer was calibrated on each day of use with a fluid of known viscosity. The viscosity was estimated at a shear rate of 230 sec.$^{-1}$ as this is thought to be in the physiological range (Whitmore, 1967; Dormandy, 1970). Immediately preoperatively 10 ml. of venous blood were anticoagulated with 125 I.U. solid lithium heparin and the viscosity was measured on 1-ml. samples. The same heparinized venous samples were used to estimate the haematocrit because of the important relationship between viscosity and red-cell concentration. Although a high haematocrit is often accompanied by a high viscosity, many patients with a markedly raised viscosity may not have an abnormally high haematocrit (Dormandy, 1970).

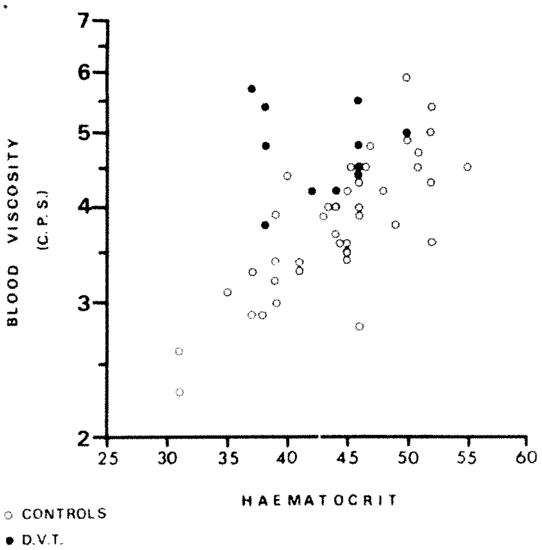

FIG. 2.—Preoperative blood viscosity plotted on a logarithmic scale against the haematocrit.

Table I.—OPERATIONS PERFORMED IN THE PRESENT SERIES

Operation		*No. of Patients*
Major thoracic		
Thoracotomy		2 (1)
Lobectomy		1 (1)
Pneumonectomy		1
	Total	4
Major abdominal		
Gastric		6 (2)
Cholecystectomy		7 (2)
Colectomy		4
Splenectomy		1
Rectal		6 (1)
Aneurysmectomy		1
	Total	25
Major gynaecological		
Hysterectomy		2 (1)
Vaginal		3 (2)
	Total	5
Minor operations		
Haemorrhoidectomy		4
Appendicectomy		2
Laparotomy		2
Ovarian cystectomy		3
Cystotomy		1 (1)
Hysterotomy		2
Incisional hernia		2
Dilatation and curettement		1
Salpingostomy		1
	Total	18

Figures in parentheses refer to the patients who developed post-operative D.V.T.

RESULTS

Eleven out of 52 patients developed D.V.T. following surgery. Further details of the patients are given in *Tables I* and *II*. The comparatively low incidence of D.V.T. was probably due to the fact that all patients above the age of 20 years were included in the trial; in fact none of the 14 patients under 40 years developed D.V.T. The patients who developed D.V.T. had a measured blood viscosity before operation 21 per cent higher than those patients who did not develop D.V.T.

It has previously been shown that there is a direct linear relationship, in the physiological range, between the red-cell concentration and the logarithm of the blood viscosity (Dormandy, 1970). This relationship can be seen in *Fig.* 2, where the blood viscosity (using a logarithmic scale) is plotted against the haematocrit. To allow a direct comparison between the blood viscosity of individual patients differences in the haematocrit have to be eliminated. Using a regression line calculated from the control results, the measured viscosities were converted to a standard haematocrit of 45 per cent. *Fig.* 3 shows the result obtained. If differences in the haematocrit of the various samples are eliminated in this way the preoperative blood viscosity of patients who later developed a D.V.T. was 29 per cent higher than the viscosity of patients who did not develop a D.V.T.

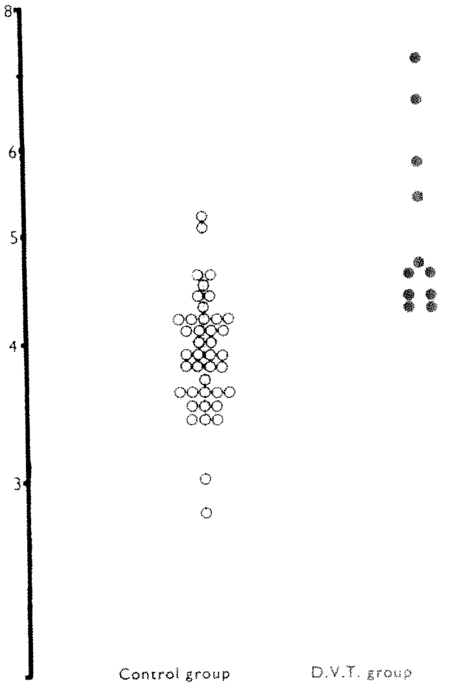

FIG. 3.—Preoperative blood viscosity in 52 patients corrected to a standard haematocrit of 45 per cent ($t = 5{\cdot}5$; $P < 0{\cdot}001$).

Table II.—DETAILS OF PATIENTS WHO DEVELOPED DEEP VENOUS THROMBOSIS

AGE AND SEX	DISEASE	OPERATION
65 M.	Carcinoma of stomach	Gastrectomy
68 F.	Gall-stones	Cholecystectomy
45 F.	Menorrhagia	Hysterectomy
54 M.	Bladder stone	Cystotomy
66 M.	Carcinoma of stomach	Gastrectomy
62 M.	Papilloma of rectum	Anterior resection
64 M.	Carcinoma of lung	Lobectomy
65 M.	Gall-stones	Cholecystectomy
66 F.	Prolapse	Hysterectomy
60 F.	Prolapse	Vaginal repair

Table III summarizes these results. Patients who developed postoperative D.V.T. had a blood viscosity prior to surgery 21 per cent higher at the measured haematocrit and 29 per cent higher at a standard haematocrit than control subjects who did not develop D.V.T. These differences were significant at the level of $P = 0{\cdot}005$ and $P = 0{\cdot}001$ respectively. All the patients who developed D.V.T. had a preoperative blood viscosity above 4·3 cP when corrected to a standard haematocrit of 45 per cent. Only 7 of the patients who did not develop a D.V.T. had a blood viscosity above this level, and 3 of these patients were under 40 years of age.

Table III.—SUMMARY OF THE RESULTS IN THE PRESENT SERIES

	NEGATIVE D.V.T.	POSITIVE D.V.T	DIFFERENCE	SIGNIFICANCE OF DIFFERENCE
Haematocrit (per cent)	44·6	42·8	−1·8	Not significant
Measured viscosity (cP)	3·93	4·75	+0·82	$P = 0{\cdot}005$
Corrected viscosity (cP)	3·95	5·12	+1·17	$P = 0{\cdot}001$

It thus appears that if a surgical patient over 40 years of age has a blood viscosity above 4·3 cP (corrected to a haematocrit of 45 per cent) before operation, he has a 73 per cent chance of developing a D.V.T. following surgery.

DISCUSSION

Although the number of patients studied was small, an important finding has emerged from this preliminary trial: an elevated blood viscosity before operation is significantly associated with the development of postoperative D.V.T. This appears to be the first physicochemical, as opposed to clinical (such as previous thrombotic episodes or age), predisposing factor to have been found in this disease. It could be used as a screening test to select patients for perioperative radioactive fibrinogen scanning or for the application of any special prophylactic measures which may be available.

While continuing with the present trial, the investigations are being extended to try to discover the reason for the high viscosity in some patients. At present very little is known about the causes of elevated blood viscosity other than a high haematocrit. There is known to be a general relationship between fibrinogen and blood viscosity (Chien, Usami, Dellenback, Gregerjen, Nanninga, and Guest, 1967; Merrill and Pelletier, 1967) and there may be a relationship between viscosity and blood-lipid patterns. An extended project, including investigation of these and other aspects, is now being undertaken.

The ideal prophylactic treatment of patients found to have a high blood viscosity prior to surgery would be direct treatment of the high viscosity; unfortunately no suitable therapy is yet available for this purpose. Low-molecular-weight dextran has been suggested as a possible agent for reducing blood viscosity; however, it has recently been shown to have no specific effect on blood viscosity other than by simple haemodilution (Dormandy, 1971). A recent *in vitro* study using small doses of heparin (Negus, Pinto, and Slack, 1971) demonstrated not only decreased platelet adhesiveness but increased lipoprotein-lipase activity after its administration. It may be that the clearing lipase activity might reduce blood viscosity by reducing the lipid level.

Acknowledgements.—This work was carried out with the help of a grant from the Royal Free Hospital Endowment Fund to one of us (J. B. E.). The rheological studies were carried out in the Department of Applied Physiology, Institute of Basic Medical Sciences, Royal College of Surgeons. We thank the surgeons and gynaecologists of the Royal Free Hospital for permission to study their patients, and Miss M. Coulter, S.R.N., and Miss E. Robinson, S.R.N., for their assistance.

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MECHANICAL SUTURES IN SURGERY

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SUMMARY

Following the original introduction of an automatic stapling instrument producing B-form staples by de Petz (1924, 1927), there has been derived from the very important first generation of Soviet stapling instruments a second generation of American stapling instruments characterized by: (1) the use of pre-loaded, pre-sterilized, and disposable staple cartridges; (2) the adaptability of one instrument to a variety of cartridges for use in a variety of tissues and operative situations; (3) the transfer from the instrument itself to the disposable cartridge of delicate and fragile moving parts simplifying the maintenance and operation of instruments. The instruments have found wide and satisfactory application in numerous areas of thoracic, vascular, gastro-intestinal, and gynaecological surgery.

MECHANICAL suture is the method of closing or anastomosing soft tissues in which the suture is made semi-automatically with a stapling apparatus activated by the surgeon's hand. The first useful stapling instrument was developed by the Hungarian de Petz (1924, 1927). Another Hungarian, Hültl (1911), had actually preceded de Petz in the development of a stapling device. Of Hültl's instrument, we know that it was extremely cumbersome, weighed 5 kg., and took 2 hours to assemble. De Petz's instrument (*Fig.* 1) provided a leak-proof, haemostatic but crushing closure of the stomach, duodenum, and colon. However, the gross staples of German or new silver, in spite of their correct B formation, were never relied upon for definite closure of the bowel. Friedrich in 1934 (*Fig.* 2), Sandor in 1936, Tomoda in 1937, and Nakayama in 1964 (*Fig.* 3) improved on de Petz's initial idea with modifications or instruments of their own.

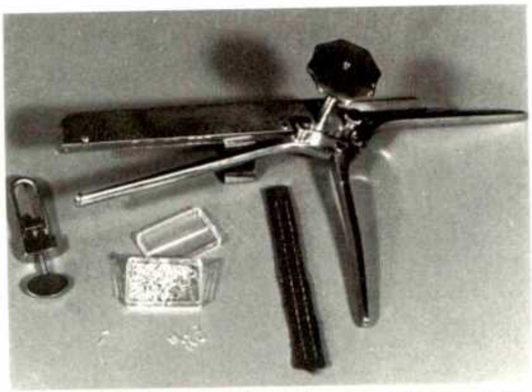

FIG. 1.—The de Petz stapler. After positioning and closing the instrument, the free ends are kept tight by the application of a U-shaped clamp shown at the left-hand side of this picture. The staples of German silver are introduced by turning the knob at the upper right-hand side of the figure in an anti-clockwise direction, thus activating a 'crémaillère' introducing one staple at a time. A double-row, finished staple line is also shown.

As interest in mechanical sutures grew, their use was extended beyond the gastro-intestinal tract. Gudov in 1951 devised an instrument for vascular anastomosis and subsequently a great impetus to mechanical suture devices was given by the Institute for Experimental Surgical Apparatus and Instruments in Moscow (Androsov, 1956, 1963, 1970; Amosov and Berezovsky, 1961; Goldman, 1964; Betts and Takaro, 1965; Gritsman, 1966; Lagache and Vankemmel, 1970) (*Figs.* 4, 5).

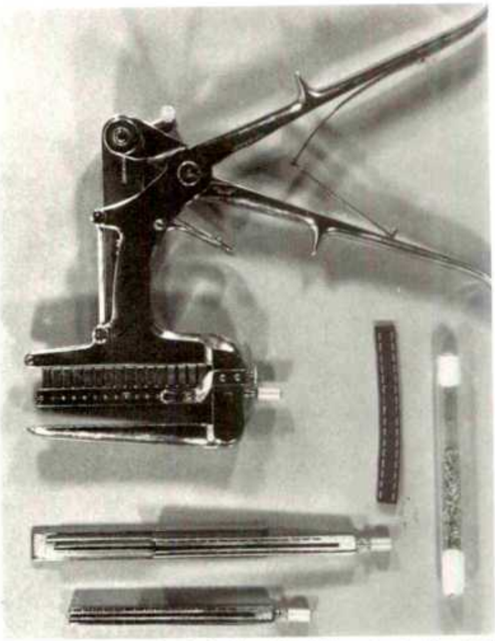

FIG. 2.—The stapler devised by Friedrich using similar staples to those of de Petz. However, exchangeable magazines are provided. Compression of the tissues to be sutured is achieved by squeezing the handle of the instrument once, approximating the jaws. A safety catch is then released and a second compression of the jaws drives the staples home.

Elsewhere Busto and Bucherl (1954) described the experimental use of staples in the closure of bronchial stumps, and Samuels in 1955 reported the use of metal clips in experimental end-to-end anastomoses of arteries. Vogelfanger and Beattie (1958) in Canada and more recently Nakayama (1964) in Japan devised instruments for vascular anastomoses, but their application is essentially limited to the suturing of non-atherosclerotic vessels since everted flanges of the opposing vessels are needed for the procedure.

Cooper, Malina, and Tolins (1967) devised and used an elegant repeating stapler, introducing one staple at a time. Their instrument is especially helpful in areas where larger instruments cannot be accommodated.

Our earlier experience with the original Soviet instruments convinced us of their potentialities (Ravitch, Brown, and Daviglus, 1959; Ravitch, Steichen, Fishbein, Knowles, and Weil, 1964; Ravitch, Rivarola, and Van Grov, 1966). Interest by American designers and manufacturers resulted in the creation of a family of six staplers; four of them were developed from the basic principles worked out by the Institute in Moscow, one was derivative only in its purpose, and one was wholly different and unique (U.S. Surgical Corp., N.Y.).

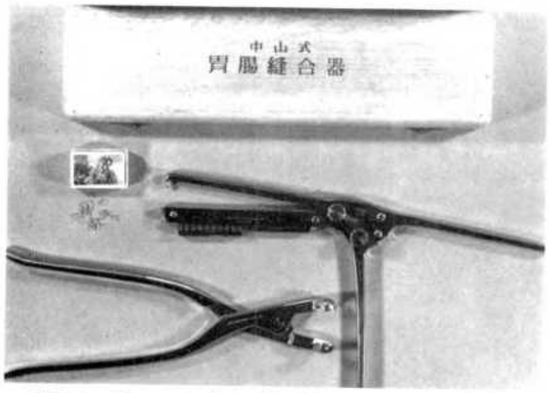

FIG. 3.—The stapler devised by Nakayama. This consists in essence of a simplified de Petz clamp. The staples are introduced by compressing the two cartridges with the heavy forceps seen at the lower left-hand side of the picture.

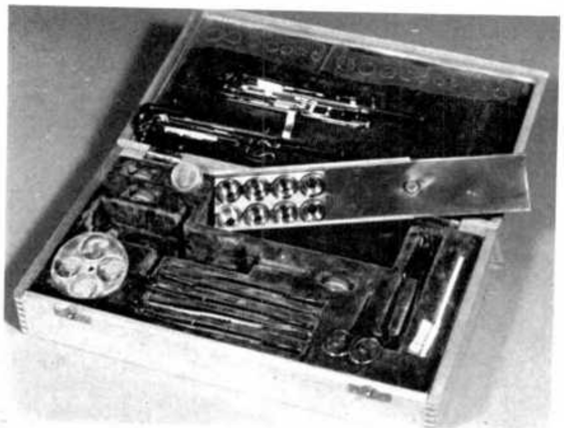

FIG. 5.—The Soviet ASTS instrument devised for the end-to-end anastomosis of vessels. While the vascular instruments do provide perfect everting sutures in healthy vessels, they are composed of many parts, their use is complicated, and the technique is applicable essentially only in normal vessels.

INSTRUMENTS

The development of pre-loaded, pre-sterilized, disposable cartridges together with disposable anvils and the incorporation of all the small moving parts in the disposable cartridge has done away with the technical limitations and the cumbersome hand-loading of the original Soviet instruments.

The very fine stainless-steel staples used as sutures are essentially non-reactive in the tissues. The size and disposition of the staples within each cartridge and the design of the corresponding anvil are adapted to the recognized need in suturing a given structure, viz., vessels, bronchus, stomach, intestines, or lung. Each instrument can accommodate a variety of cartridges so as to reduce the required number of instruments to a minimum.

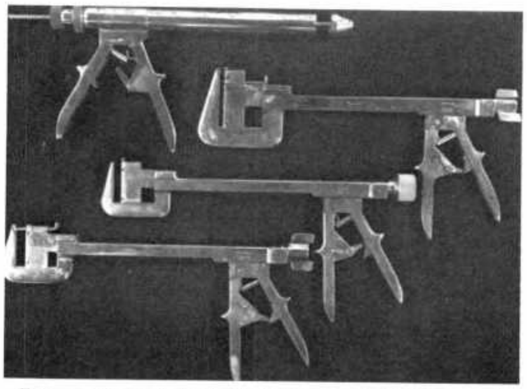

FIG. 4.—Three of the instruments of the UKB (25, 40, 60) variety devised by the Institute for Experimental Surgical Apparatus and Instruments in Moscow are seen superposed from left to right. In the upper left-hand side of the figure is shown the PKS which is used for end-to-end inverting anastomoses in low anterior rectal resections. The instrument is introduced through the anus. For oesophagogastric or oesophagojejunal anastomoses it has to be introduced through a stab wound in the bowel.

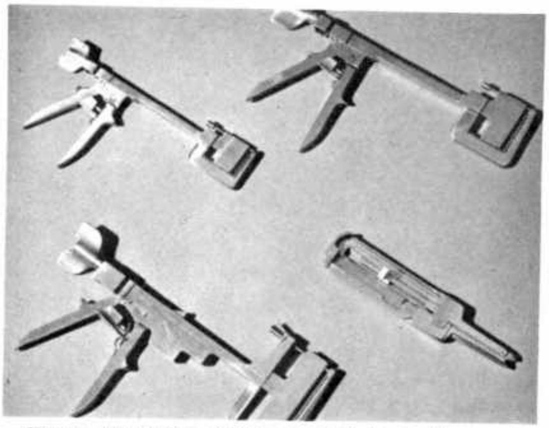

FIG. 6.—From left to right in an anticlockwise direction are shown the TA-90, TA-30, TA-55, and GIA. The TA instruments are used for linear sutures and closures in gastro-intestinal, pulmonary, gynaecological, and vascular surgery. The GIA instrument is employed for transection and simultaneous closure of the intestine and lung, as well as for anastomoses in the gastro-intestinal tract.

The six instruments are used for: (1) linear sutures and closures in gastro-intestinal, pulmonary, gynaecological, and vascular surgery; (2) transection and simultaneous closure of the intestine; (3) anastomoses in gastro-intestinal surgery; (4) ligating and dividing vessels; (5) closing skin and fascia. There are three linear suture instruments (the TA-30, 55, 90), one anastomosing instrument (the GIA), one ligating and dividing instrument (the LDS), and one instrument for closing of fascia and skin.

With the three TA or linear instruments (*Fig.* 6) the tissues to be sutured are first gently compressed between the jaws of the clamp. An entire suture line is then driven home, the size of the staples and the length and pattern of the suture line depending upon the cartridge employed. The designations 30, 55, and 90 refer to the length in mm. of the double staggered row of staples inserted, these instruments placing simultaneously 11, 18, and 33 staples repeatedly.

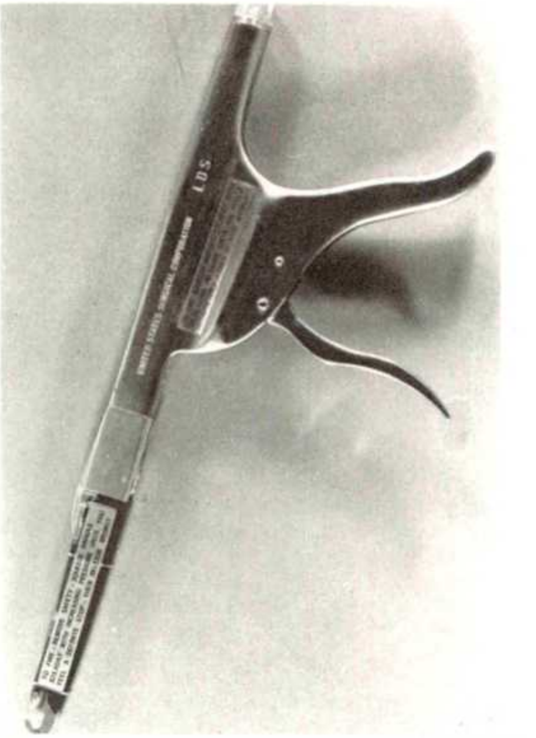

FIG. 7.—The LDS stapler with cartridge. In one operation this instrument doubly ligates and divides between staples tissue contained within the hook located at the tip of the cartridge, which can be operated thus 15 times before reloading.

The GIA (*Fig.* 6) consists of two interlocking halves forming a flat handle with two projecting limbs. With the instrument open, its limbs grasp between them the walls of the organs to be anastomosed or of tissue to be sutured and transected. The basic anastomosis is serosa to serosa and side to side. The cartridges provide two double rows placed simultaneously, thus avoiding the need for the reinforcing sutures required in the single-row Russian instrument. The staggering of the pushers for the introduction of the double rows of staples, the disposable knife, and the transfer of the innumerable tiny staple drivers into the disposable cartridge make the instrument easy to activate and maintain.

One of the most interesting instruments is the LDS (*Fig.* 7), which is the product of 8 years of hard work and innumerable models based on a wide variety of principles, as regards staple design, jaw design, and method of activation (Ravitch, Hirsch, and Noiles, 1973). The instrument as used with a pre-loaded, pre-sterilized, and disposable magazine does the following things: (1) it isolates safely within it by a positive mechanism whatever tissue is delivered to it, not relying on the operator to judge the amount of tissue which might or might not be safely grasped; (2) it doubly ligates this tissue with absolute security whether it is a tiny delicate isolated vein or a mass of fat and blood-vessels; (3) when the handle is squeezed the instrument doubly staples the tissue enclosed and divides it between the staples in the same operation.

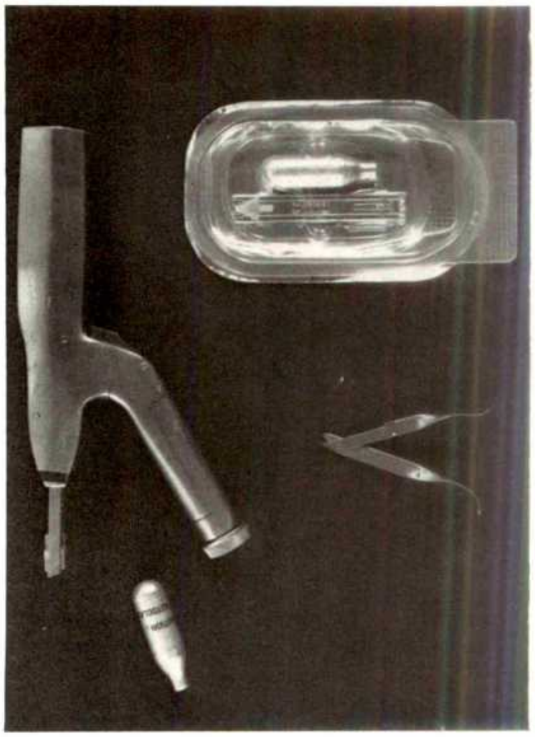

FIG. 8.—The skin stapler is shown together with a cartridge containing 25 staples and the staple remover, which is not unlike the one used for the removal of Michel clips. The sterile package contains a small CO_2 cylinder which provides the driving force in the instrument, as well as the staple cartridge.

A totally different kind of instrument in conception and historical background is the skin stapler (*Fig.* 8). This instrument is powered by a CO_2 cartridge. The disposable, pre-loaded, pre-sterilized magazine contains 24 staples which when closed form in a complete rectangle. The time-saving obtained with this instrument is substantial.

SURGICAL TECHNIQUES

With increasing experience and confidence in the instruments, we have found that they can be used in a wide variety of operative procedures. In the Billroth-II type of gastric resection (Ravitch and Steichen, 1973) the LDS is used for the ligating and dividing of vessels along the curvatures, the duodenum and stomach are closed with the TA instruments, a side-to-side gastrojejunostomy is performed with the GIA, and the stab wounds used to introduce the limbs of the GIA are closed with a TA instrument. We prefer an antecolic anastomosis placed on the anterior wall of the stomach (Ravitch and others, 1964), although retrocolic and posterior anastomoses can be performed with equal ease.

If a Billroth-I reconstruction is contemplated the gastroduodenal continuity may be established by a triangulating, partially inverting, partially everting, end-to-end anastomosis with the help of the TA-55 stapler (McGinty, 1970; Ravitch and Steichen, 1973) after the proximal portion of the stomach has been sealed by a double staggered staple row applied by the TA-90 and a portion corresponding to the width of the duodenum has been excised from this closure along the greater curvature. Another elegant technique for this reconstruction is Reynolds's (1973) application of the GIA instrument to Poth's (1950) technique of gastrectomy and gastroduodenostomy, in which a 'step-like' resection of the body of the stomach, starting at the lesser curvature, results in the creation of a tube along the greater curvature. This tube is fashioned so as to present a circumference matching the one of the duodenum and it may then be anastomosed to the duodenum manually or by using the triangulating, partially inverting, partially everting, end-to-end anastomosis.

For the excision of a gastric ulcer the TA-90 has been used (Ravitch and Steichen, 1973). If the ulcer is situated on the posterior wall of the stomach, for instance, the vessels along the greater and lesser curvatures are cleared with the LDS instrument sufficiently to allow for mobilization of the stomach. The gastric wall is then grasped with Babcock clamps on either side of the ulcer; the ulcer and surrounding normal gastric wall are introduced between the jaws of the TA-90 instrument. An elliptical resection results, leaving a transverse closure of the posterior wall of the stomach. The TA-55 serves admirably for everting, mucosa-to-mucosa, non-obstructing transverse closure of the Heineke-Mikulicz pyloroplasty, while the GIA is used routinely for Finney pyloroplasty and gastro-enterostomy (Ravitch and Steichen, 1973).

In small- and large-bowel surgery a special type of functional end-to-end anastomosis—previously described in a manual suture technique by Poth (1950)—in which the cut ends of two loops of bowel are placed together in a shotgun fashion, the septum between them is divided with this instrument, and then the open end of the bowel is closed over with the TA-55, or sometimes the TA-90 is utilized (Steichen, 1968). Currently, we usually divide the small and large intestines between the arms of the GIA instrument, thus closing at the moment of transection each end with two rows of the extremely fine staples, whatever might be the ultimate plan of anastomosis or resection (Ravitch and Steichen, 1973). The anastomotic clamp also serves very well to divide the spur of a Mikulicz enterostomy or of the Duhamel operation for Hirschsprung's disease in one stage and at the same time as the original operative procedure (Steichen, Talbert, and Ravitch, 1968).

With the use of these instruments there is an important saving of time in such extensive procedures as colon by-pass, colon interposition with lower oesophagectomy, and especially colon replacemen and total oesophagectomy in one stage (Steichen 1971). In the latter procedure double suture line and transection of the gastric fundus, functiona end-to-end colocolostomy or ileocolostomy, end-to-side cologastrostomy, end-to-side cervical or thoracic oesophagocolostomy, and incidental appendectomy are all performed with the help of staplers In patients undergoing oesophagogastrectomy the stomach is mobilized along the greater and lesser curvatures with the LDS and the body of the stomach is transected between two TA-90 suture lines Intrathoracic end-to-side oesophagogastrostomy is then performed with the GIA. We have used the TA-55 instrument in the closure of oesophageal and pharyngeal diverticula and the GIA in the creation of a reversed gastric tube for the palliative by-pass o inoperable oesophageal carcinoma (Ravitch and Steichen, 1973).

In thoracic surgery the TA-90 or TA-55 instrument is used in the excision of emphysematous blebs (Steichen, 1971). The individual bleb is grasped and held up with Babcock clamps and then slipped into the jaws of the stapling instrument at the junction of the bleb with the relatively normal lung tissue. Following the stapling of the neck of the bleb, the latter is removed distal to the instrument, obtaining a haemostatic and air-tight closure. The very narrow suture line does not encroach on the expansion of the underlying lung tissue. Wedge and segmenta resections may be performed similarly, by holding the wedge or segment to be resected and introducing the TA-90 or TA-55 instrument proximal to the lesion to be excised (Steichen, 1971). Following staple closure of the lung at the elected site of resection a tangential excision of the specimen may then be performed. If this excision represents all or most of a given segment, ligation of the corresponding segmental artery is advisable. In wedge resections the GIA instrument may also be used in a double application, producing a pie-shaped excision of the specimen and surrounding tissue with automatic transection and closure of both the remaining lung and the specimen (Steichen, 1971).

The TA-30 instrument using cartridges containing the 4·5-mm. staples is employed in the closure of the main bronchus after pneumonectomy, and the same instrument using staples of 3·8 mm. in the closure of lobar bronchi (Dart, Scott, and Takaro, 1970 Steichen, 1971). A third cartridge containing very fine staples may be used with the same instrument in the closure of the pulmonary artery after pneumonectomy and the pulmonary vein(s) after lobectomy or pneumonectomy (Steichen, 1971). A not-anticipated use of the TA-90 or TA-55 instrument is the division of an incomplete pulmonary fissure in pulmonary lobectomy; the GIA instrument may also be used for this purpose (Steichen, 1971). Following control of the hilus after closure and transection o the vessels and the bronchus, the remaining bridge between the two lobes, the dissection of which results so frequently in an oozing and bubbling surface, is closed with a row of staples. This suture line is narrow and avoids any compromise of the expanding remaining lobe.

The vascular staples contained in one of the fou cartridges that fit the TA-30 have been used fo closure of the patent ductus arteriosus and more recently for closure of the Potts aortopulmonary anastomosis (Leand, Bender, Martz, Crisler, Agnew, and Gott, 1971) at the time of the definitive open-heart correction of the tetralogy of Fallot. The vascular staples are equally useful in the closure of the hepatic end of the portal vein in end-to-side portacaval shunts (Steichen, 1971). The TA-30 instrument accommodates a special cartridge for the compartmentation of the inferior vena cava in the prevention of pulmonary embolism (Ravitch, Snodgrass, McEnany, and Rivarola, 1966).

Table I.—OVER-ALL EXPERIENCE WITH AUTOSUTURE INSTRUMENTS DURING THE PERIOD FROM 6 JUNE, 1967, TO 15 SEPTEMBER, 1971

TYPE OF SURGERY	NO. OF PATIENTS	NO. OF OPERATIONS	NO. OF PROCEDURES	NO. OF COMPLICATIONS	NO. OF DEATHS
Gastric	69*	70	167	6	—
Intestinal	60†‡	62	120	3	—
Oesophageal	15	15	55	2	—
Pulmonary	49§	50	104	6	1
Vascular	14	14	16	—	—
Gynaecological	8	8	8	—	—
Miscellaneous	3*	3	7	—	—
Total	218	222	477	17	1

Four patients were operated on twice with autosuture instruments:—
* Inguinal herniorrhaphy and gastrectomy.
† Closure of fistulae and ileocolectomy.
‡ Ileocolectomy and Duhamel procedure.
§ Staged bilateral resection of pulmonary blebs.

In gynaecological operations we have used the TA-55 for the closure of the vaginal cuff in abdominal hysterectomies (Kahn, 1968) and the GIA for the suturing of the broad ligament in vaginal hysterectomies.

INSTRUMENT AND STAPLE CHARACTERISTICS

Mechanical suturing assures many of the factors which are desirable in a bowel anastomosis or tissue closure, such as: fixation and coaptation of the structures to be sutured; avoiding the shifting and minimal tearing that occur in even the most carefully hand-performed suture; needle and suture holes that are of the same fine calibre, since the staple is both a needle and a suture; speed and neatness resulting in minimal trauma to and oedema of the wound edges; and finally minimal inflammation and necrosis because of the non-strangulating nature of the tissue closure involved in the B shape of the closed staple. The quality of the actual suturing depends little on the surgeon's experience and skill, although he still has to learn when and how to use the instruments, how to prepare the tissues, etc. As in other areas of human endeavour, machines cannot replace or improve man's thinking; if used properly they can, however, add precision, neatness, and speed in the execution and completion of his decisions.

Studies have shown that the tissues distal to the staple line remain viable, and that in the gastro-intestinal tract the mucosa-to-mucosa approximation does not require inversion or reinforcement (Ravitch, Lane, Cornell, Rivarola, and McEnany, 1966; Ravitch and Rivarola, 1966; Steichen, 1968). Healing is accelerated because of minimal trauma and oedema and the non-reactive nature of the stainless-steel staples. Staples have not been deformed or damaged over the 4-year period that we have been able to follow some of our patients. The staples have not shifted, with the exception of those in inverting intestinal anastomoses which may be eliminated into the bowel lumen with time. In gastric and intestinal surgery we have been consistently impressed with the immediate patency of anastomoses and the early return of intestinal transit (Weil and Steichen, 1970; Steichen, 1971). Air-leaks or haemorrhagic oozing following pulmonary blebectomy, wedge resection, segmentectomy, and division of an incomplete fissure have been virtually eliminated by the stapling techniques.

RESULTS

From June, 1967, to September, 1971, a total of 218 patients have undergone 222 operations (*Table I*). These amounted to 477 individual staple procedures. The definition of a 'staple procedure' is best illustrated by a Billroth-II gastrectomy, in which four stapling procedures would be involved: (1) ligating and dividing vessels, (2) duodenal closure, (3) gastric closure, and (4) gastrojejunostomy. In addition, the skin was closed with the staples in some 150 patients.

In these 477 staple procedures we encountered 13 complications related to the use of the instruments (*Table II*). There was postoperative anastomotic bleeding in 5 patients, 3 of whom required reoperation. There were 5 suture-line leaks, of which 4 were temporary and self-limiting. One occurred some 3 weeks after an emergency gastrectomy for bleeding from a duodenal ulcer. In this patient the duodenal stump had been drained, which is not our usual technique. Leakage of bile occurred at a time when the patient was already at home and eating a regular diet. The leak was limited and healed spontaneously. In the second patient, a 10-day-old baby with a right colectomy for in utero caecal perforation and neonatal obstruction from the resulting inflammatory mass, a small amount of faeces was discharged from the wound on one occasion at a time when normal transit was already established. Seventeen days later the child demonstrated the classic picture of Hirschsprung's disease; hence the anastomosis had been performed proximal to a mechanical obstruction. In 1 patient who had a total oesophagectomy and oesophagocologastrostomy performed in one stage there was a small and temporary discharge of saliva through the neck incision. One leak in a heavily irradiated colon was manifested after 2 weeks with no complications and apparent recovery following colostomy closure. The radiation had been given 12 years previously for treatment of an adenocarcinoma of the uterus. At that time, severe radiation colitis had resulted; however, evaluation prior to closure of the colostomy did not contra-indicate an attempt at reconstructing normal bowel passage. Finally, a leak occurred after a technically difficult colorectal anastomosis. It was treated by local drainage alone. The patient left the hospital with a healed and well-functioning anastomosis.

Table II.—COMPLICATIONS RELATED TO THE USE OF AUTOSUTURE INSTRUMENTS

COMPLICATION	OPERATION	NO. OF COMPLICATIONS	
		Related	Questionable
Suture leak			
Late	Duodenal closure	1	—
Small	Ileocolic anastomosis	1	—
	Oesophagocolic anastomosis	1	—
Post-irradiation	Colocolic anastomosis	1	—
Limited	Colorectal anastomosis	1	—
Postoperative bleeding			
Reoperation (2)	Gastrectomy	4	—
	Cologastrostomy	—	1
Limited	Wedge gastrectomy	1	—
	Pulmonary wedge	—	3
Air leak			
Limited	Pulmonary wedge	2	—
Bronchopleural fistula			
Expired	Pulmonary lobectomy	1	—
	Total	13 (5·8 per cent)	4 (1·8 per cent)

Pulmonary air leaks for 24–36 hours were observed in 2 patients with a wedge resection. A bronchopleural fistula after a right lower lobectomy for pulmonary suppuration in advanced Wegener's granulomatosis was fatal in 1 patient.

In another 4 patients the postoperative complications were questionably related to the use of the instruments. In 3 of these patients there was some postoperative bleeding through chest tubes after a pulmonary wedge resection, 2 of these patients having had, in addition, extensive decortications.

In the fourth patient there was presumed slow intraperitoneal bleeding over a 24-hour period following a tangential wedge resection of the stomach for a posterior penetrating ulcer. No blood was aspirated through the nasogastric tube in this patient and he recovered without reoperation.

DISCUSSION

Mechanical suture instruments do not make a virtuoso out of a tiro and do not make difficult surgery possible for the unskilled or untrained. Nor is it possible to use these instruments in all situations and on all patients or on all lesions. Nevertheless, the suturing and anastomosing instruments, for instance, deliver their staples with a uniform degree of compression, with a uniform spacing in a manner that the best of us cannot achieve manually, and without the trauma involved in picking up bowel bronchus or blood-vessels with a forceps, penetratir it with a needle, pulling through the thread, takir it up again, and penetrating it once more. In tl Soviet Union where distances between hospitals a great and transportation of very sick patients difficult at times, these instruments were original created partly in order to increase technical abili and safety in the hands of the isolated surgeon pe forming major operations only occasionally. In con paring large series of gastrectomies Gritsman in 19 reported a mortality of 3·2 per cent in gastrectomi performed manually for gastric and duodenal ulce as compared with 1 per cent if staplers were use Mortality in gastrectomy for carcinoma was 10·4 ar 3·6 per cent respectively. The number of new ar ingenious ways in which these instruments can l employed is becoming apparent as they are beir used more widely, and satisfaction with them seen to be general.

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THE EFFECT OF ANTRAL ACIDIFICATION ON ACID SECRETION STIMULATED BY PENTAGASTRIN*

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SUMMARY

In 6 dogs with innervated antral pouches (4 with vagally innervated fundic pouches and 2 with vagally denervated fundic pouches) the effect of irrigating the antral pouches with acid on the pentagastrin-induced secretion from the fundic pouches was assessed. A range of doses of pentagastrin (0·25–8·0 μg. per kg. body-weight per hour) was given by intravenous infusion for 3 hours at a constant rate, each dose being given on six occasions in separate experiments carried out on separate days. No consistent inhibition of secretion was observed in either preparation. The results do not support the concept of either an inhibitory hormone or an inhibitory neural reflex of antral origin active against pentagastrin-stimulated acid secretion.

Previous studies from the Surgical Unit, Royal Infirmary, Cardiff, suggested that a neural reflex might be responsible, in part, for the inhibition of pentagastrin-induced gastric secretion by antral acidification in the dog (Williams and Forrest, 1969). Similar conclusions were reached by Coelho, Bombeck, Pissidis, and Nyhus (1971) in respect of both meat and pentagastrin.

The experiments of Williams and Forrest (1969) were carried out in dogs with vagally innervated and denervated fundic pouches and vagally innervated antral pouches of the stomach. The stimulus of gastric secretion was pentagastrin given in sequential doses in a single experiment. Inhibition by perfusion of the antral pouch with acid was observed only in dogs with vagally innervated fundic pouches stimulated by submaximal doses of pentagastrin.

The studies now reported extend these observations in dogs in which varying doses of pentagastrin were given, each in a single test.

MATERIALS AND METHODS

The studies were carried out in 6 mongrel dogs with body-weights ranging from 9 to 13 kg. Four were prepared with vagally innervated (mucosal septal) fundic pouches (Hollander and Jemerin, 1938; Thomas, 1942) using the modifications described by Gregory, Hallenbeck, and Code (1942). The remaining 2 animals were prepared with vagally denervated (separated) fundic pouches (Heidenhain, 1879). The presence or absence of vagal nerve-supply to the pouch was confirmed by an insulin test, which was performed once in each dog (Jemerin, Hollander, and Weinstein, 1943). The total acid output in the 3 hours following an intravenous injection of 0·5 U. of insulin per kg. body-weight ranged from 2·9 to 13·0 mEq. in the case of the innervated preparations and was zero in the denervated pouches.

At a second operation performed 4 weeks later an innervated antral pouch was made by the construction of a mucosal septum between the body and the antrum (Forrest, 1956), gastro-intestinal continuity being re-established by gastroduodenostomy. The distal end of the antrum was exteriorized to form a mucocutaneous fistula. Definition of the junction between the body and the antrum at operation was made using *p*H-indicator paper after a subcutaneous injection of 1 mg. histamine dihydrochloride, as described by Olbe (1963). A strip of mucous membrane, 1–2 cm. wide, was excised along both sides of the junction in order to be as certain as possible that the antral pouch contained no parietal cells. No oxyntic cells were seen in random biopsies taken from the margins of the remaining antral mucosa in any of the dogs. As further confirmation, *p*H measurements of the antral contents were made during experiments in which gastric secretion was stimulated. In all the dogs it remained above *p*H 7·0. Confirmation of the absence of duodenal mucosa in the distal antrum was also obtained by histological examination.

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* Based on a communication to the Surgical Research Society in July, 1971.

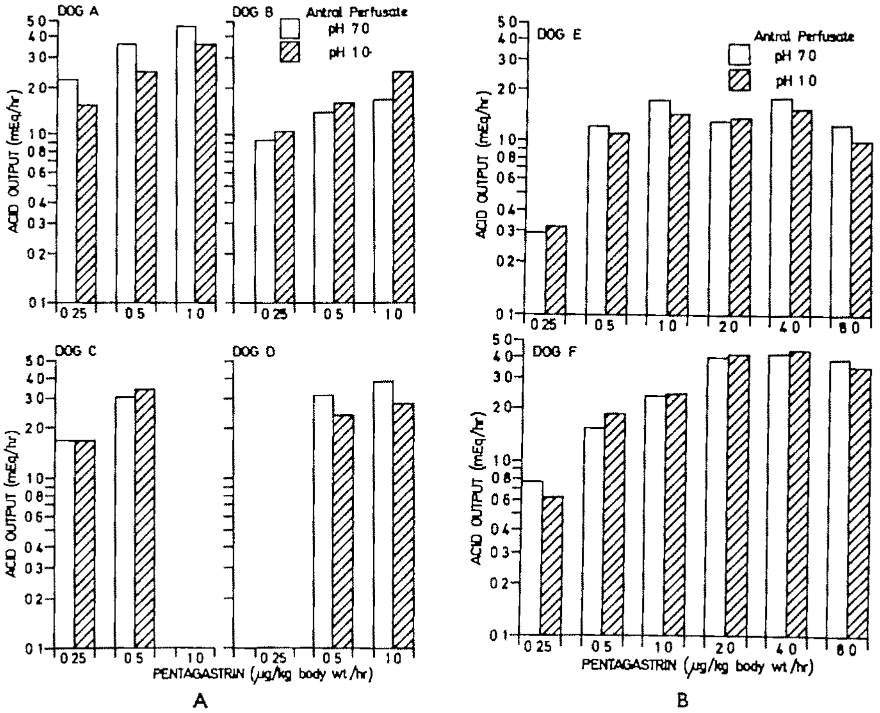

FIG. 1.—Acid secretory responses to intravenous infusions of pentagastrin in (A) 4 dogs with vagally innervated fundic pouches and (B) 2 dogs with vagally denervated fundic pouches during antral pouch perfusion with (i) isotonic saline at *p*H 7·0 and (ii) isotonic saline at *p*H 1·0. Each column represents the mean of the final hour outputs of acid for each dose obtained in a 3-hour test performed three times in each animal. The mean acid outputs have been plotted on a logarithmic scale. Three doses of pentagastrin were employed in dogs A and B, two doses in dogs C and D, and six doses in dogs E and F.

The septal integrity of all the mucosal septal pouches was established by feeding the animals milk on at least three occasions. Tests of secretion were commenced 6 weeks after operation. Before each test the animals were fasted for at least 18 hours and a rest of 48 hours was allowed between tests. Any test in which an animal vomited or showed excess restlessness or salivation was terminated.

The acid secretory response to a range of doses of pentagastrin (Peptavlon, I.C.I. 50, 123, Imperial Chemical Industries Ltd.) was determined. Each dose of pentagastrin was given in a separate experiment by intravenous infusion for 3 hours. The doses of pentagastrin were 0·25, 0·5, and 1·0 µg. per kg. body-weight per hour in the dogs with innervated fundic pouches, and 0·25, 0·5, 1·0, 2·0, 4·0, and 8·0 µg. per kg. body-weight per hour in those with denervated fundic pouches.

The infusion was injected into a foreleg vein at a rate of 6·7 ml. per hour, irrespective of the dose, using a Palmer slow-infusion pump (C. F. Palmer, London).

Fifteen minutes before the start of the pentagastrin infusion and after the collection of at least one 15-minute basal specimen of gastric juice, perfusion of the antral pouch was commenced with isotonic saline at *p*H 7·0 or an isotonic solution of HCl in saline at *p*H 1·0 and continued throughout the test. Confi mation of equal osmolality of the two solutions was l estimation of the depression of the freezing poir using a semi-micro osmometer (Knauer, Berlin).

The antral perfusate was delivered by a peristalt pump (Type MHRE, Watson-Marlow Ltd., Marlo Bucks.), at a rate of 1 ml. per minute via the narro inner lumen of a double-lumen Kay gastroston tube (J. G. Franklin and Sons Ltd., London). fluid escaped from the antrum through the wide out lumen of the tube and as the balloon of the cathet was not inflated, distension of the antrum w avoided. At hourly intervals the *p*H of the perfusa returning from the antrum was measured; it nev varied from that of the entering fluid.

Three tests were performed on each dog for ea dose of pentagastrin and at each *p*H of the ant perfusate, i.e., 6 tests for each dose of pentagastri The antral perfusate used in any one experiment w selected randomly.

During the tests the gastric juice was collected 15-minute samples. The volume was measured in n and the concentration of acid determined by titrati with 0·01 NaOH to a *p*H of 7·0 using an EIL Model Titrimeter (Electronic Instruments Ltd., Richmon Surrey). From these estimations the acid output w calculated in mEq. per 15 minutes.

The results were analysed by a statistical compa son of the outputs of acid during the last hour (mE per hour) of the tests when the antrum was perfus at *p*H 7·0 with the outputs when the *p*H of t perfusate was 1·0. As acid outputs appear to follow a log-normal distribution (Forrest and Code, 1954) the logarithms of the individual values for each test were used in the analysis (Gaddum, 1945). In a further analysis the outputs during the third half-hour (mEq. per 30 minutes) of each test were similarly compared. The latter period was chosen as it coincided with that which appeared in the data presented by Williams and Forrest (1969) and which was found to give the greatest differences.

Table I.—EFFECT OF ANTRAL ACIDIFICATION ON THE ACID SECRETORY RESPONSE TO PENTAGASTRIN ADMINISTERED BY CONTINUOUS INTRAVENOUS INFUSION

DOG	DIFFERENCE BETWEEN LOG ACID OUTPUT DURING ANTRAL PERFUSION AT pH 7·0 AND pH 1·0		
	Mean	± S.E.M.	*P*
A	0·138	0·024	< 0·001
B	−0·091	0·049	N.S.
C	−0·024	0·058	N.S.
D	0·134	0·051	< 0·05
Group I (4 dogs)	0·039	0·058*	N.S.
E	0·038	0·050	N.S.
F	0·016	0·039	N.S.
Group II (2 dogs)	0·027	0·032†	N.S.
Group I − group II	0·012	0·066	N.S.

* Calculated from between-dog variation as this group of dogs differed significantly in response among themselves.

† Calculated from within-dog variation in the absence of significant between-dog variation.

N.S., Not significant ($P > 0·05$).

The initial analysis was to determine if any effect of antral acidification was dose-dependent. Differences between fundic-pouch outputs during antral perfusion at pH 7·0 and 1·0 were examined over the whole range of pentagastrin doses and the results compared by an analysis of variance.

Since no dose-dependence was demonstrated, the mean difference in acid output obtained from all the doses was used in the main analysis. The standard errors of these differences were calculated from a pooled variance obtained from all the doses and their significance assessed by *t*-tests.

RESULTS

The mean acid output during the final hour of the 3-hour tests on the individual dogs is shown in *Fig.* 1 at each dose of pentagastrin and with each perfusate.

As one would expect, the dose of stimulant had a noticeable effect on the level of acid output; increasing the dose increased acid secretion. Nevertheless, the difference between acid output from the fundic pouches during perfusions of the antrum at pH 7·0 and 1·0 was not substantially affected by the dose of pentagastrin. The absence of a statistically significant effect of dose on this difference was shown by an analysis of variance. In no dog was the result significant at even the 20 per cent level.

In the absence of any apparent dose effect comparisons of response to antral perfusion at individual doses were not worth while. Instead, the mean difference between acid output during antral perfusion at pH 7·0 and 1·0 obtained from all doses was considered for each dog. *Table I* shows the mean difference for each dog together with the standard error of this difference. Neither of the animals with denervated fundic pouches exhibited significant inhibition.

Table II.—EFFECT OF ANTRAL ACIDIFICATION ON THE ACID SECRETORY RESPONSE TO PENTAGASTRIN ADMINISTERED BY CONTINUOUS INTRAVENOUS INFUSION

DOG	DIFFERENCE BETWEEN LOG ACID OUTPUT DURING ANTRAL PERFUSION AT pH 7·0 AND pH 1·0		
	Mean	± S.E.M.	*P*
A	0·151	0·040	< 0·005
B	−0·016	0·067	N.S.
C	−0·144	0·094	N.S.
D	0·129	0·080	N.S.
Group I (4 dogs)	0·030	0·069*	N.S.
E	0·023	0·068	N.S.
F	−0·028	0·045	N.S.
Group II (2 dogs)	−0·003	0·041†	N.S.
Group I − group II	0·033	0·080	N.S.

* Calculated from between-dog variation.

† Calculated from within-dog variation.

N.S., Not significant ($P > 0·05$).

Two of the dogs with innervated fundic pouches showed significantly lower acid output when the antrum was perfused at pH 1·0 as compared with pH 7·0. However, 1 dog in this group showed a higher output at pH 1·0 which reached significance at the 10 per cent level. The dogs with the innervated fundic pouches considered as a group did not demonstrate significant inhibition.

A comparison of the mean effect of antral acidification on the acid output of the dogs with denervated fundic pouches and of the dogs with innervated fundic pouches failed to demonstrate any statistically significant difference between the two groups (*Table I*).

A similar analysis was applied to the third half-hour of each test instead of the final hour. This is summarized in *Table II*. Although the results of this analysis were less precise, because of a greater degree of variation leading to larger standard errors, the conclusions matched those described above.

DISCUSSION

Since pentagastrin has the same active terminal tetrapeptide and physiological properties as gastrin (Tracy and Gregory, 1964), its action should be inhibited by any mechanism which inhibits gastrin-stimulated secretion. The demonstration of such inhibition would indicate that acidification of the antrum inhibits gastric secretion by a mechanism other than suppression of gastrin release. In vagally denervated fundic pouches this could only be by a hormonal mechanism.

Our failure to demonstrate inhibition in this preparation is further evidence against the existence of such an antral inhibitory hormone. These findings are in agreement with those of Williams and Forrest (1969), who also used pentagastrin-stimulated secretion, and of Gillespie and Grossman (1962), Andersson and Olbe (1964), and Rheault, Semb, Harkins, and Nyhus (1965), who stimulated secretion with hog gastrin.

Contrary findings were reported by Coelho and others (1971) using pentagastrin to stimulate gastric secretion, and by Thompson, Davidson, Miller, and Davies (1964), who used hog gastrin. Both these groups of workers claimed that antral acidification inhibited the secretion from denervated fundic pouches. Full details of the experiments of Coelho and others have not yet been published.

The studies of Olbe (1964) suggested that the 'resting' innervated antral pouch releases small quantities of gastrin which might influence the secretory response of a fundic pouch to other stimuli. If this is so, then antral acidification, by reducing this subthreshold gastrin release, would result in a diminished response of a fundic pouch. Clearly the case for the antral chalone diminishes when this argument is evoked. However, Andersson and Grossman (1966) did not think that the amount of gastrin released spontaneously from the excluded innervated antrum was sufficient to increase significantly the response of a fundic pouch to exogenous gastrin.

In the present study there was no consistent inhibition of pentagastrin-induced acid secretion from innervated fundic pouches following acidification of the innervated antral pouch. The doses of pentagastrin chosen were those which gave the maximal inhibition previously noted (Williams and Forrest, 1969). Although 2 dogs did show some inhibition, the extent of this was less than that observed in the earlier study and there was no difference in the means of the 4 dogs considered as a group.

Our failure to demonstrate consistent inhibition in the animals with innervated antral and innervated fundic pouches is in agreement with the results of Preshaw (1967). Preshaw was also interested in the possibility of a neural inhibitory mechanism triggered by antral acidification and carried out studies in which he irrigated innervated antral pouches with 50 m*N* and 100 m*N* HCl in dogs with gastric fistulae. No inhibition of gastrin-stimulated secretion was observed. In these animals inhibition of a sham-feeding response was noted, indicating that antral acidification could suppress the release of vagally stimulated gastrin.

The experiments described here were undertaken in an attempt to confirm our previous findings. In the tests which we reported earlier (Williams and Forrest, 1969) sequential doses of pentagastrin were given in a single experiment and antral perfusion was performed using a gravity-feed system. In the current studies each dose of pentagastrin was given in a single test on different days, and a constant-rate perfusion system employing a peristaltic pump was used. Whether these differences explain our inability to confirm the inhibition observed previously, we do not know. Certainly, we have failed to obtain further evidence for a possible neural reflex of antral origin active against pentagastrin-induced acid secretion.

Acknowledgements.—This work was supported by the Wellcome Trust, from whom M. H. Wheeler received a full-time grant.

The authors are grateful to Mrs. M. Coyle for her technical assistance.

The pentagastrin used in this study was generously supplied by Imperial Chemical Industries Ltd., England.

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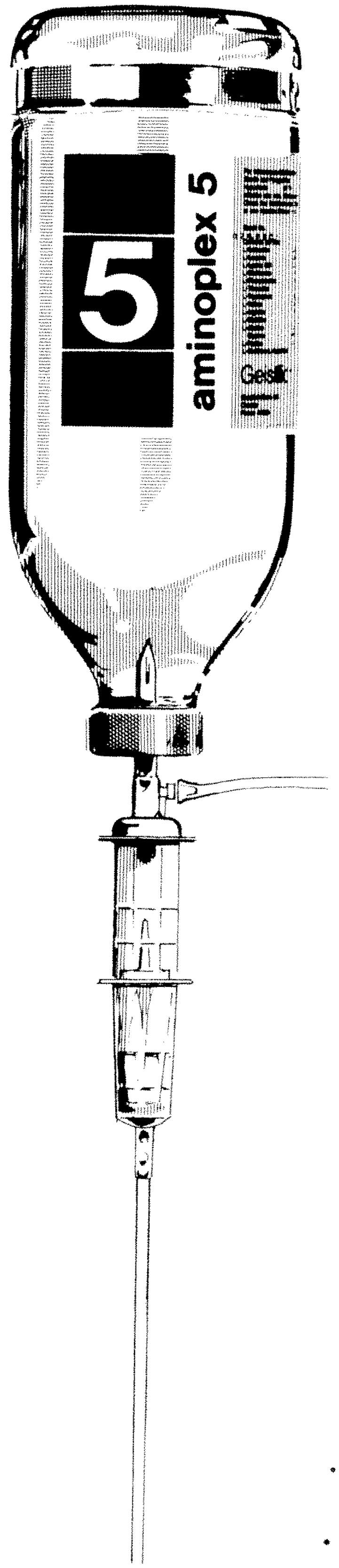

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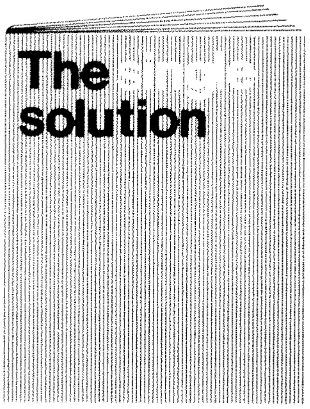

THE CONTROLLED USE OF VASODILATOR DRUGS IN THE MANAGEMENT OF HYPOVOLAEMIA COMPLICATED BY DIMINISHED CARDIAC FUNCTION

By K. M. PAGLIERO, A. K. YATES, AND D. G. HILL
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SUMMARY

The fundamental importance of precise measurement of cutaneous temperature rather than the cursory assessment with the back of the hand in cases of shock or diminished tissue perfusion has been well described by Ross, Brock, and Aynsley-Green (1969). They showed examples where core/toe temperature gradients reflected hypovolaemia in postoperative cardiac surgical patients and further showed how this information could be used to guide α-blockade therapy to overcome peripheral vasoconstriction, thus allowing rapid correction of hypovolaemia by transfusion.

One criticism levelled by antagonists to this form of treatment is that α-blockade drugs cause hypotension. This article shows that with careful control α-blockade should not cause significant hypotension. Furthermore, in patients with hypotension of cardiogenic origin, α-blockade may be safely used in the treatment of coincidental hypovolaemia.

PERIPHERAL cutaneous temperature is dependent on the degree of cutaneous vasoconstriction and will therefore in standard environmental conditions reflect the degree of increased peripheral resistance found in shock, whatever its cause. Peripheral resistance can be calculated knowing the cardiac output and systemic pressure. However, measurement of cardiac output at the bedside is tedious, costly, and beyond the scope of all but the most sophisticated of units. Measurement of cutaneous temperature, on the other hand, is easy to perform, inexpensive, and non-invasive. Conceivably, the skin could be vasodilated in the presence of vasoconstriction in other organs. Cutaneous temperature measurement would therefore be of no value. However, our clinical findings show that a warm periphery (as measured in the big toe) corresponds to generalized vasodilatation with normal consciousness, good urinary output, and maintenance of normal acid-base balance which indicates that the degree of overall peripheral resistance is reflected by the cutaneous temperature.

α-Blockade is used to overcome vasoconstriction resulting from the physiological output of adrenaline and noradrenaline, this physiological response being the same for any form of shock whether cardiogenic, hypovolaemic, or peripheral in type (Block, Pierce, Manesc, and Lillehei, 1965). In the Thoracic Surgical Unit at Guy's Hospital chlorpromazine, 2·5–5 mg. intravenously, is used in repeated doses if an initial lack of response makes them necessary. Chlorpromazine has been reported by Dietzman and Lillehei (1968) as a 'moderately' effective α-blocking agent with a central nervous depression effect which is not always desirable in shock. Accordingly, Dietzman and Lillehei use phenoxbenzamine. Our own experience is that chlorpromazine is satisfactory and we have never needed to resort to more powerful drugs. Any associated mild cerebral sedation appears to be beneficial.

The vasodilatation caused by α-blockade is initially reflected by a fall in venous pressure corresponding with the increase in volume of the vascular bed. There will therefore be a concomitant fall in arterial pressure. The undesirable effect of this hypotension can be avoided by simultaneous intravenous transfusion to maintain the venous pressure.

CASE REPORTS

Case 1.—*Fig.* 1 shows the parameters for the first 5 postoperative hours of a 53-year-old woman who had undergone mitral valve replacement. On her return from the operating theatre she had poor peripheral perfusion and required an intravenous infusion of isoprenaline (0·2 mg. per cent at 4 drops per minute) to maintain her cardiac output at acceptable levels. Two doses of 2·5 mg. of chlorpromazine were given to initiate vasodilatation. Simultaneous transfusion, however, was not sufficient to maintain the central venous pressure. Each injection was followed by a fall in the central venous pressure and arterial blood-pressure with no improvement in the haemodynamic state. A fall of 30 points of blood-pressure is noteworthy in this patient and had the original pressure been 80–90 mm. Hg systolic could have been catastrophic.

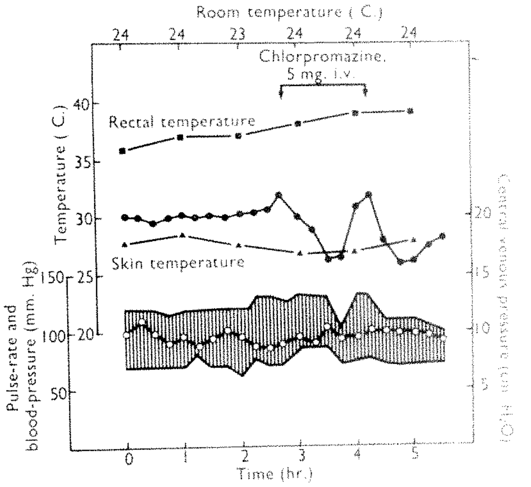

FIG. 1.—*Case* 1. Chart of the parameters for the first 5 hours after mitral valve replacement.

A patient with cardiogenic shock will be particularly susceptible to a fall in the central venous pressure. Hypovolaemia must nevertheless be corrected and therefore attention must be paid to expanding the effective blood-volume at the same time as inducing peripheral vasodilatation by α-blockade. Expansion of the blood-volume is achieved by transfusion at such a rate that the central venous pressure does not fall. Minute-by-minute monitoring of the venous pressure may be necessary. The vasodilator effect of intravenous chlorpromazine is usually seen within 2 or 3 minutes if the dose is adequate. If these criteria are satisfied there will be no fall in the central venous pressure, no reduction in venous return to the heart, and no hypotension. The following cases illustrate these points.

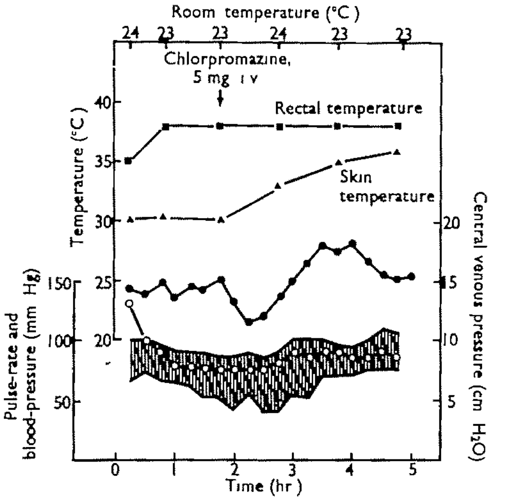

FIG. 2.—*Case* 2 Chart of the parameters for the first 5 hours after aortic valve replacement.

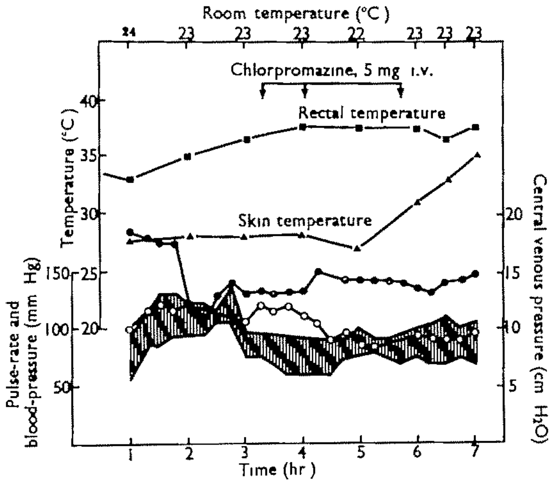

FIG 3—*Case* 3 Chart of the parameters for the first 7 hours after mitral valve replacement

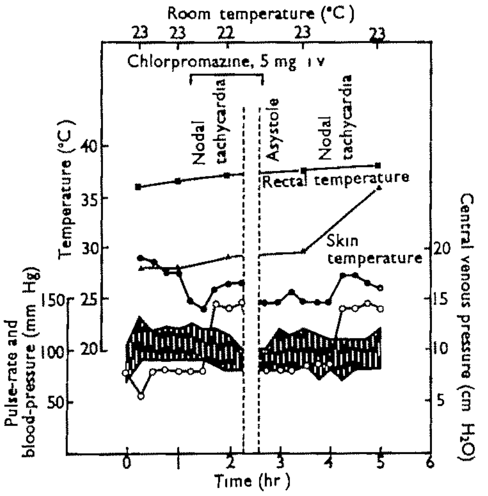

FIG. 4—*Case* 4. Chart of the parameters for the first 5 hours after mitral valve replacement

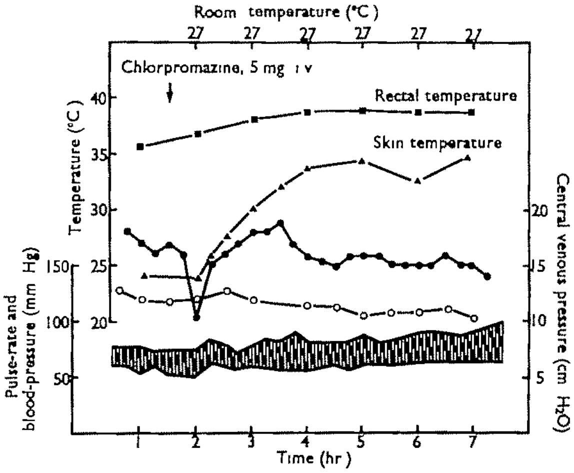

FIG 5—*Case* 5. Chart of the parameters for the first 7 hours after emergency aortic valve replacement.

Case 2.—*Fig.* 2 shows the parameters of a man of 50 years who had undergone aortic valve replacement for aortic stenosis while in severe cardiac failure. For 2½ hours after operation there was a declining blood-pressure. The peripheral temperature of 30° C. indicated vasoconstriction despite a central venous pressure maintained at 14–15 cm. water. Chlorpromazine, 5 mg. i.v., was therefore given while the venous pressure was maintained by increased blood transfusion. The blood-pressure showed progressive improvement with increasing peripheral perfusion, as indicated by a decreasing core/toe temperature gradient.

This case illustrates that the controlled administration of chlorpromazine at a systolic blood-pressure of 85 mm. Hg resulted in no further hypotension.

Case 3.—*Fig.* 3 is the chart of a 45-year-old woman who had undergone mitral valve replacement for mitral regurgitation. The initial picture is one of instability: peripheral vasoconstriction and low urinary output indicated low cardiac output and hypovolaemia. In addition, heat-loss during the 6-hour operation had caused depression of the central temperature to 33° C. In this case chlorpromazine was withheld until metabolic heat had produced a rise in the central temperature to 37° C. (Although vasodilatation risks loss of heat and depression of the central temperature, chlorpromazine may be safely given to patients with central hypopyrexia if an adequate environmental temperature is maintained.) Three separate intravenous injections of 5 mg. of chlorpromazine were necessary before a vasodilator response was gained, as indicated by the need for rapid transfusion to maintain the central venous pressure. Subsequently, vasodilatation and normovolaemia were indicated by a satisfactory rise in the peripheral temperature, increase in urinary output, and return of consciousness. Despite the three doses of chlorpromazine there was no significant change in the systolic blood-pressure, which remained at 90–100 mm. Hg throughout this period of treatment.

In retrospect vasodilator therapy should have been initiated earlier in the postoperative period and the injections of chlorpromazine should have been repeated more rapidly, e.g., at 15–20-minute intervals until the vasodilator response was obtained.

Case 4.—*Fig.* 4 shows the chart of a 51-year-old man who underwent mitral valve replacement. He returned to the ward with a satisfactory blood-pressure, venous pressure, and pulse-rate; however, vasoconstriction persisted, indicating concealed hypovolaemia. There was no response to an initial dose of chlorpromazine. Half an hour later a nodal tachycardia occurred and the blood-pressure dropped to 100 mm. Hg systolic. Subsequently, myocardial instability persisted and a period of asystole occurred. Despite the precarious situation, having achieved a return of heart-beat it was considered essential to correct the hypovolaemia. A further dose of chlorpromazine was given together with increased transfusion to maintain the venous pressure. Over the next 1½ hours this treatment was rewarded by vasodilatation with no adverse effect on the cardiovascular state.

Case 5.—*Fig.* 5 is the chart of a man of 52 years who underwent emergency aortic valve replacement. His postoperative condition was critical and his blood-pressure was only 70 mm. Hg systolic despite cardiac stimulants and vasopressors. Concealed hypovolaemia was indicated by a low peripheral temperature and therefore the patient was given chlorpromazine, 5 mg. i.v., despite his hypotension. A fall in the venous pressure was corrected by transfusion and was maintained at a satisfactory level. Peripheral vasoconstriction relented, urine excretion became satisfactory, and the patient became conscious. The blood-pressure continued to be low, indicating reduced cardiac function, but this was not aggravated by our treatment.

CONCLUSION

The use of α-blockade to facilitate and to allow speedy correction of hypovolaemia has been previously recommended by Ibsen (1967). Other workers (Block and others, 1965; Dietzman and Lillehei, 1968) have advocated the use of vasodilators in cardiogenic shock. Although this latter treatment is far from universally accepted, it would, however, seem a reasonable and safe policy to combine these two treatments to aid the correction of hypovolaemia in the presence of cardiogenic and other forms of shock.

The cases illustrated in this article serve as examples of this policy. At no time have we had cause to regret its use. However, it cannot be overemphasized that α-blockade without careful attention to the central venous pressure and central temperature can be highly dangerous. Its indiscriminate and uncontrolled use could result in dangerous degrees of hypotension or central hypothermia.

Once again, the measurement of the core/toe temperature gradient has been shown to be of value in the understanding and management of shock.

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FURTHER PROGRESS WITH RECONSTRUCTION OF THE EXSTROPHIED BLADDER

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SUMMARY

Two series of primary reconstructions of the classic exstrophied bladder are reviewed and a brief description of the operative procedure is given.

There has been a significant improvement in the results since 1963 and a discussion of the possible reasons is given along with a policy for the future.

EXSTROPHY of the urinary bladder continues to be a formidable problem in paediatric urology. This paper brings up to date the treatment of this condition under the care of the senior author (D. I. W.) at the Hospital for Sick Children, Great Ormond Street, and the St. Peter's Group of Hospitals, London. The last reported results from these hospitals cover a period from 1949 to 1963 (Williams and Savage, 1966). During this period 80 cases of exstrophy of the urinary bladder were treated, with primary closure of 51 cases. The late follow-up shows that 5 cases have acceptable continence. This is a dismal result but is better than when we first reported this series (Williams and Savage, 1966). At the time of the initial report a policy for the future was decided upon. We decided to be more selective in the choice of which exstrophied bladder to reconstruct. This depended mainly upon the size, suppleness, and condition of the bladder. Also less attempt was made to obtain a tight closure of the bladder neck and the closure was done at a later age. In the first series the average age of closure was 8–12 months, whereas in the second series it was 16 months.

PRESENT SERIES

From July, 1963 to July, 1969, 36 cases of classic exstrophy of the bladder have been treated. This report is limited to the common complete form of exstrophy of the bladder. Epispadias, ectopic cloaca, and the split-symphysis variants are excluded. Clearly the incomplete forms of exstrophy are more amenable to reconstruction and their inclusion in this series would give a false impression of the results to be expected.

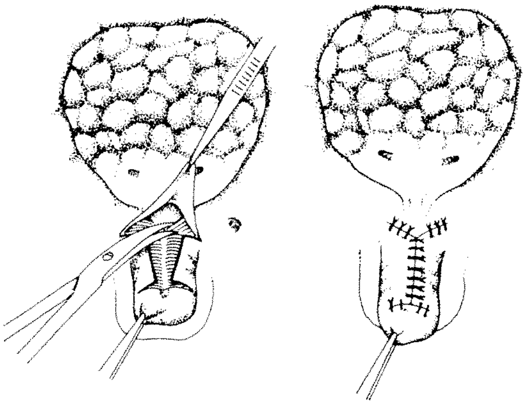

FIG. 1.—Urethral lengthening procedure. A, A V-shaped incision is based near the verumontanum and has its apex near the coronal sulcus. The urethra is dissected back and the dorsal fibrous attachments of the corpora cavernosa are freed. B, Skin closure is in the form of a Y.

The sex distribution was in the ratio of 2 males to 1 female, which has changed from that of the original series of 3 males to 1 female. Of the 36 cases, 17 were considered unsuitable for closure because of the small size and rigidity of the bladder. These 17 cases had a urinary diversion, of which 11 were ileal conduits, 5 were sigmoid conduits, and 1 was a cutaneous ureterostomy. Nineteen cases were primarily reconstructed and the details of these cases are reported here.

OPERATION

The basic procedure is unchanged from that of the earlier series and has been described in detail in the previous article (Williams and Savage, 1966). The essential features are as follows.

In the male infant upward chordee correction is performed about 6 months prior to the actual closure of the bladder. The simplest method of chordee correction is by elongation of the urethra based on a V–Y plasty, bringing around preputial skin (*Fig.* 1). After a transverse or V-shaped incision in the urethral strip the proximal end is dissected off the corpora cavernosa up to the point at which these separate from one another. The corpora are then laid bare on either side and traced upwards until the bands which tether them to the pubic tubercles can be severed. The defect in skin cover created by correction of the chordee may be corrected by the use of preputial flaps, either brought around the side or over the top with a button-hole method, but in some cases there is insufficient preputial tissue and one has to use scrotal skin. An opening is made in the skin of the anterior scrotal wall and the skin of the penis is then circumcised. The whole penis is displaced under this anterior scrotal skin and the glans is brought up through the button-hole. This adds a lot to the urethral length although it does, of course, require a further operative procedure to release it and to enclose the penis completely in supple skin. The correction of the chordee helps not only with subsequent closure of the bladder but also in later life with sexual intercourse.

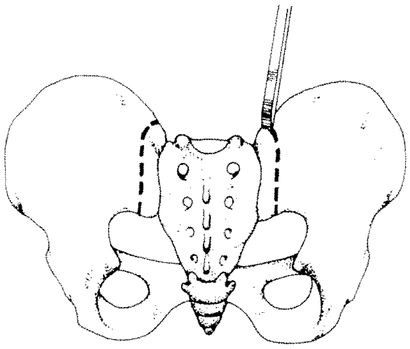

FIG. 2.—Iliac osteotomy. A vertical incision is made a little lateral to the sacro-iliac joint. The muscle is cut and the periosteum is stripped and the bone is cut with an osteotome down to the greater sciatic notch.

The female genital defect is less serious, since the upper vagina, uterus, ovaries, and tubes are almost always normally formed. The vaginal introitus is, however, stenosed and anteriorly displaced. An episiotomy in later childhood or adolescence will usually suffice to make intercourse satisfactory and most of these girls are capable of child-bearing.

The actual closure consists first of bilateral pelvic osteotomy (*Fig.* 2). This was done in 16 of the 19 patients in this series of cases, but it has not been attempted where the child has been past the age of 2 years as it has not been found that sufficient mobility is obtained after this age. Briefly, the child is laid face down with a sandbag supporting the pelvis anteriorly; a vertical incision is made 1–2 cm. lateral to the sacro-iliac joint. The gluteal muscles are incised and the periosteum is stripped from the ileum down to the sacro-iliac notch. A bone lever is inserted into the notch and with an osteotome the ileum is then cut through 1 or 2 cm. lateral to the sacro-iliac joint. When the cut is complete the bone can be hinged inwards by pressure on the femora. The muscle layer is then sutured with catgut and the wound is closed. In many cases the child has then been turned over for immediate reconstruction of the bladder. In others a period of 48 hours has elapsed before the closure operation. After pelvic osteotomy the child has been suspended by the legs in a gallow's splint for 3 weeks.

The reconstructive procedure (*Fig.* 3) is commenced by an incision around the mucocutaneous junction of the bladder and urethra, excising also the umbilical scar superiorly. The incision is deepened so that the retropubic space is opened up on either side and the apex of the bladder is mobilized completely. Towards the base of the bladder the mobilization is carried out against the inner aspect of the pubis so that the fibromuscular fibres joining the bladder to the bone are severed far laterally, thus avoiding the ureters and neurovascular supply of the bladder. After mobilization, the bladder-neck area is narrowed by lateral incisions and the urethral strip is mobilized a little at its edges. Before the bladder is closed a decision must be taken concerning the ureters. Reflux prevention is likely to be required at some stage in the reconstructive programme and if the bladder is large and supple an immediate re-implantation of the ureters by a tunnel technique is practical. If, however, the bladder is small and thick it may be extremely difficult to accomplish a satisfactory reimplant at the same time as bladder closure, and it may be preferable to leave this aspect of the reconstruction until a later date. The bladder and urethra are then closed by two layers of catgut suture in the anterior midline with a suprapubic drain for the bladder and, if necessary, separate drains for the two ureters. The fibromuscular tissue which has been freed from the pubis is wrapped around the front of the bladder-neck area if possible. The rectus sheath is then sutured in the midline with strong catgut or silk. Pressure on the iliac crest during closure of the suture line will enable a simple midline closure to be performed if an osteotomy has preceded this operation; if not, flaps of rectus sheath must be mobilized (*Fig.* 4) and turned inwards to cover the bladder. Similarly, the skin may be closed by simple suture in the midline after osteotomy, while in other cases flaps are required. Postoperatively bladder drainage is continued for 10–14 days and long-term chemotherapy for at least 3 months. In all cases it is usually at least a year before it can be decided whether continence is to be obtained and during this period careful supervision by intravenous pyelography and urinary analysis is vital as infection and upper-tract dilatation are by no means rare complications.

The variants of the closure have been to use isolated segments of ileum or colon in cases where a small bladder needed to be enlarged. In our second series this was only performed once and satisfactory continence was not obtained postoperatively. We have performed bilateral nephrostomies preoperatively in only 2 of the 19 patients and an anti-reflux procedure was done at the time of closure in 4 of the 19 patients.

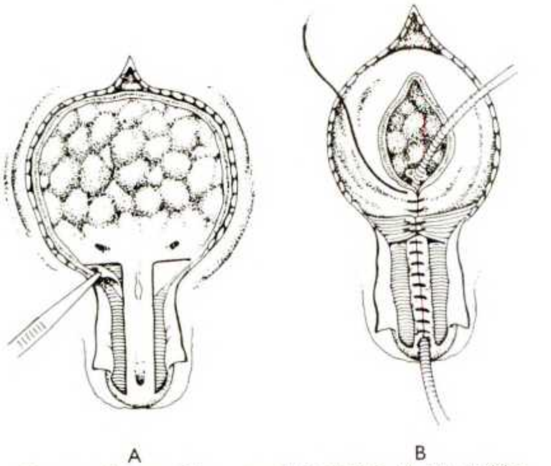

FIG. 3.—Closure of the exstrophied bladder. A, The incision is made along the mucocutaneous junction of the bladder and urethra. Triangles of mucosa are excised from the trigone to create a bladder neck. B, Closure of the bladder and urethra together with the fibromuscular bands across the bladder-neck area.

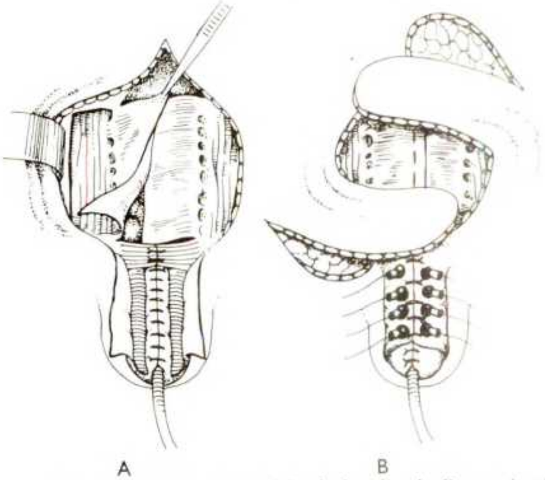

FIG. 4.—Closure of the abdominal wall. A, Rectus-sheath flaps are formed which hinge on the medial border to cover the bladder. B, Skin closure can be obtained by the rotation of broad-based flaps.

RESULTS

The first series of cases from 1949 to 1963 has been reviewed afresh and to a certain extent the results are better than appeared at the time of the original publication (*Table I*). The late follow-up of these 80 cases, of which 51 were reconstructed, shows that acceptable continence was obtained in 5 cases, 3 have rather poor control and are using some sort of external appliance, and 38 have had a secondary diversion. Four patients have died; 1 of these deaths was due to acute poliomyelitis which developed soon after the operation, 1 patient died on the twenty-fifth postoperative day of uncertain cause but possibly related to postoperative sepsis, and 2 have died several years after the reconstructive procedure while under the care of another hospital for a secondary diversion. One case has been lost to follow-up.

Table I.—RESULTS OF RECONSTRUCTION IN THE FIRST SERIES OF CASES FROM 1949 TO 1963

	No. of Cases
Total No. of cases seen	80
Functional reconstruction attempted in	51
Results of reconstruction	
Acceptable continence	5*
Poor control and using appliance	3
Secondary diversion	38
Lost to follow-up	1
Died	4

* Continence: 6·2 per cent of total cases; 9·8 per cent of reconstructed cases.

Examination of the continent patients shows the oldest patient to be 14 years post-reconstruction and the youngest to be 7 years post-reconstruction. Two of these patients have perfect control, no infections, and normal pyelograms. In the other 3 patients infections have occurred but have been cleared satisfactorily. One of these patients had stones in the earlier period but has none at the present time.

The second series of cases was treated between July, 1963, and July, 1969 (*Table II*). During this time a total of 36 cases was referred for treatment and functional reconstruction was attempted in 19. Of these 19 cases, acceptable continence with a normal intravenous pyelogram was obtained in 6. In 3 of these patients the urine is sterile, whereas the other 3 are on maintenance antibiotics for infection. Secondary diversion has been performed in 8 other cases because of failure of continence, and 4 cases are still incontinent and awaiting further treatment. One patient had perfect continence, but hydronephrosis necessitated a urinary diversion. Comparing now the first and second series it will be clear that we have obtained a very satisfactory improvement of continence. In the first series only 6·2 per cent of the total cases and 9·8 per cent of the reconstructed cases were continent, whereas in the second series the figures are 17 and 31 per cent respectively.

Table II.—RESULTS OF RECONSTRUCTION IN THE SECOND SERIES OF CASES FROM 1963 TO 1969

	No. of Cases
Total No. of cases seen	36
Functional reconstruction attempted in	19
Results of reconstruction	
Acceptable continence	6*
Perfect continence but hydronephrosis requiring diversion	1
Secondary diversion	8
Incontinent and awaiting further treatment	4

* Continence: 17 per cent of total cases; 31 per cent of reconstructed cases.

Table III.—COMPLICATIONS OF RECONSTRUCTION IN THE FIRST SERIES OF CASES FROM 1949 TO 1963

Complications	*No. of Cases*		*Percentage Incidence*
Early			
Breakdown		9	
Complete	4		
Partial	5		
Fistula		9	
Stricture		7	
Other		4	
Intestinal obstruction	1		
Severe ileus	1		
Ureteric obstruction	1		
Poliomyelitis	1		
Late			
Persistent pyuria	27 out of 37		73
Pyelographic deterioration	12 out of 35		34
Stone	10 out of 47		21
Reflux	15 out of 18		83

COMPLICATIONS

A depressing feature of the early series was the number of complications (*Table III*). Of the early complications, some breakdown of the wound was common; this usually occurred before osteotomy was undertaken. In the late follow-up the incidence of infection, reflux, pyelonephritis, and stone formation was extremely worrying. In the second series the complications have been less, particularly the late complications (*Table IV*). There have been no stones, infection has not been uncommon but radiological evidence of pyelonephritis has been relatively rare and slight, and it is clear that with better techniques and more careful supervision no serious harm has been done to the upper urinary tract in these children.

Table IV.—COMPLICATIONS OF RECONSTRUCTION IN THE SECOND SERIES OF CASES FROM 1963 TO 1969

Complications	*No. of Cases*		*Percentage Incidence*
Early			
Breakdown		8	
Complete	2		
Partial	6		
Fistula		3	
Stricture		1	
Other		3	
Pulmonary oedema	1		
Intestinal obstruction	1		
Bilateral hydronephrosis (required temporary diversion)	1		
Late			
Persistent pyuria	10 out of 19		53
Pyelographic deterioration	4 out of 19		21
Stone	0 out of 0		0
Reflux	7 out of 9		77

In the second series the 2 complete breakdowns of the wound were in patients whose bladders were closed at a few weeks of life. A reconstruction was attempted at an older age, but both of the patients required later diversion for incontinence. The 6 partial breakdowns were treated conservatively and they healed with time. Suprapubic fistula occurred in 3 cases and again these were treated conservatively and subsequently healed. Stricture occurred much less in the second series and this improvement is possibly explained by the attempt now not to get too tight a closure at the bladder neck and urethra. Again there was the occasional complication as listed in *Table IV*. The intestinal obstruction required an exploratory laparotomy and lysis of adhesions. The bilateral hydronephrosis required temporary nephrostomy tubes.

DISCUSSION

After review of our second series of patients it would seem that we have improved our results and reduced the complications to the point where closure of exstrophied bladders should be attempted in selected cases. The reported figures are certainly sufficiently encouraging for us to believe that functional reconstruction has an important part to play in the treatment of exstrophy, even though the majority of cases will still require diversion. We have attempted to review the various features of the reconstructive procedure to determine what has been useful and what has not.

The penile-lengthening procedure has certainly an important part to play in the achievement of normal erections and genital function, but it has not had any very obvious influence on the attainment of urinary continence. Pelvic osteotomy has made wound closure much more satisfactory and in the long run the abdominal wall has remained sound after this procedure. However, radiographs have shown in all cases that the pubes have sprung apart and there has been no contribution at all towards the achievement of continence. The significance of the results is a little hard to assess since osteotomy was not performed in the older children and it is well known that these children have a better chance of obtaining control.

However, in both the first and second series continence after osteotomy was very poor and we have decided not to perform this manœuvre unless the gap in the pubes is very wide.

The part played by the tightness of the bladder-neck closure has been very hard to assess since we have no accurate measurement of this factor. The general impression has been that the best results have been obtained where the muscle tissue in the region of the bladder neck is well formed and where extreme narrowness of the neck has not been aimed at. In the earlier series it was shown that a bladder of very small capacity did not obtain continence and in the second series such cases were excluded from the reconstructed group. Only 52 per cent of the total cases seen were reconstructed in the second series as opposed to 63 per cent in the first series. Attempts were made in a few cases to enlarge the bladder capacity by colocystoplasty or ileocystoplasty. In none of these was continence obtained.

It is clear that reflux has been a serious factor in some of the postoperative cases and has accounted for early upper-tract dilatation in some. In 1 case there was an extremely satisfactory return to pyelographic normality after a secondary reflux-preventing operation in a patient who was almost completely continent. The choice of larger capacity bladders, reflux prevention, and the more careful control of infection by chemotherapy appear to have been responsible for the absence of stones and only very slight evidence of pyelonephritis in the second series.

Our results compare favourably with the recently reported results of Smith and Lattimer (1966), Fisher and Retik (1969), Ezell and Carlson (1970), Marshall and Muecke (1970), and Jeffs (1971). The approaches of these authors are somewhat similar to ours though Fisher and Retik (1969) have been keen to postpone the primary reconstruction of the bladder neck until adolescence. Marshall and Muecke (1970) perform preliminary bilateral nephrostomies and bilateral reimplantations at the time of the initial closure with fascial covering of the abdominal wall and no osteotomies.

Our conclusion in relation to reconstruction of exstrophy is that about one-half of the number of classic exstrophy cases will be suitable for reconstruction. In the present series only one-third of that group were successfully treated, but one would certainly hope to raise the success rate with improved techniques so that perhaps ultimately one-third of the total number might be successfully treated in this way. Two-thirds of the cases will still need to be diverted.

Our policy for the future will be first to undertake in males penile-lengthening procedures which will avoid any interference with the area of the verumontanum. Secondly, in those patients in whom it can be postponed we will close the bladder later than previously, possibly waiting until the second or third year of life. We will be prepared to do a closure operation which will not, in the first instance, aim at complete bladder-neck correction or reflux prevention and to follow it with a second operation some years later. Thirdly, in the definitive reconstruction we shall not undertake pelvic osteotomy unless the symphysial gap is enormous, but will aim to get abdominal wall closure by large rectus-sheath flaps. We shall aim at a very long posterior urethra constructed out of the bladder base with reimplantation of the ureters at a higher level and with a reflux-preventing submucosal course. This procedure demands a potentially large bladder capacity and if such is not available at the initial closure, then the two-stage procedure of covering over and awaiting events seems the right line of action. One must conclude that however an exstrophy is treated, by reconstruction or diversion, we must accept the child as a patient for the rest of our professional careers, as follow-up will be essential no matter what course we take.

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AN ANALYSIS OF 59 CASES OF TRACHEAL STENOSIS FOLLOWING TRACHEOSTOMY WITH CUFFED TUBE AND ASSISTED VENTILATION, WITH SPECIAL REFERENCE TO DIAGNOSIS AND TREATMENT

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SUMMARY

An analysis of 59 cases of tracheal stenosis after tracheostomy with cuffed tube and assisted ventilation is reported. Special emphasis is placed upon diagnosis and treatment. The detection of severe strictures is usually easily achieved, but mild to moderate degrees of stenosis may present difficulties in diagnosis and may remain undetected for some time.

Management of the strictures included dilatation (14 cases), segmental tracheal resection with primary end-to-end anastomosis (34 cases), staged plastic reconstruction (2 cases), and permanent tracheostomy (4 cases). No treatment was given in 5 cases.

Dilatation achieved a good result in 6 cases and a satisfactory one in 8. Of 34 strictures treated by segmental resection, a good result was obtained in 29 cases, although 7 required a second operation for restenosis. Three cases had an unsatisfactory result and there were 2 operative deaths. Postoperative complications are discussed.

Mild strictures may be satisfactorily managed by dilatation, but some mild strictures and all severe strictures are best treated by segmental resection with primary end-to-end anastomosis. Segmental defects ranging from 0·5 to 5·5 cm. in length can be satisfactorily resected.

TRACHEOSTOMY with cuffed tube and assisted ventilation has been used with increasing frequency in the management of respiratory insufficiency over the past 15 years, and tracheal stenosis has become a well-recognized complication of this type of therapy (Deverall, 1967; Gibson, 1967; Pearson, Goldberg, and da Silva, 1968; Grillo, 1970; Andrews, 1971; Andrews and Pearson, 1971). The present paper is an analysis of 59 symptomatic tracheal strictures treated at Toronto General Hospital between 1963 and 1970, and the diagnosis and treatment of these strictures are discussed. Thirty-two of the strictures were seen during a 3-year period of a prospective study which was designed to determine the true incidence of this complication, and to clarify the pathogenesis of tracheal injury in those patients requiring tracheostomy and assisted ventilation. The results of this prospective study have been previously reported (Andrews, 1971; Andrews and Pearson, 1971).

MATERIAL

Fifty-nine symptomatic tracheal strictures were treated by the Thoracic Surgical Service at Toronto General Hospital during the 8-year period 1963–70. Thirty-five strictures occurred at the site of the original tracheostomy, and 24 occurred at the level of the inflatable cuff of the tracheostomy tube.

Tables I and *II* summarize some pertinent data relating to the 59 tracheal strictures.

Table I.—DETAILS OF THE 59 PATIENTS WITH TRACHEAL STRICTURES IN THE PRESENT SERIES

	STOMAL STRICTURES (35 cases)	CUFF STRICTURES (24 cases)
Sex		
Male	22	9
Female	13	15
Age		
Range	17–76	15–83
Mean	52·0	45·5
Size of tracheostomy tube		
Male		
Range	11–14	11–14
Mean	12·6	12·0
Female		
Range	9–13	9–13
Mean	10·9	11·0
Duration of intubation (d.)		
Range	4–330	7–42
Mean	30	18

The prospective study mentioned previously (Andrews, 1971; Andrews and Pearson, 1971) indicated the following conclusions:—

1. Tracheostomy tubes of large diameter were associated with an increased incidence of strictures at the level of the original tracheostome.
2. The presence of airway infection predisposes to stomal, and probably to cuff, stenosis formation.
3. Females had a significantly higher incidence of strictures at the level of the inflatable cuff of the tracheostomy tube.
4. Older patients and those with pre-existing lung disease might be more likely to develop stomal stenosis.
5. The duration of cuffed-tube tracheostomy with assisted ventilation did not appear to be important in the development of tracheal stenosis.

The data recorded in *Tables I* and *II* show similarities to those obtained from the prospective study. The sex ratio, mean age of patient, mean size of tracheostomy tube used, and percentage of patients with pre-existing lung disease in both the stomal and cuff stenosis groups are similar to those found in the prospective study.

Table II.—Conditions requiring Tracheostomy and Assisted Ventilation and the Presence of Pre-existing Lung Disease in 59 Patients with Tracheal Strictures in the Present Series

	Stomal Strictures (35 cases)		Cuff Strictures (24 cases)	
	No	Per cent	No	Per cent
Conditions requiring tracheostomy and assisted ventilation				
Chest trauma	10	28 6	10	41 7
Postoperative respiratory insufficiency	13	37 5	6	25 0
Acute and chronic lung diseases	9	25 7	4	16 7
Miscellaneous	3	8 2	4	16 7
Presence of pre-existing lung disease	24	68 6	12	50

DIAGNOSIS OF TRACHEAL STRICTURES

Symptoms and Signs.—Awareness of the complication of tracheal stenosis following tracheostomy and assisted ventilation facilitates diagnosis. However, detection of severe degrees of stenosis should not be difficult since these patients have stridor at rest, usually predominant during inspiration, but this only occurs when the tracheal lumen is reduced to a diameter of 5 mm. or less.

The mild or moderate degrees of tracheal stenosis are more difficult to diagnose. Stridor at rest is usually absent and may become apparent only on exertion or on rapid, deep breathing. However, dyspnoea on exertion is almost an invariable complaint with these milder degrees of stenosis but may be overlooked in patients with chronic respiratory disease (36 out of 59 strictures in the present series), who may have had this symptom prior to tracheostomy. Patients with chronic chest diseases often have a chronic cough with sputum and may find difficulty in raising their secretions if they develop a tracheal stricture. A characteristic brassy cough is also common in patients with functionally significant tracheal narrowing.

Most of the 59 strictures in this series were recognized by the presence of the symptoms and signs detailed above. In fact, 40 patients had stridor at rest, and a further 9 had stridor elicited on rapid, deep breathing. Fifty patients had dyspnoea on exertion, and 31 had difficulty in raising their secretions. The presence of the characteristic brassy cough was recorded in only 5 patients. Forty-five of the 59 strictures (76·5 per cent) were diagnosed clinically, 4 (6·8 per cent) were diagnosed by bronchoscopy, and 10 strictures (17 per cent) were recognized on routine radiography.

One of the 4 cases diagnosed bronchoscopically was recognized at routine bronchoscopy performed on all the patients in the prospective study (Andrews, 1971; Andrews and Pearson, 1971) at the time of the final removal of the cuffed tracheostomy tube.

Nine of the 10 strictures diagnosed radiologically were recognized by the use of routine radiography in the prospective study, and the tenth stricture was recognized on routine chest radiography.

The length of time between extubation and the recognition of stenosis varied between 1 day and 2 years. Details are summarized in *Table III*. It is apparent that about half of the strictures were recognized within 1 month of the final removal of the cuffed tracheostomy tube, and that the majority of the strictures were recognized within 3 months of extubation (49 strictures; 83 per cent).

Table III.—Length of Time between Extubation and Recognition of Stenosis in 59 Patients

Time after Extubation	No. of Strictures recognized	Time after Extubation	No. of Strictures recognized
0–1 wk	6		
1–2 wk	5	0–2 wk	11
2–4 wk	17	0–1 mth.	28
1–2 mth.	17	0–2 mth.	45
2–3 mth.	4	0–3 mth	49
3–6 mth	4	0–6 mth	53
6–12 mth	3	0–12 mth	56
1–2 yr.	3	0–2 yr	59

Precise Diagnosis.—The definitive diagnosis of tracheal stenosis was established at bronchoscopy (usually performed under local anaesthesia) or by the use of tracheal tomograms or cine-tracheograms.

Bronchoscopy allowed assessment of the state of the stricture, special attention being directed to the pliability or rigidity of the stricture, to the presence or absence of coexistent inflammation or ulceration, and to whether the stricture was epithelialized or mature. Often bronchoscopic assessment allowed determination of the level of the stricture (i.e., at the site of the original tracheostome or at the level of the inflatable cuff of the tracheostomy tube). However, accurate perception of the depth or length of a stricture through a bronchoscope is difficult, and the exact position and length are best defined by either tracheal tomograms or, better still, by cine-tracheograms.

Bronchoscopy was used in the precise diagnosis of 30 of the 59 strictures (51 per cent), tomograms in 18 of the strictures (30·5 per cent), and cine-tracheograms in 11 cases (18·5 per cent).

The lengths of the strictures recorded by this precise diagnosis varied from 0·5 to 5·5 cm. (*Fig.* 1), and the diameter of the tracheal lumen was reduced to 5 mm. or less in 40 strictures (68 per cent), whilst the remaining 19 strictures (32 per cent) all had their airway diameter reduced by 50 per cent or more.

THE MANAGEMENT OF TRACHEAL STRICTURES

The management of each of the 59 symptomatic tracheal strictures fell into one of the categories outlined in *Table IV*.

The severity of the stricture is the major factor in deciding which method of treatment to use. Severe strictures (characterized by stridor) in which the diameter of the tracheal lumen is reduced to 5 mm. or less tend to be treated surgically (segmental resection or plastic reconstruction) since there is no evidence that they can be managed nearly as effectively by dilatation (Grillo, 1970), although dilatation is usually used to maintain a satisfactory airway while awaiting the optimum time for surgical intervention. Mild or moderate degrees of stenosis (characterized by an absence of stridor but having exertional dyspnoea and difficulty in raising sputum) in which the tracheal luminal diameter is greater than 5 mm. but less than 50 per cent of normal are usually treated by dilatation.

Table IV.—MANAGEMENT OF 59 CASES OF TRACHEAL STRICTURE

	No of Cases
1 Dilatation	
Endoscopic	11
Long tracheostomy tube	1
Laryngeal stent	2
2. Segmental resection (often preceded by dilatation)	
Circumferential	32
Wedge	2
3. Staged plastic reconstruction	2
	1 (plus 1 after failed segmental resection)
4. Tracheostomy	
Awaiting resection	8
Permanent	4
5 No treatment	5

Table V.—TREATMENT OF 14 TRACHEAL STRICTURES BY DILATATION

Type of Dilatation	*No. of Cases*
Endoscopy	8 stomal strictures 3 cuff strictures
Long tracheostomy tube	1 cuff stricture
Laryngeal stent	2 stomal strictures

Results. Good 6; satisfactory 8.

1. **Dilatation.**—Dilatation was used as the initial step in the treatment in almost all of the 59 cases of tracheal stricture. It was usually achieved by oral bronchoscopy using the bronchoscope as a dilator. The number of dilatations required, and the frequency with which they were performed, varied from case to case and was determined by the progress achieved.

Three patients with strictures at the level of the cuff of the tracheostomy tube had their tracheostomy re-established through the original cervical stoma and a metal tube of large diameter and appropriate length was passed through the stenosis as a method of achieving dilatation. A 5-month period of this type of dilatation was successful in 1 patient; the other 2 patients ultimately required segmental resection of the stricture after 4 months of attempted dilatation.

Re-establishment of the tracheostomy was required in 2 further patients so that a laryngotracheal stent could be used to achieve dilatation.

Table V summarizes the management of 14 tracheal strictures treated solely by dilatation. In general, management by dilatation alone was successful in the patients with mild to moderate degrees of stenosis, and in fact only 1 of the 14 cases had a tracheal luminal diameter of less than 5 mm. Restoration of a satisfactory airway was achieved in all 14 cases, and 8 of these had no clinical evidence of a reduced airway diameter.

2. **Segmental Resection of the Trachea with Primary End-to-end Anastomosis.**—In 34 of the 59 strictures (57·5 per cent) (16 strictures at the level of the original tracheostome, 18 at the level of the inflatable cuff) adequate treatment of the stricture ultimately required a local segmental resection of the tracheal stricture with reconstruction by primary end-to-end anastomosis. Operative details have been reported in a previous publication (Pearson and Andrews, 1971) and are similar to those used by others (Flavell, 1959; Mathey, Bines, Galey, Evrard Lemoine, and Denis, 1966; Gibson, 1967; Grillo 1970). The majority of the 34 cases had strictures classified as severe (diameter of the tracheal lumen reduced to 5 mm. or less), and only 3 of the strictures requiring resection had a tracheal luminal diameter greater than 5 mm.

Most of the 34 cases had initial treatment by some form of dilatation but without adequate improvement. The length of time over which dilatation was attempted prior to segmental resection varied from 1 week to 1 year (*Table VI*). The number of dilatations used in each patient was between one and ten, although 4 patients had multiple dilatations prior to resection. Two patients were dilated by a long tracheostomy tube prior to segmental resection and 6 other patients required tracheostomy.

Segmental resection of the stricture was the treatment of choice in most of the 34 strictures and was not used simply because dilatation had failed to restore a satisfactory airway. In the majority of severe strictures dilatation cannot achieve a satisfactory result, but repeated bronchoscopic dilatation can maintain an adequate airway until such time as segmental resection can be performed under favourable conditions.

Table VI.—LENGTH OF TIME OF ATTEMPTED DILATATION PRIOR TO SEGMENTAL RESECTION IN 34 CASES

Time of Dilatation (mth.)	*No of Cases*
0–1	14
1–2	10
2–6	8
6–12	2

Segmental resection and tracheal anastomoses are best performed through healthy rather than through softened, inflamed, and infected tissues so that the complication of restenosis is avoided. Endoscopic dilatation was used to maintain an adequate airway until the gross inflammatory changes found above and below the stricture had subsided and re-epithelization of the trachea had occurred. The stricture itself did not always epithelialize but segmental resection was delayed if possible until inflammation appeared minimal.

Operative Exposure.—Details of the operative technique used have been described in a previous publication (Pearson and Andrews, 1971). A cervical (collar) incision allows adequate exposure of the trachea to the mid-mediastinal level and was the most commonly used incision (28 out of 34 cases). During the early part of the series median sternotomy was used with the collar incision (3 cases) since it allows access to the entire trachea. It has since been found to be unnecessary, since with correct techniques a sufficient length of the mediastinal trachea is exposed with the collar incision. In 3 cases in which exposure of the distal 5 cm. of the mediastinal trachea was required, median sternotomy (1 case), right posterolateral thoracotomy (1 case), and median sternotomy with right posterolateral thoracotomy (1 case) were used for operative exposure.

Length of Trachea resected.—Circumferential segments of strictured trachea were resected in 32 cases nd 2 lesions were managed by anterolateral wedge esection with preservation of the normal posterior membranous trachea. The length of trachea esected varied between 0·5 and 5·5 cm. There was ood correlation between the length resected at operation and the length of the trachea shown to be nvolved in the stricture measurements of the radiographs (tracheal tomograms and cine-tracheograms), s may be seen from *Fig.* 1.

Pathology.—Of the 34 strictures resected (16 at he level of the tracheostome, 18 at the level of the nflatable cuff), 28 (12 at the stomal level, 16 at the uff level) were fibrous strictures (i.e. of a rigid and ibrous nature) and 6 (4 at the stoma, 2 at the cuff) were collapsing or malacic, the tracheal wall remaining soft and pliable at the level of the defect owing to oss of cartilaginous support of a short segment of the tracheal wall.

At operation a sufficient length of trachea was esected on either side of the stricture to allow rimary end-to-end anastomosis through healthy pithelialized trachea rather than through softened, nflamed, and infected tissue. The cut ends of the rachea were examined and categorized as inflamed, ot epithelialized, or healthy and epithelialized.

Twenty-five strictures (11 stomal, 14 cuff) were esected at the optimum time, the anastomosis being erformed through healthy epithelialized tissue, preoperative dilatations having been continued until the tricture was mature and inflammation in and round the stricture had subsided. Five patients (2 tomal, 3 cuff strictures) had anastomoses performed hrough inflamed tissue, 2 patients (both cuff trictures) had anastomoses performed through nepithelialized trachea, and in 2 cases (both cuff trictures) the state of the cut ends was not recorded.

The Results of Segmental Resection with Primary End-to-end Anastomosis.—*Table VII* summarizes the esults of segmental resection of 34 tracheal strictures

Table VII.—Results of Segmental Resection of 34 Strictures

Result	16 Stomal Strictures	18 Cuff Strictures
Good	13 (including 3 reoperations)	16 (including 2 reoperations)
Unsatisfactory	2	1 (after reoperation)
Deaths	1	1 (after reoperation)
Reoperation	3	4

with primary end-to-end anastomosis. There were 9 good results and these patients had complete bsence of symptoms or signs of airway obstruction no stridor, dyspnoea on exertion, or retention of racheobronchial secretions) following operation, and ad an airway diameter greater than 50 per cent of normal in all radii at the site of the end-to-end nastomosis. None of these patients was lost to ollow-up, which consisted of clinical assessment and racheograms obtained at least 6 months after operation.

There were 3 unsatisfactory results. One of these ollowed a wedge resection of a stomal stricture; a moderate degree of restenosis occurred at the site of anastomosis and was being treated by endoscopic dilatation at the time of the patient's suicide. A second unsatisfactory result followed a circumferential wedge resection of a 3-cm. length of cuff stricture. The anastomosis was performed through inflamed trachea on each side of the anastomosis and an early postoperative anastomotic dehiscence occurred with extensive loss of trachea on both sides of the anastomosis. The resulting long defect required reconstruction, which was performed by Dr. H. C. Grillo in Boston using his own technique of staged replacement with bipedicled skin-flaps (Grillo, 1970). The third unsatisfactory result followed a severe degree of infection in the anastomotic site during the immediate postoperative period with a resultant moderate degree of symptomatic restenosis in a debilitated patient. A second operation was not recommended.

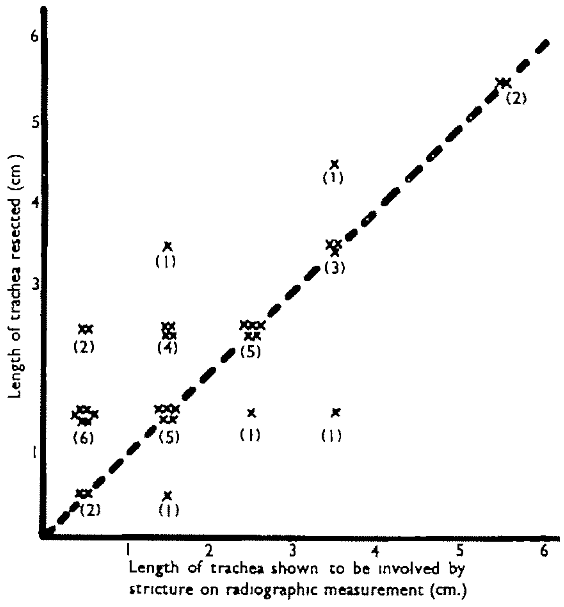

Fig. 1.—The correlation between the length of trachea resected at operation and the length of trachea shown to be involved by stricture on radiographic measurement.

One of the 2 operative deaths should have been avoided, the patient having an hypoxic cardiac arrest following the development of unrecognized laryngeal oedema and airway obstruction due to a haematoma in the neck wound in the immediate postoperative period. The other operative death was caused by erosion of the adjacent innominate artery 12 days after a second resection for restenosis of the mediastinal trachea.

Second Operation for Restenosis.—Seven of the 34 patients managed by segmental resection and primary anastomosis developed significant restenosis at the anastomosis (3 stomal strictures, 4 cuff strictures). Restenosis probably results from performing the anastomosis through an inflamed and infected trachea (4 cases). On the other hand, 3 patients having an anastomosis performed through unhealthy trachea tissue did not develop restenosis. Extensive mobilization may impair the circulation of the trachea, resulting in restenosis (3 cases).

Of the 7 patients requiring reoperation, 5 had a good result following the further segmental resection, 1 required staged reconstruction (as previously mentioned), and 1 died from erosion of the adjacent innominate artery 12 days after operation.

Postoperative Complications of Segmental Resection with Primary End-to-end Anastomosis.—

Dehiscence of the Anastomosis: Partial or total dehiscence of the primary end-to-end anastomosis may occur in the postoperative period (usually because the anastomosis was performed through unhealthy tracheal tissue) and results in restenosis. Seven of the 34 cases treated by segmental resection developed a partial dehiscence (3 had inflamed tissue included in the anastomosis and in 1 the tracheal wall used for anastomosis was not epithelialized). In 5 of these subsequent restenosis was severe enough to warrant reoperation, and in 2 the subsequent stenosis was satisfactorily treated by endoscopic dilatation.

Ischaemia of the anastomosis: Local ischaemia of the anastomotic site may have resulted from the extensive mobilization of the trachea, with subsequent impairment of the blood-supply, that is required in the resection of longer strictures. The local ischaemia caused restenosis either as a direct consequence (3 cases) or by bringing about partial dehiscence of the anastomosis (2 cases). In 3 cases of restenosis caused by ischaemia further operation was required and 2 other cases accounted for 2 of the unsatisfactory results of segmental resection already cited.

Infection of the anastomosis: In 1 case gross infection of the anastomosis was added to local ischaemia and resulted in a degree of restenosis which accounted for the third unsatisfactory result of segmental resection.

Haematoma formation: Two patients had a haematoma develop in the operative wound in the immediate postoperative period. In 1 of the patients it was unrecognized and resulted in obstruction of the airway which was followed by a fatal hypoxic cardiac arrest. The formation of a haematoma was recognized in the second patient. Evacuation and ligation of a small bleeding artery were performed.

Erosion of the adjacent innominate artery: In 1 case requiring further surgery for restenosis in the mediastinal trachea death occurred on the twelfth postoperative day following erosion of the adjacent innominate artery at the site of tracheal anastomosis. Infection was presumably the precipitating factor.

3. **Staged Plastic Reconstructions.**—A staged plastic reconstruction using pedicled flaps of cervical skin was used in 2 patients. Both strictures were in the subglottic area and extended above the lo border of the thyroid cartilage. Lesions at this le are not amenable to segmental resection and very difficult to manage effectively. One patient ha good result following this type of procedure and now asymptomatic. The other patient is m improved but has some clinical evidence of air obstruction. A third patient was treated by Dr. H. Grillo using a staged replacement with bipedic skin-flaps to deal with a restenosis after an early po operative anastomotic dehiscence following segmen resection with primary end-to-end anastomosis.

Details of the operative management of th patients will be reported subsequently. This type staged plastic reconstruction has been repor previously by McComb (1967) and Grillo (1969)

4. **Tracheostomy.**—Eight patients requi tracheostomy to relieve their airway obstruction u inflammation in and around their strictures subsided and segmental resection could be satisf torily performed. In these cases endoscopic dilatati could not maintain a satisfactory airway. This particularly true with collapsing or malacic strictu

Four further patients were so debilitated tha permanent tracheostomy was considered to be only feasible treatment. All 4 have since died of th primary disease.

5. **No Treatment.**—There were 5 patients had no treatment for their strictures. Two of th refused treatment for their severe stomal strictu and later died from airway obstruction due to acute episode of retained tracheobronchial secreti blocking an already compromised tracheal lum Another patient also refused treatment and still dyspnoea on exertion and difficulty in raising sputum. Two other patients have died of th primary condition since diagnosis of their stricture

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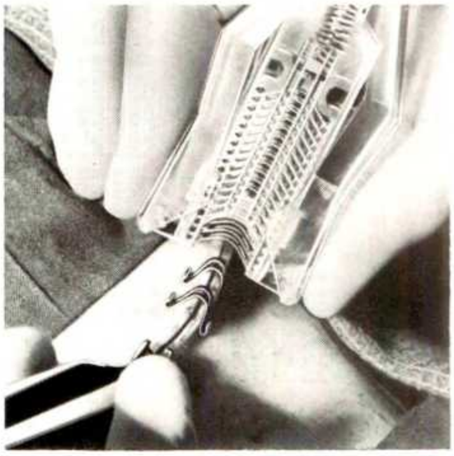

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ACALCULOUS GALL-BLADDER DISEASE

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SUMMARY

A prospective study of 130 consecutive unselected patients submitted to cholecystectomy for biliary disease has been made. Nineteen patients (14·6 per cent) were found to have acalculous gall-bladder disease. The clinical history of these patients did not differ significantly from those with calculous disease, whilst the radiological and histopathological findings in this group were variable.

Eleven of these 19 patients were completely relieved of their symptoms by surgery and it appeared that cholecystectomy was most successful in the patients with a history of either severe pain or previous acute cholecystitis. It is concluded that chronic gall-bladder disease may be acalculous and that, despite the lack of a homogeneous pathological background, surgery is of considerable value in a high proportion of such cases.

THE association between chronic gall-bladder disease and gall-stones, though not fully understood, is well recognized, and few would dispute that patients with biliary symptoms and demonstrable calculi are best treated by cholecystectomy. The condition of acalculous biliary disease is, however, less widely accepted. Several series of patients with acalculous gall-bladder disease have been reported (Mackey, 1934; Glenn and Mannix, 1956; Hoerr and Hazard, 1966; Munster and Brown, 1967), but these have all suffered from being retrospective and the reports have tended to leave in doubt the true proportion of cases in which stones were definitely absent. It is thus not surprising that the existence of acalculous biliary disease has been doubted by many who would maintain that such a diagnosis reflects either an error in investigation or a failure to recognize associated conditions responsible for the symptoms (Clark, 1968); proponents of this view maintain that the results of cholecystectomy are uniformly bad in patients in whom gall-stones are not demonstrable and it is, therefore, understandable that many surgeons are reluctant to operate on such cases (Glenn and Mannix, 1956).

Between December, 1968, and April, 1970, a prospective study of all the patients undergoing biliary surgery (excluding those operated on for malignant disease) in one surgical unit at the Manchester Royal Infirmary was undertaken. A full preoperative examination of each patient was made by one of us (A. G.), and detailed findings at operation, including those noted on operative cholangiography, were recorded; these were later correlated with the radiological and histopathological data. All the patients were followed up for a period of between 12 and 20 months after operation with a mean follow-up time of 15 months.

A surprisingly high proportion of these patients were found to have chronic acalculous biliary disease. The absolute number of such cases was small, but because of the doubts that surround this clinical entity we thought it worth while to record and analyse our experience of this group of patients.

FINDINGS

Incidence.—During the period of study 130 patients were submitted to cholecystectomy and in 19 cases (14·6 per cent) no stones were present in the biliary system. In a further 4 patients stones were present in the common bile-duct but not in the gall-bladder; such cases were not included in this series.

Clinical Features.—All the patients with acalculous biliary disease were Caucasian. There were 15 women and 4 men and the age-range was from 27 to 64 years (median age 47 years; mean age 46·8 years).

The duration of symptoms before surgery ranged from 1 month to 17 years with a mean duration of just over 3 years. All the patients had suffered pain, and in 11 patients this was described as severe; in 3 patients the pain was of moderate intensity, whilst in 5 the pain was described as mild or as an ache. The pain was in the upper abdomen except in 1 patient who had retrosternal pain, and in 10 patients the pain radiated through to the scapular regions. In 12 patients the pain was associated with vomiting; 3 patients seen during an attack of pain had clinical signs of acute cholecystitis.

Biochemical Findings.—Three patients had a raised serum bilirubin at some stage of their illness (levels of 1·3, 2·9, and 5 mg. per cent respectively), with an obstructive cause suggested by the serum-transaminase and alkaline-phosphatase readings. A further 7 patients had a raised serum alkaline phosphatase ranging from 16·5 to 20 K.A. units.

Radiology.—A preoperative cholecystogram or intravenous cholangiogram was performed on all but 1 of the patients. In 5 cases the gall-bladder was reported as non-functioning or as showing only minimal opacification. In 3 cases a polyp was visualized on cholecystography and in a further 2 cases the presence of a polyp was queried but could not be confirmed because of poor opacification of the gall-bladder. In 2 patients it was thought that stones were visible in the gall-bladder on cholecystography but in 1 of these opacification was poor and the evidence for the presence of a stone was unconvincing; in the other patient, however, several small stones did appear to be visible. In 3 patients septa were seen in the gall-bladder but in only 1 of these did the appearances suggest adenomyosis. In 3 patients the cholecystogram showed an apparently normal gall-bladder.

Histopathology.—Six of the removed gall-bladders were histologically normal whilst 4 showed an active chronic inflammation; mucosal hyperplasia was present in 7 gall-bladders whilst cholesterolosis was found in 3, in 2 cases this being coexistent with a mucosal hyperplasia.

Results of Surgery.—Eleven of the 19 patients were completely relieved of their symptoms by cholecystectomy whilst 5 showed no improvement. One patient was symptom-free for 20 months after her operation but then suffered a return of her symptoms. One further patient gained only slight relief of her symptoms from surgical intervention, whilst 1 patient died in the immediate postoperative period from a cerebral haemorrhage.

Table I.—DETAILS OF THE PATIENTS WHOSE SYMPTOMS WERE COMPLETELY RELIEVED BY CHOLECYSTECTOMY

AGE AND SEX	DURATION OF SYMPTOMS	SEVERITY OF PAIN	CLINICAL ACUTE CHOLECYSTITIS	RADIOGRAPHIC FINDINGS	PATHOLOGY
48 F.	7 yr.	Severe	No	Polyp seen	Mucosal polyp
44 F.	7 mth.	Severe	No	Normal	Normal
47 M.	8 mth.	Severe	Yes	? Small stones	Mucosal hyperplasia
37 F.	5 mth.	Moderate	Yes	Minimal opacification	Mucosal hyperplasia
32 F.	17 yr.	Severe	No	Non-functioning gall-bladder	Active chronic inflammation
56 F.	10 yr.	Severe	No	Septum present	Mucosal hyperplasia
56 F.	2 yr.	Severe	No	2 polypi seen	Mucosal hyperplasia + cholesterolosis
43 M.	5 mth.	Severe	Yes	Non-functioning gall-bladder	Active chronic inflammation
51 F.	4 yr.	Severe	No	Doubtful polyp reported	Normal
38 F.	16 mth.	Severe	No	Septum	Normal
62 F.	7 mth.	Severe	No	Polyp	Cholesterolosis, cholesterol polyp

Table II.—DETAILS OF THE PATIENTS WITH A POOR RESPONSE TO CHOLECYSTECTOMY

AGE AND SEX	DURATION OF SYMPTOMS	SEVERITY OF PAIN	CLINICAL ACUTE CHOLECYSTITIS	RADIOGRAPHIC FINDINGS	PATHOLOGY
64 F.	6 mth.	Mild	No	Minimal opacification	Active chronic inflammation
52 F.	8 mth.	Mild	No	Doubtful polyp reported	Normal
57 F.	7 mth.	Mild	No	? Stone	Normal
27 F.	1 yr.	Mild	No	Septum	Mucosal hyperplasia
47 F.	3 yr.	Mild	No	Normal	Cholesterolosis + mucosal hyperplasia
35 F.	5 yr.	Severe	No	Normal	Normal
35 M.	4 yr.	Mild	No	Not done	Mucosal hyperplasia
59 M.	1 mth.	Mild	No	Non-functioning gall-bladder	Active chronic inflammation*

* Patient died postoperatively from cerebral haemorrhage.

Correlation of Clinical Features and Results of Surgery.—An attempt was made to correlate the results obtained by cholecystectomy in acalculous biliary disease with the clinical history, the radiological investigations, and the histopathology of the removed gall-bladder. The results are shown in *Tables I* and *II*.

DISCUSSION

The results in this series suggest that stones are absent from the biliary tract of a relatively high proportion of patients with symptoms suggestive of chronic biliary disease and that such patients often benefit considerably from cholecystectomy. It is emphasized that each gall-bladder in this series was opened immediately after removal and the presence or absence of stones was noted at that time. We believe that retrospective examination of case notes does not clearly show which gall-bladder contained stones and that most retrospective series probably underestimate the true incidence of gall-stones.

A surgeon is, therefore, going to be faced with patients in whom a history strongly suggestive of gall-bladder disease is apparently belied by an absence of demonstrable calculi. It is recognized, of course, that it is not possible in every case to come to a firm conclusion about the absence or presence of stones preoperatively; it is well known, for example, that a normal cholecystogram may be found in patients with a stone in the cystic duct (Large, 1968), whilst faulty opacification of the gall-bladder may leave the issue in doubt. Nevertheless, the operative results reported here indicate that, if careful investigation fails to reveal disease elsewhere, cholecystectomy is a worth-while procedure in acalculous cases. Eleven of the 18 surviving patients in this series were completely relieved of their symptoms by surgery, a result which, whilst not as good as that achieved by operating on calculous gall-bladders, is nevertheless in opposition to the view that cholecystectomy is rarely of value in acalculous patients.

It is, therefore, unfortunate that these patients do not form a homogeneous group and that relatively few factors emerge from this study which could indicate to the surgeon those patients in whom there is a likelihood of success resulting from operative intervention. The symptoms of acalculous gall-bladder disease do not differ in any significant way from those of calculous disease (LeQuesne and Ranger, 1957; Munster and Brown, 1967), but quite a high proportion of patients with acalculous disease complain of severe pain and it is these who benefit most from cholecystectomy; thus, whilst 10 out of 11 patients with severe pain obtained complete symptomatic relief from surgery this was true for only 1 out of 7 patients with mild pain. A further point that may indicate a successful outcome from surgery is a history of acute cholecystitis; all the patients in this series who suffered a clinical attack of acute cholecystitis became completely symptom-free after operative treatment.

The radiological findings in this series were varied. Patients with normal cholecystograms do not usually benefit from cholecystectomy (Glenn and Mannix, 1956; Cronin and Middleton, 1963), and indeed only 1 out of 3 such patients in our series improved following operation. This is not to say that a normal cholecystogram indicates a normal gall-bladder (Large, 1968), and it is worth adding that gall-bladders containing cholesterol polyps or even small stones may look and feel normal at operation (Lahey, 1927). Patients with a non-visualized gall-bladder on cholecystography usually benefit from surgery if they have severe biliary symptoms and if there is no reason to suspect failure of absorption or excretion of the contrast medium. In clinically doubtful cases, however, an intravenous cholangiogram or a repeat cholecystogram after an interval of 2–3 months may be rewarding. Presumably, acalculous gall-bladders fail to visualize on cholecystography because of a diseased mucosa, for in 4 out of our 5 cases there was histological evidence of active chronic inflammation.

These were 3 patients with convincing evidence of polyps of the gall-bladder, all of whom had severe symptoms and all of whom improved after cholecystectomy. Two further patients had questionable radiological evidence of polyps, 1 of whom had severe symptoms which were relieved by surgery. Thus, cholecystectomy can be recommended for patients with severe pain and a polyp visible on the cholecystogram. When symptoms are minimal the decision is not so easy. Tabah and McNeer (1953) have indicated the risk of carcinoma developing in papillomas of the gall-bladder, and the problem is made more difficult by the inability to differentiate radiologically between inflammatory, adenomatous, and cholesterol polyps of the gall-bladder (Ochsner, 1962). Most polyps, however, are cholesterol, and Eelkema, Hodgson, and Stauffer (1962) traced 113 out of 226 patients with radiological polyps and found no cases of carcinoma of the gall-bladder after 15 years. Procrastination in these patients would, therefore, seem reasonable although follow-up cholecystography may be wise. LeQuesne and Ranger (1957) advise operation for acalculous cases of adenomyomatosis, and more recently Heald (1970) has emphasized both the need for an awareness of this condition and the good results obtained by cholecystectomy if the patient has severe symptoms. The radiological criteria for the diagnosis of adenomyomatosis have been summarized by Colquhoun (1961). Diverticulae of the gall-bladder are easily seen if looked for, but the significance of a septum is not so easily defined and Jutras (1960) believes many of these to be 'segmented manifestations of hyperkinesis'. Thus, in our series septa up to 3 mm. in width appeared only as a slight narrowing or a waist in the opened gall-bladder.

The histopathological findings in this series were also variable and there was no clear-cut relationship between the histological findings and the results obtained by cholecystectomy. Six of the removed gall-bladders were histologically normal and this incidence of normality is somewhat greater than that found in gall-bladders removed for calculous disease; however, 3 of these patients, all of whom had suffered severe pain, were completely freed of their symptoms by cholecystectomy. The incidence of gall-bladders showing active inflammation was approximately the same as that in calculous gall-bladders seen at this hospital, but 1 of the 3 surviving patients with an actively inflamed gall-bladder failed to improve after surgery. Perhaps the most striking histological feature in this series was the relatively high incidence of mucosal hyperplasia. Mucosal hyperplasia can occur in calculous biliary disease, but the incidence of this histological abnormality in this acalculous series was much higher than that seen in gall-bladders with stones. Primary acalculous mucosal hyperplasia is well recognized and has been claimed by some workers to be a potent cause of biliary symptoms (Jutras, 1960; Elfving, Lehtonen, and Teir, 1967); nevertheless, in the present series there was no clear relationship between mucosal hyperplasia and benefit from cholecystectomy, 4 patients becoming symptom-free after surgery and 3 failing to improve.

It would appear, therefore, that acalculous biliary disease does exist as a clinical entity but that its pathological basis is variable. The surgeon faced with such cases can expect cholecystectomy to produce symptomatic relief in a considerable proportion of patients, this being especially so for those with a history of severe pain or of acute cholecystitis.

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THE INFLUENCE OF THE VAGUS NERVES ON THE BILIAR

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VAGOTOMY has become accepted as a standard operation for the treatment of peptic ulcer during the past 15 years. Although used to treat a specific lesion in the stomach or duodenum, vagus division can have a much wider effect on the digestive system, but little attention has been paid by most surgeons to the effects of the vagus on other organs and it is timely to review the influence of the vagus nerves on the biliary system.

In 1887 Ruggero Oddi suggested that the sphincter which is named after him was partly controlled by a nervous reflex. Since then many anatomists, physiologists, and clinicians have investigated the effects of the vagus nerves on the biliary system. The anatomical distribution of the vagus nerve and its hepatic and coeliac branches has been more thoroughly worked out than have their physiological effects.

ANATOMY

Mitchell (1963) described 'two to four hepatic branches of the anterior vagal trunk or the greater anterior gastric nerve.... It is often possible to trace filaments to the common and cystic ducts and to the gall-bladder.' The posterior vagal trunk gives a large branch to the coeliac plexus. 'Owing to the multiple intricate inter-connections in the coeliac plexus it is impossible to trace the ultimate distribution of individual bundles but the coeliac branch must contain most of the para-sympathetic vagal fibres for abdominal viscera.'

It has been confirmed that in the dog fibres from the left vagus pass by the hepatic branch of the nerve to the gall-bladder, but the destination of fibres in the coeliac branch of the right vagus is still in doubt (Staveney, Kato, Griffiths, Nyhus, and Harkins, 1963).

The common bile-duct and hepatic duct are surrounded by numerous nerve-fibres which extend from the coeliac plexus up to the gall-bladder and down to the region where the bile-duct enters the duodenum (Kirk, 1944; Burnett, Gairns, and Bacsich, 1964; Libman, 1964; Libman and Sutherland, 1966). Kirk (1944) described a constant, well-defined nerve running down the common bile-duct and he thought that it originated in the dorsal vagus nerve.

PHYSIOLOGY

The evidence for neurological control of the gall-bladder and sphincter of Oddi is mainly circumstantial and has been derived from animal experiments and clinical studies.

Oddi (1887) observed that sphincter resistance was increased after irritating the duodenal mucosa and postulated the existence of a nervous reflex through the spinal cord.

Mitchell and Steifel (1916) considered that the sphincter response to vagal stimulation was equivocal, but Westphal (1923), after experimen
pigs, concluded that vagal stimulat
gall-bladder contraction and rela
sphincter of Oddi. Best and Hicken
Doyen (1894), who wrote 'excitatio
nerves provoked dilatation of the sphin
surrounding the lower end of the co
parallel to the contraction of the gal
(1934) reviewed the current concepts
and common bile-duct innervation.
that 'reciprocal innervation' between
and the sphincter of Oddi probab
stimulation of the vagus probably cau
of the gall-bladder and relaxation of

Lueth (1931) stimulated the vagal
He recorded on different occasions a
bile-duct pressure with stimulation of
or left vagus nerve. Cutting the right
in a fall in pressure in 6 dogs and a ris
1 dog, while cutting the left vagus h
the pressure.

Johnson and Boyden (1943) infer
experiments on cats that the righ
contained both motor fibres to the g
inhibitory fibres to the sphincter of O
left vagus nerve contained only mot
gall-bladder. They suggested that th
true in man.

Watts and Dunphy (1966) stimul
thoracic vagal trunks and measured th
pressure in isolated segments of the co
in dogs. They found that the press
fall within 2–3 seconds of applying
they were unable to demonstrate a sig
of pressure change or to explain w
were inconsistent.

Wyatt (1967), who worked in Dunp
obtained evidence in the dog of a
between the gall-bladder and the sp
and between the gastric antrum, the je
sphincter. Both electrical stimulation
irritation of the gall-bladder and an
reflex relaxation of the sphincter of Od
the duodenum produced equivocal
then excised the coeliac ganglion and
abolished the gall-bladder sphincter
division of the common bile-duct near
with the cystic duct. Division of the d
did not affect the reflex. He postulat
reflex arc mediated through the nerv
the cystic duct, upper common bi
coeliac ganglion, and thence to the sp
Vagotomy or splanchnicectomy did n
reflex.

Two papers published in 1969 repo
experimental results. Schein, Rosen
Gleedman (1969) recorded a fall in
'choledochoduodenal junction' passa
the dog in response to total bilateral tr

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* Present address: County Hospital, York.

suggesting that the vagi act to maintain both sphincter and gall-bladder tone. This was supported by the observation that intravenous pilocarpine causes a rise in pressure in the dog after vagotomy. (Pilocarpine is a parasympathetic drug.) It is, however, pertinent to note that Lueth in 1931 showed that the intraduodenal pressure rose after administering pilocarpine, and it was possibly this rise in duodenal pressure which stopped the bile-flow in the experiments of Schein and others (1969). In contradiction to those results Williams and Huang (1969) recorded the gall-bladder pressure of fasting dogs before and after bilateral vagotomy and found a significant rise in pressure and a concomitant increase in gall-bladder volume. They concluded that these changes were due to increased sphincter resistance, suggesting that the vagi had an inhibiting influence on the tone of the sphincter of Oddi.

It is evident from these apparently contradictory results that the various investigators have been conducting experiments which were insufficiently controlled or else not comparable in the terms of their results. Several sources of error or confusion are definable in most of the experiments.

Stimulation of the vagal trunks, which are mixed nerves with a wide distribution, produces responses which are not confined to the biliary tract. Gastric secretions entering the duodenum could cause changes in the common bile-duct pressure, and studies under anaesthesia, though initially easier to carry out, may produce abnormal results.

In order to eliminate some of these sources of possible error and confusion Hopton and White (1971) prepared dogs with electrodes affixed to the hepatic and coeliac branches of the vagus nerves. A cannula was placed in the common bile-duct through the cystic duct stump and the gall-bladder was removed. A Thomas fistula (gastric-antral fistula; Thomas, 1941) was fashioned and the animals were allowed to recover for 2 weeks.

In 200 electrical stimulations of the hepatic and coeliac nerves using various currents and frequencies no change in the common bile-duct pressure which was attributable to the stimulation was recorded. The dogs were fully conscious throughout these studies and duodenal stimulation from gastric secretions was eliminated by drainage through the Thomas fistula. This study suggests that the vagal branches do not have a direct effect on the tone of the sphincter of Oddi.

CLINICAL EVIDENCE

The clinical interest in this apparently esoteric topic arises because of the well-documented evidence that the gall-bladder dilates after gastrectomy or vagotomy (Johnson and Boyden, 1952; Cox, Doherty, and Kerr, 1958; Griffith, 1962; Burge, 1964; Ruddick and Hutchinson, 1964). (During a gastrectomy the left gastric artery is ligated and thus damage or interruption of the hepatic branch of the left vagus nerve and of the coeliac branch of the posterior vagal nerve is usually present.)

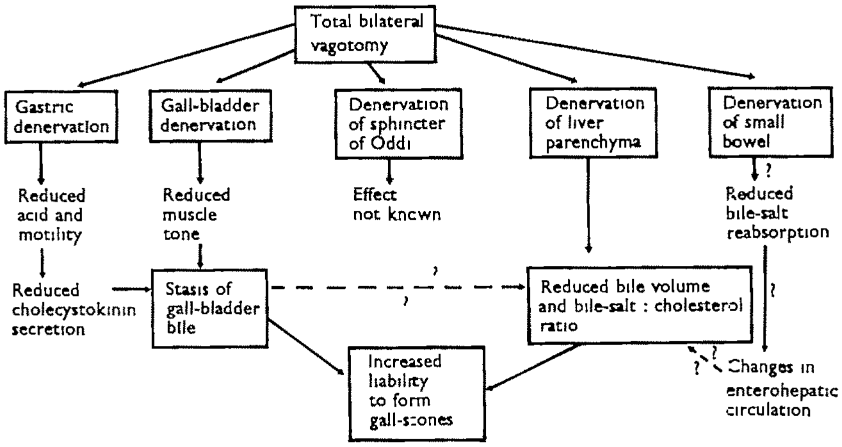
Total bilateral vagotomy
Gastric denervation
Gall-bladder denervation
Denervation of sphincter of Oddi
Denervation of liver parenchyma
Denervation of small bowel
Reduced acid and motility
Reduced muscle tone
Effect not known
?
Reduced bile-salt reabsorption
Reduced cholecystokinin secretion
Stasis of gall-bladder bile
?
?
Reduced bile volume and bile-salt : cholesterol ratio
?
Increased liability to form gall-stones
? ? Changes in enterohepatic circulation

FIG. 1.—Probable effects of vagotomy on the biliary system.

Griffith (1962) and Burge (1964) have also suggested that any effect on the gall-bladder would be abolished if only a selective vagotomy were carried out, so preserving the hepatic branch of the anterior vagus nerve and possibly also the coeliac branch of the posterior vagus nerve. This has been discredited by the work of Tinker and Cox (1969), who showed that gall-bladder emptying in response to insulin-induced hypoglycaemia and cholinergic and hormonal stimulation with carbachol and cholecystokinin was the same in patients after truncal or selective vagotomy.

Evidence of increased disease of the biliary tract after gastric surgery has been described in several papers but this is more difficult to substantiate than the radiological demonstration of gall-bladder dilatation. Krause (1963) found an incidence of biliary disease of 25 per cent occurring after Billroth-I gastrectomy, compared with an incidence of 12–13 per cent after conservative treatment of comparable patients. A smaller increase in biliary disease following Billroth-II gastrectomy was reported by Lundman, Orinius, and Thorsen (1964) and Schrieber and Luchman (1965). Nobles (1966) recorded an 18·2 per cent incidence of biliary disease in patients 12 years after vagotomy and gastro-enterostomy. Possibly more significant than the overall percentage is the apparent change in the sex ratio of gall-stone formation. In control subjects the female-to-male ratio was

5·8 : 1, but after Billroth-I gastrectomy the ratio was 1 : 2 (Majoor and Suren, 1947).

In order to interpret the clinical consequences of vagal section it is necessary to look further than the localized mechanical effects of changes in muscle tone. The hepatic branch of the vagus supplies the liver parenchyma and might, therefore, be expected to influence the rate of bile secretion and the composition of bile; the effects of the vagus on the stomach and small bowel must also be considered.

CHEMICAL CHANGES IN THE BILE

Recent publications indicate that there are changes in the bile composition as a consequence of vagotomy. Schein and others (1969) described an increased viscosity of canine gall-bladder bile after vagotomy. They also noted that particulate matter was visible in this bile and that after vagotomy canine gall-bladder bile was no longer able to dissolve human cholesterol gall-stones. Some of the dogs with human gall-stones in their gall-bladders developed a syndrome similar to that of acute cholecystitis (also noted by Hilbun and Barnett, 1965).

Fletcher and Clarke (1969) measured the flow-rate and composition of common bile-duct bile before and after vagotomy in dogs. They found that vagotomy markedly reduced the bile volume secreted in response to a fatty meal and that there was a fall in the bile-salt content. The concentration of phospholipids and cholesterol in the bile was not affected by vagotomy and therefore the net result was a fall in the ratio of bile-salt and cholesterol concentrations.

A decrease in the bile-salt : cholesterol ratio endangers the solubility of the cholesterol in the micelles formed by the phospholipids and bile-salts (Small, 1968). Thus, the experimental results of Fletcher and Clarke (1969) in dogs are significant in indicating that vagotomy causes changes in the hepatic bile which increase the possibility of cholesterol precipitation which could in turn increase the risk of gall-stone formation.

VAGAL INFLUENCES THROUGH OTHER ORGANS

To consider the biliary system in isolation in its relation to the vagus nerves would omit possibly important factors mediated through the stomach and small bowel. Vagotomy, by reducing gastric acidity and possibly modifying the rate of gastric emptying, could decrease the rate and amount of secretion of cholecystokinin by the duodenum. This in turn would reduce gall-bladder contraction. Denervation of the small bowel may interfere with the reabsorption of cholate and thus affect the bile-salt enterohepatic circulation and possibly cause a shift in the cholate : cholesterol ratio. Such changes are, however, still conjectural and await experimental demonstration.

CONCLUSIONS

1. The anterior vagus nerve maintains gall-bladder muscle tone through its hepatic branch.
2. The tone of the sphincter of Oddi may be influenced through the coeliac branch of the posterior vagus nerve. This has not been either demonstrated or disproved conclusively.
3. There is a nervous reflex between the gall-bladder and sphincter of Oddi which can be abolished by dividing the common bile-duct and its surrounding nerve plexus.
4. The hepatic branch influences the hepatic bile composition to maintain the bile-salt : cholesterol ratio.
5. Division of the vagus nerves increases the risk of gall-stone formation. *Fig.* 1 shows the probable effects of vagotomy on the biliary system.

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COELIAC AND HEPATIC NERVE FUNCTION FOLLOWING SELECTIVE VAGOTOMY*

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SUMMARY

1. In the intact patient insulin hypoglycaemia increases the output of amylase and bile-acids despite the exclusion of acid from the duodenum.

2. This effect is abolished by truncal vagotomy.

3. After selective vagotomy a partial response from the pancreas occurs consistent with preservation of a direct route in the coeliac nerve and the loss of vagally released pancreatic secretagogues. A similar effect in the biliary system could not be demonstrated.

SELECTIVE vagotomy for duodenal ulcer has been advocated because it may reduce the incidence of episodic diarrhoea compared with truncal vagotomy (Kennedy and Connell, 1970). Selective vagotomy involves preservation of the coeliac and hepatic branches supplying the biliary system, the pancreas, and the midgut, but the relation of these nerves to the local reflexes and humoral mechanisms is not known.

Pancreatic secretion in man increases in response to the sight or smell of food (Sarles, Dani, Prezelin, Souville, and Figarella, 1968). The pancreas also secretes in response to hypoglycaemia provided that the vagus nerves are intact (Dreiling, Druckerman, and Hollander, 1952). Hypoglycaemia similarly stimulates the exocrine functions of the biliary system until vagotomy is performed (Baldwin, Heer, Albo, Peloso, Ruby, and Wilen, 1966; Tinker and Cox, 1969). The pathways involved may be direct, through the coeliac and hepatic nerves, or indirect, through the vagal release of antral hormones (Lenninger, Magee, and White, 1965; Nahrwold, Cooke, and Grossman, 1967).

Clinical assessment of selective vagotomy is handicapped by uncertainty regarding the integrity of function in the preserved branches. A study was planned to examine the effect of hypoglycaemia as a central stimulant of these extragastric branches of the vagus nerves in order to determine whether selective vagotomy preserves parasympathetic influence on the pancreas and biliary system.

MATERIALS AND METHODS

Fifteen patients with Hollander-negative selective vagotomy and pyloroplasty were studied more than 1 year after operation for duodenal ulcer. Control studies were performed on 12 patients with Hollander-negative truncal vagotomy and pyloroplasty and also 14 patients with uncomplicated duodenal ulcer who had never had gastric surgery.

Following an overnight fast, a double-lumen tube (Dreiling) was positioned under fluoroscopic control so that the proximal limb drained the body and antrum of the stomach and the distal limb drained the second, third, and fourth parts of the duodenum. Basal secretion was aspirated continuously for 1 hour into a container at 0° C. Following the intravenous injection of 20 U. of soluble insulin, the stimulated secretion was collected similarly for 2 hours in eight fractions. The blood-sugar was measured before and at 30 and 45 minutes after the injection of insulin. In all the patients a hypoglycaemia of less than 50 mg. per 100 ml. was achieved.

Using phenol red as an indicator, the acid concentration of the gastric juice was measured by titration against 0·1 N NaOH. The collection of gastric juice provided information on the completeness of the gastric denervation and also prevented acid from entering the duodenum.

The duodenal samples were analysed for content of amylase and total bile-acids.

Amylase was measured by an automated procedure using the Technicon Auto Analyzer, in which prediluted aliquots of duodenal juice were introduced into a diluent stream of modified starch substrate and incubated at 37° C. for 3 minutes (Strumeyer, 1967). The reducing sugar formed was then dialysed into a recipient stream of alkaline potassium ferricyanide solution. The resultant reduction of the ferricyanide was measured colorimetrically at 420 nm. Pure glucose solutions were used as standards and the results determined as mg. of glucose liberated from the substrate in 3 minutes per 100 ml. of duodenal juice. The total amylase secreted in each collecting period was calculated.

Total bile-acids were measured by a method in which diluted aliquots of duodenal juice in saturated sodium chloride solution were acidified and then extracted with a diethylether/ethanol mixture (3 parts diethylether to 1 part ethanol; Sjovall, 1959). A portion of each extract was then evaporated to dryness in a water-bath at 37° C., and then 50 per cent sulphuric acid was added to the dried residue. The resultant colour reaction with the sulphuric acid was measured in a spectrophotometer at 340 nm. after allowing the colour to stabilize for 1 hour at room temperature in the dark. Test samples were read against cholic acid standards which had been carried through the extraction process along with the test solutions. The results were determined as mg. of bile-acid per 100 ml. of duodenal juice. The total bile-acid secreted in each collecting period was then calculated.

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* Based on a communication to the Surgical Research Society in January, 1970.

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RESULTS

The results for both pancreatic and biliary secretion were expressed in a logarithmic form because of wide variation in the level of secretion between the individuals in each group. The basal secretion of each group was compared with the secretion in the maximal hour after stimulation. In addition, the magnitude of the responses in the postoperative groups was compared with the response of the preoperative patients.

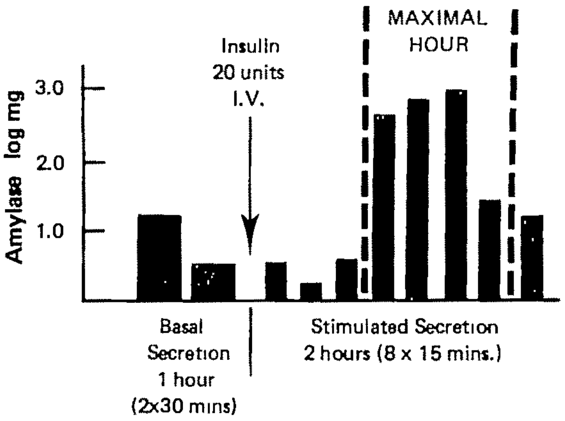

FIG. 1.—Pattern of amylase secretion in a preoperative patient.

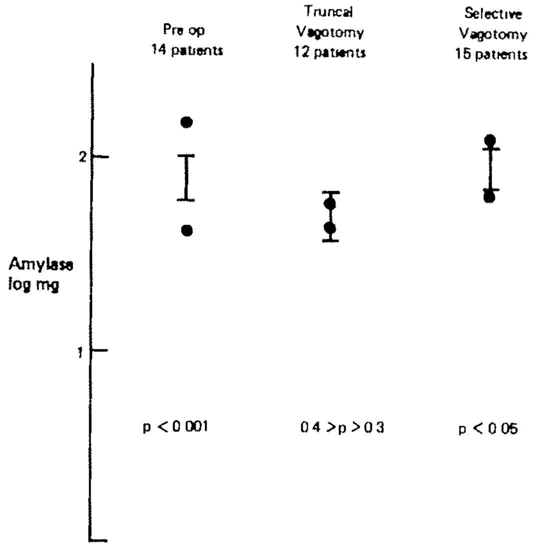

FIG. 3.—Pancreatic response to hypoglycaemia in pre- and postoperative patients. In each group the mean secretion in the basal hour and the mean secretion in the maximal hour are shown, together with 2 S.E. of the difference between the means.

In the preoperative patients the secretion of amylase in the maximal hour after stimulation was 3·6 times that of the basal secretion ($P < 0\cdot001$) (*Figs.* 1, 3). Simultaneously the output of bile-acids rose 3·1 times ($P < 0\cdot05$) (*Figs.* 2, 4).

In the patients with Hollander-negative truncal vagotomy, secretion of amylase in the maximal hour after hypoglycaemia was not different from that in the basal hour (*Fig.* 3). The response was significantly less than that observed in preoperative patients ($P < 0\cdot05$). The output of bile-acids also failed to increase (*Fig.* 4) and differed from the response observed in the preoperative patients ($P < 0\cdot05$).

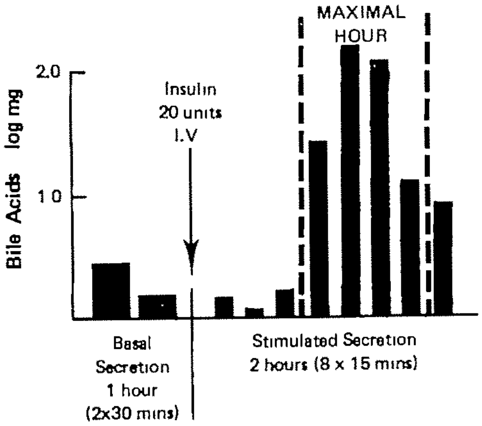

FIG. 2.—Pattern of bile-acid secretion in a preoperative patient.

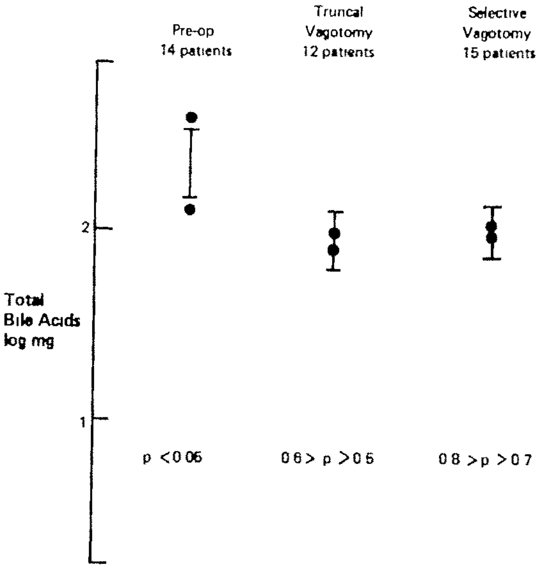

FIG. 4.—Biliary response to hypoglycaemia in pre- and postoperative patients. In each group the mean secretion in the basal hour and the secretion in the maximal hour are shown, together with 2 S.E. of the difference between the means.

In the patients with Hollander-negative selective vagotomy the output of amylase in the maximal hour after stimulation was 1·8 times that in the basal hour ($P < 0\cdot05$) (*Fig.* 3). This increment did not differ significantly from that found in preoperative patients ($0\cdot1 > P > 0\cdot05$). However, a response was not observed from the biliary system (*Fig.* 4) and this was significantly different from that observed in the preoperative patients ($P < 0\cdot05$).

DISCUSSION

In the preoperative patients amylase secretion could be readily increased by inducing hypoglycaemia.

This occurred despite the exclusion of acid from the duodenum and is consistent with the findings of Dreiling and others (1952). Similarly the output of total bile-acids into the duodenal lumen was increased. Evidence that the formation of bile-acids is influenced by the activity of the vagus or vagally released hormones has not been recorded. The biliary response may therefore be due to emptying of the gall-bladder, as reported by Tinker and Cox (1969).

Truncal vagotomy abolished the pancreatic and biliary responses to hypoglycaemia. This finding is consistent with complete interruption of all the vagal pathways to the pancreas and biliary system.

The performance of the patients with selective vagotomy is more difficult to interpret. No evidence was found that this operation preserves vagal influence on the biliary system in response to hypoglycaemia. Similar observations have been reported by Tinker and Cox (1969) using cholecystography to measure the response to hypoglycaemia. On the other hand, a pancreatic response was observed which was statistically significant ($P < 0{\cdot}05$).

Selective vagotomy may preserve the direct innervation of the pancreas through the coeliac nerve while abolishing indirect stimulation through the vagal release of antral hormones. This would account for the diminished, though significant, response. This interpretation is compatible with evidence that vagal stimulation of the antrum augments pancreatic secretion (Preshaw, Cooke, and Grossman, 1966). Alternatively, the diminished response may be due to operative failure to preserve the extragastric nerves in some cases. Such operative failures would obviously make the results of clinical trials of selective vagotomy difficult to interpret. It is possible that the technique used in this study could be adapted to the recognition of patients in whom the operation of selective vagotomy was a technical failure.

The lower incidence of diarrhoea which has been reported after selective vagotomy is difficult to attribute to preservation of pancreatic function. The episodic pattern of this complaint is not consistent with denervation. Malabsorption is not a specific feature of patients with episodic postvagotomy diarrhoea.

Uncontrolled gastric emptying occurs after vagotomy and drainage and is an aetiological factor in postvagotomy diarrhoea (McKelvey, 1970). Patients without diarrhoea after vagotomy can tolerate uncontrolled emptying into the small bowel better than those with diarrhoea. It is possible that preservation of the nerve-supply of the midgut enhances this tolerance. This would be consistent with the observation of Alvarez, Hosoi, Overgard, and Ascanio (1929) that the vagotomized gut is irritable, and of Gutierrez, Kocak, and Cox (1971) that it is supersensitive when subjected to physical and chemical stimuli.

Acknowledgements.—We wish to acknowledge the following for their advice and assistance: Professor H. W. Rodgers, Mr. D. W. Neill, Staff Nurse E. Crawford, and Mrs. M. R. Foster. This work was undertaken during the tenure of a Royal Victoria Hospital Research Fellowship.

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THE KIRSCHNER OPERATION—A FORGOTTEN PROCEDURE

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SUMMARY

Kirschner, in 1920, described an operation for benign stricture of the oesophagus. This entails division of the cervical oesophagus, closing the distal portion, bringing the stomach to the neck, and anastomosing the fundus to the proximal divided portion of the oesophagus. This operation has not been performed since, because of the tedious anastomosis between the divided abdominal oesophagus and the jejunum. However, it may be applied in the treatment of malignant oesophagobronchial fistula when it is desirable to isolate the fistula from the upper alimentary tract. This paper describes the operation as carried out in the treatment of 18 cases of advanced oesophageal carcinoma, 6 of whom had a oesophagobronchial fistula. When the operation was successful the patients could eat a normal diet without spasms of cough.

IN 1920 Kirschner described an operation in which, after mobilizing the stomach, he brought it subcutaneously to the neck and there anastomosed it to the divided cervical oesophagus. In his first case he had difficulty in bringing the fundus of the stomach sufficiently high to make a direct anastomosis between it and the cervical oesophagus. However, he managed to restore the oesophagogastric continuity by interposing skin. Subsequently, he succeeded in making a direct anastomosis between the stomach and the oesophagus. At the lower divided end of the oesophagus he performed a Roux-en-Y anastomosis. No report of this operation has been made since, and in 1944 Yudin condemned it as dangerous because of the added anastomosis between the lower end of the oesophagus and the jejunum.

Ong and Kwong (1970) advocated isolating a malignant oesophagobronchial fistula from the rest of the upper alimentary tract by performing a double by-pass with jejunum. The Kirschner operation, however, may be an alternative method of achieving the same end. During the period from March, 1970, to June, 1971, 18 such operations have been performed at the Queen Mary Hospital, Hong Kong.

MATERIALS AND METHODS

All the cases were in an advanced stage of malignant disease in which resection was not possible. Of the total 18 cases, there were 14 males and 4 females. The age-range was from 42 to 81 years, with an average of 59 years.

Clinical Features.—All the patients complained of dysphagia, ranging from 1 week to as long as 18 months in duration. All but 1 of the patients had received no previous treatment. The history was typical of carcinoma of the oesophagus with dysphagia, there being difficulty in swallowing first solids, then semiliquids, and finally fluids. In addition, 6 cases coughed out food on swallowing, indicating the possibility of an oesophagobronchial fistula.

There was marked loss of weight, ranging from 3·6 to as much as 11 kg., with an average of 9 kg. over the period of illness.

Blood-streaked sputum was encountered in 5 of the patients. The sputum itself varied in amount; in some cases as much as 140 ml. of sputum were coughed out during 24 hours, and it was usually purulent with a lot of froth but occasionally the fluid component was excessive.

Examination.—The general health was good only in 1 case; 3 patients were so ill that they could not even sit up in bed. The remaining 14 patients also had poor health. Detailed examination showed evidence of marked loss of weight, and at bronchoscopy invasion of the carcinoma into the trachea or the right or left bronchus was found in all the cases. In addition, an oesophagobronchial or tracheal fistula was demonstrated in 6 patients.

Oesophagoscopy.—The growths were all found to be fixed; in 3 cases the tumour was situated in the upper thoracic part of the oesophagus, while in the other 15 cases the growth was in the mid-thoracic section. In 2 cases chest radiographs showed extensive tuberculosis; in 1 of these a pneumonectomy had been performed in 1968 for a destroyed right lung. The oesophagobronchial fistula was demonstrated in the left bronchus. In another case there was collapse of the right lower lobe of the lung in addition to extensive pneumonitis. Of the 18 cases, the lung was free from infection in only 1 case.

Preoperative Preparation.—Intravenous feeding is usually necessary for the patients who have total dysphagia and in most of these cases a gastrostomy should be performed soon afterwards. In the majorit of cases some weight-gain is apparent after a shor period of feeding.

Tracheostomy for toilet is necessary in cases wher there is profuse sputum, especially in the patients wh have difficulty in expectorating their sputum.

Operation.—As soon as the patient is thought t be strong enough, operation is performed. Before th induction of anaesthesia, bronchial toilet is carrie out through either a bronchoscope or, in those case with a tracheostomy, by suction with a catheter Oesophagoscopy is also done, so that the accumulate secretion proximal to the point of obstruction can b sucked out.

A midline incision extending from the xiphisternum to approximately 2 cm. below the umbilicus is made A generous incision facilitates the subsequen abdominal part of the operation.

Exploration of the abdomen is carried out first afte opening the peritoneum, and if there are metastase in the liver then it would be wise to abandon th operation. If there are no metastases in the abdomina cavity the stomach is mobilized. This is done b dividing the gastrocolic omentum, preserving th arterial arcade on the greater curvature, and dividin the vasa brevia from the lieno-renal ligament. In th process of dividing the uppermost vas brevis (whic is sometimes very short) the spleen is occasionall damaged, necessitating its removal. The lesser curvature of the stomach is then freed. This is done easil by cutting through the lesser omentum and coagulating the few small vessels running over it. As soon a the greater and lesser curvatures are completel free an extensive Kocher manœuvre to expose th aorta and the inferior vena cava is carried out. Th junction between the second and the third parts o the duodenum with the reflection of the transvers mesocolon is freed, so that the duodenum now lie almost in a straight line.

Examination of the biliary tract is important becaus occasionally symptomless gall-stones may be present When the stomach is brought up into the thorax o neck the common bile-duct comes to lie transversel across the abdomen. This change of position of th common bile-duct could cause stagnation of bile i the gall-bladder and stones might become impacte in the cystic duct. This could give rise to empyema o the gall-bladder in the immediate postoperative period

Pyloromyotomy is then performed. There may b some difficulty at this stage as the duodenal mucos may be opened accidentally. Part of the pylori sphincter should be excised and the transverse circula muscle can then be dissected out and a segment of i removed.

After the pyloromyotomy has been completed transection of the stomach is done. The junctio between the oesophagus and the cardiac portion of th stomach is divided; in order to facilitate anastomosi a small portion of the cardia should be left wit the divided oesophagus. The divided cardiac portio of the stomach is then closed with two layers o atraumatic catgut and the stomach is laid aside. A loop of jejunum about 15 cm. from the duodenojejuna junction is prepared. Only one main branch of th jejunal vessel needs to be divided. This should giv sufficient length for the divided distal loop to b brought up to the lower end of the oesophagu without tension. After dividing the jejunum, the vertical limb is brought to the lesser sac through the transverse mesocolon in which a window has been made, usually to the left of the middle colic artery. This loop is then anastomosed to the lower end of the divided abdominal oesophagus with two layers of atraumatic catgut.

Continuity of the jejunum is restored by making a one-layer end-to-side anastomosis between the divided proximal jejunum and the vertical limb. This anastomosis should be at least 45 cm. from the oesophagojejunal anastomosis.

Anastomosis between the Stomach and Divided Cervical Oesophagus.—Having completed the abdominal anastomosis, the stomach is brought up to the neck through a subcutaneous tunnel made with a pair of long scissors of the Albee type. By opening the blades of the scissors a tunnel is created which is sufficiently large to allow the stomach to pass through. There is some danger of damaging the perforating branches of the internal mammary artery in making the tunnel. Should this happen, the skin should be slit open and the bleeding controlled. If bleeding were to take place undetected, the blood might track down into the abdominal cavity, causing hypovolaemic shock and possibly death.

After the subcutaneous tunnel has been completed, a transverse incision is made in the neck. The incision is enlarged and a skin-flap raised so that the anterior border of the left sternomastoid muscle is exposed. This muscle is divided at its attachment to the clavicle and the sternum. By dissecting into the carotid sheath the internal carotid artery and internal jugular vein are exposed.

The middle thyroid and the superior thyroid veins occasionally need to be divided. The inferior thyroid artery is then dissected out behind the carotid sheath and this is ligated and divided. The oesophagus then comes into view. By dissecting close to the oesophagus and gently retracting the trachea, the oesophagus is freed with exposure of the recurrent laryngeal nerves. Care has to be taken not to damage these nerves. The oesophagus, after having been freed completely from its bed, is retracted. It is divided as low as possible but allowing good clearance of the tumour. The lower end of the cervical oesophagus is closed with two layers of atraumatic catgut after the contents have been sucked out. The proximal divided end is brought out after it has been freed so that it can lie subcutaneously without tension. The divided sternomastoid muscle is fixed to the prevertebral muscle and fascia with stout stitches, so that a space is created in which the stomach can be comfortably lodged.

A disk of the fundus of the stomach, usually at the level of the second or the third vas brevis, is removed. This should not be larger than the circumference of the oesophagus to which it is to be anastomosed. After the vessels supplying the fundus of the stomach have been stitched, the anastomosis is made with one layer of interrupted silk sutures. The posterior layer of the anastomosis is made first, and just before the anterior layer is started a nasogastric tube is inserted into the stomach. The proximal end of the tube is threaded into the pharynx and brought out through the nose by the anaesthetist. The anterior anastomosis is then completed. The neck wound is closed with a drain, and the abdomen is finally closed.

Just before the patient is returned to the ward, bronchial toilet is performed again as sputum may have accumulated during the operation, especially in patients with an oesophagobronchial fistula.

Postoperative Care.—Occasionally, the general condition of the patient is so poor that respiratory aid is needed. Blood-gas estimation is done immediately on the patient's return to the ward. If the Po_2 is low a respirator should be used until the patient is able to breathe on his own. Metabolic acidosis might have to be corrected if the pH is low. Blood-gas estimation is repeated every 6 hours for the next 24 hours and then daily for about a week or so.

Intravenous Feeding.—Blood usually has to be given because either the patients are anaemic or their general condition is very poor. Intravenous feeding might have to be continued for the next 4 or 5 days until the stomach has sufficiently recovered its tone and healing has taken place.

Care of the Tracheostomy.—When a tracheostomy has been carried out frequent suction of the tracheostomy must be performed, especially in patients with a malignant oesophagobronchial fistula. This prevents accumulation of sputum and enables the pneumonitis to subside.

Antibiotics.—Antibiotics should be given postoperatively. The benefit of these is most obvious in patients with a malignant oesophagobronchial fistula when the amount of sputum is large. Culture of the sputum and a sensitivity test of the organisms should be carried out, and Terramycin or one of the broad-spectrum antibiotics used in controlling pulmonary infections.

Gastric Aspiration.—Decompression of the stomach is important as accumulation of gastric secretion might occur. If this is not aspirated through the nasogastric tube the accumulation of gastric contents might be regurgitated and then aspirated into the bronchus, which would further aggravate the pulmonary infection. The tube should not be removed until the patient is able to swallow and radiographic examination reveals no leakage at the site of the anastomosis. Once the tube has been removed it is difficult to replace it.

Oral Alimentation.—A Gastrografin swallow should be done on the sixth postoperative day. If no leakage is demonstrated and the patient is comfortable, fluids may be given. A normal diet is started within 7–10 days. At this stage intravenous feeding is discontinued and the patient is allowed to get out of bed.

RESULTS

Of the 18 cases operated on, 4 died in the immediate postoperative period—9, 15, 17, and 14 days after operation respectively. Of these 4 cases, 2 had pulmonary tuberculosis and had been treated for this condition. Three patients died of respiratory insufficiency, while the remaining case had a leak in the jejunojejunal anastomosis. The chest was in a poor state before operation in each case.

Complications.—

Pulmonary Infection.—This was by far the most common complication. All the 6 cases with an oesophagobronchial fistula had severe infection before operation. Eleven cases had pneumonitis befor operation, and in only 1 case were the lungs clear of infection. However, after the operation all the cases with infection had aggravation of their condition and required extensive physiotherapy for its control.

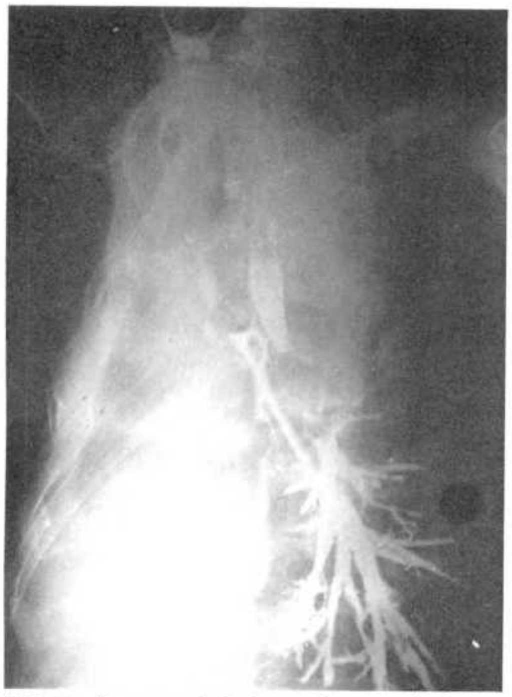

FIG. 1.—*Case* 15. A barium-swallow examination was accidentally carried out in this patient and demonstrated an oesophagobronchial fistula.

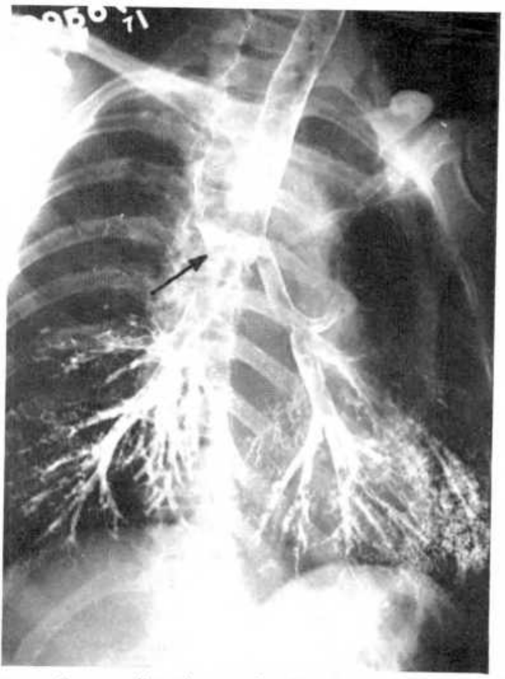

FIG. 3.—*Case* 10. Bronchogram showing an oesophagobronchial fistula (arrow).

CASE REPORT.—

Case 15.—W. H. S., a 65-year-old male, presented complaining of dysphagia for a period of 2 months and weight-loss. He was known to have had pulmonary tuberculosis for a long time, and in 1968 a right pneumonectomy had been done. There was a considerable amount of sputum, an average of 84 ml. being expectorated each day. Before admission on the present occasion the patient had received irradiation to a carcinoma of the oesophagus and had developed an oesophagobronchial fistula which was demonstrated radiographically. The left lung showed pneumonitis (*Figs.* 1, 2). Oesophagoscopic examination confirmed the diagnosis of carcinoma of the oesophagus which even after an irradiation of 3420 rad still gave positive results. Bronchoscopy revealed a fistula between the left main bronchus and the oesophagus. A gastrostomy was performed at the time of bronchoscopy. Operation was carried out on 21 Dec., 1970. After the operation the patient was able to breathe very well without any respiratory aid. Although the sputum lessened initially it began to reaccumulate, and a radiograph of the chest showed that there was extensive infection of the remaining lung. Tracheostomy was performed and bronchial toilet was carried out repeatedly. The patient died on the fifteenth day after operation, and post-mortem examination revealed acute infection of the remaining lung. There was a small leak at the site of the anastomosis. This could have healed spontaneously. The cause of death was respiratory infection.

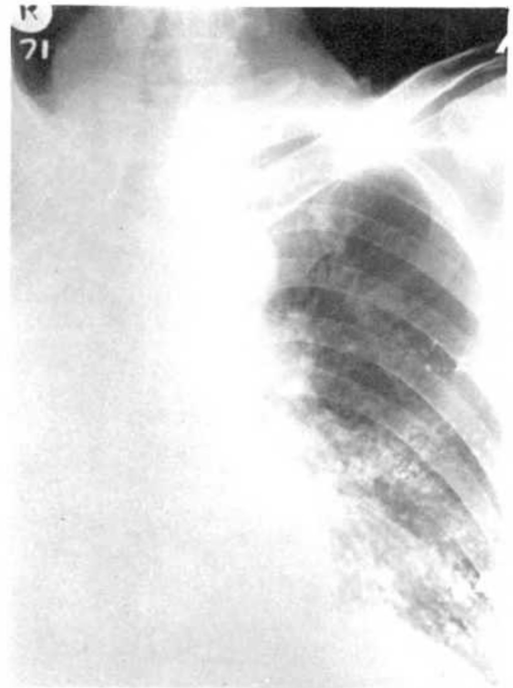

FIG. 2.—*Case* 15. Plain radiograph of the chest showing pneumonitis in the lung with residual barium.

Leakage at the Site of the Neck Anastomosis.—Of the 18 cases, only 5 had primary healing at the site of the anastomosis. The remaining 13 had a varying amount of leakage, usually of the outer anastomosis. However, of these 13 cases, only 2 required a secondary repair. The others healed spontaneously except in 1 case who died 2 weeks after operation. The other patients were able to eat soon after the operation, but in 2 oral feeding was delayed for 2 or 3 weeks.

In 1 case the anastomosis healed by primary intention and the patient was able to eat normally.

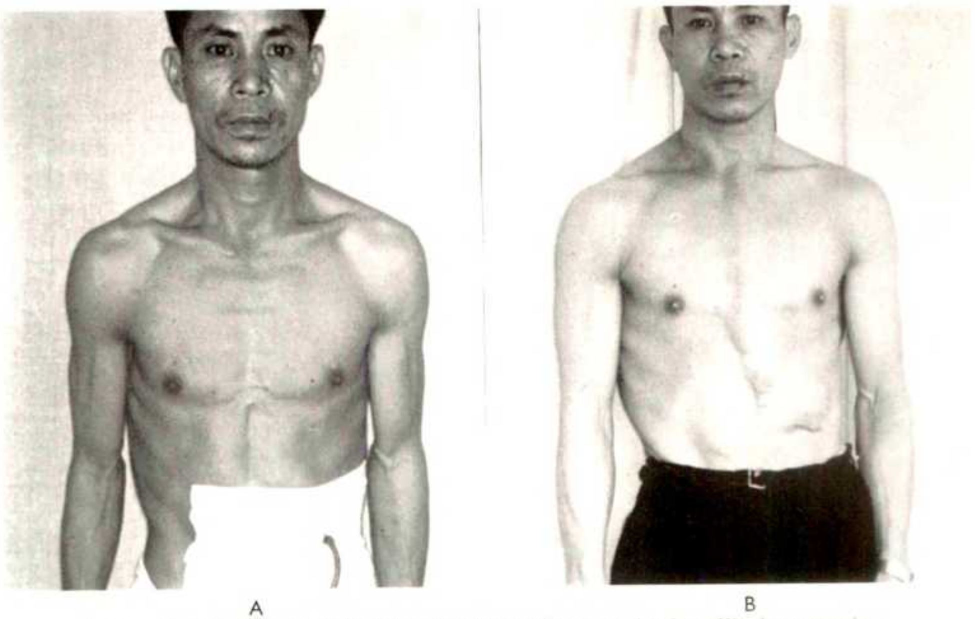

FIG. 4.—*Case* 10. The patient (A) before operation and (B) 14 months after a Kirschner operation.

Table I.—DETAILS OF 18 PATIENTS WHO UNDERWENT A KIRSCHNER OPERATION FOR CARCINOMA OF THE OESOPHAGUS

CASE	AGE AND SEX	STATE OF DISEASE	LENGTH OF SURVIVAL	ABILITY TO SWALLOW
1. A. T. T.	54 M.	Penetration of left bronchus	3 mth.	Normal diet
2. C. K.	74 M.	Penetration of left bronchus	2 mth.	Fluids
3. K. M.	58 M.	Penetration of left bronchus and lungs	3 mth.	Normal diet
4. K. C. S.	53 M.	Penetration of right bronchus	9 d.	—
5. L. C. Y.	68 F.	Penetration of trachea	Discharged: lost to follow-up	Normal diet at time of discharge
6. L. M. S.	50 M.	Oesophagobronchial fistula	8 mth.	Normal diet
7. L. T.	51 M.	Fistula at trachea	1 mth.	Fluids
8. L. K. C.	81 M.	Penetration of trachea	1½ mth.	Fluids
9. L. K.	47 M.	Penetration of trachea	2 mth.	Normal diet
10. L. F.	42 M.	Oesophagobronchial fistula	14 mth.	Normal diet
11. L. S.	75 M.	Penetration of trachea	9 mth.	Normal diet
12. L. Y. C.	79 F.	Oesophagotracheal fistula	2 wk.	—
13. P. H. S.	47 F.	Penetration of left bronchus	3 mth.	Normal diet
14. T. M. F.	50 F.	Oesophagotracheal fistula	2 mth.	Fluids
15. W. H. S.	65 M.	Oesophagobronchial fistula	15 d	—
16. Y. K. S.	64 M.	Penetration of trachea	17 d.	—
17. W. L. S.	50 M.	Penetration of trachea	1½ mth.	Normal diet
18. W. C.	55 M.	Penetration of trachea	1 mth.	Fluids

Two months later, the wound broke down completely and revealed the presence of a large fistula. Under local anaesthesia an attempt was made to repair this fistula. However, on exploration it was found that the site of the fistula was not at the anastomosis but near the point where the stomach was anchored to the prevertebral fascia. The stomach wall had completely thinned out and the fistula was the result of tissue breakdown in a dying patient.

One patient survived for 16 months and was able to swallow a normal diet despite the fact that he continued to have an oesophagobronchial fistula.

CASE REPORT.—

Case 10.—L. F., a 42-year-old male, had a mid-oesophageal lesion which at bronchoscopy was found to have developed a fistula at the left main bronchus. He had lost 9 kg. in weight and had been coughing up 84 ml. of sputum daily. He also had difficulty in swallowing—an act which was usually followed by spasms of cough.

A gastrostomy was done and after 9 days the patient was deemed to be fit for a major operation. He was operated upon on 27 April, 1970. There were no complications, he was able to eat soon after operation, and he was discharged from hospital 30 days after his admission.

Postoperatively he had a course of radiotherapy of 4560 rad. This enlarged the fistula (*Fig.* 3). He was quite well for 14 months and gained over 9 kg. in weight (*Fig.* 4). He was readmitted 14 months after the operation because of haemoptysis. Examination showed that there was a large fistula and recurrence of the carcinoma, which was confirmed by a biopsy taken during oesophagoscopy. A second course of irradiation of 3040 rad was given and the patient was discharged. Despite the large fistula he was able to eat normally. He lived for another 2 months after his discharge and died suddenly at home. No post-mortem examination was carried out.

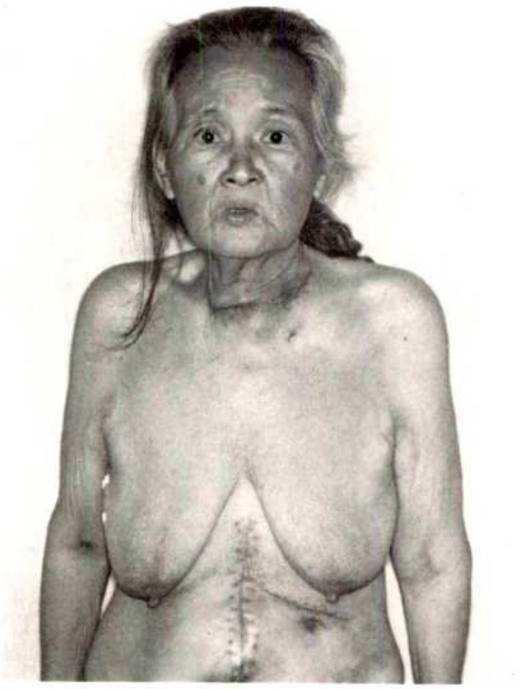

FIG. 5.—*Case* 5. The patient after operation in which the stomach was placed behind the sternum.

Leakage of the Abdominal Anastomosis.—In 1 case there was a leak at the jejunojejunostomy. This was in a patient in whom the anastomosis was made in one layer. The anterior anastomosis was defective and as a result it leaked. It was not detected early so that subsequently the condition deteriorated and breakdown of the anastomosis occurred. The patient died of peritonitis after repair of the anastomosis.

The results of the operation in 18 cases are shown in *Table I*.

DISCUSSION

The Kirschner Operation.—The Kirschner operation is certainly not the best operation for benign stricture of the oesophagus because when the fundus of the stomach is brought up to the neck for anastomosis to the cervical oesophagus the lower end of the oesophagus has to be divided. This necessitates an extra anastomosis, which, according to Yudin (1944), is dangerous. However, by using either the colon or the jejunum one can achieve a by-pass of the stricture without an extra oesophageal anastomosis. When applied to advanced malignant disease such as oesophagobronchial fistula where it is not possible to resect the oesophagus, this procedure allows a complete isolation of the fistula from the upper alimentary tract.

The use of a loop of jejunum to perform a double by-pass also isolates the oesophagobronchial fistula from the upper gastro-intestinal tract so that the patient can eat without spasms of cough. The Kirschner operation fulfils this requirement but instead of using the jejunum the stomach is used for the anastomosis. In effect using the stomach gives the same result. There is no difficulty in stretching the stomach to the neck for anastomosis to the cervical oesophagus, and also the blood-supply of the stomach from the right gastric and right gastro-epiploic vessels is more than adequate. It is a much simpler operation and is less time-consuming. These considerations should be taken into account as in an already moribund patient the operative risk is high.

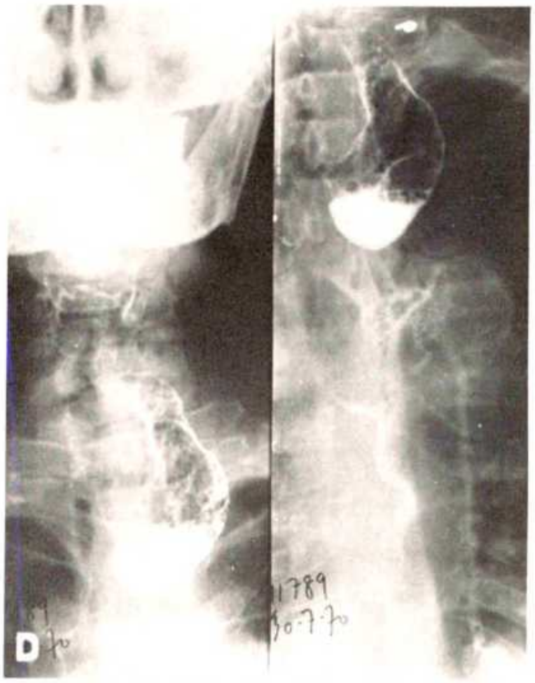

FIG. 6.—*Case* 5. Postoperative barium-swallow film, showing a slight hold-up at the level of the clavicle but the contrast medium cleared satisfactorily.

The route through which the stomach is delivered into the neck may be either subcutaneous or retrosternal. A subcutaneous route has the advantage of being safer and, if leakage should develop, it would be less likely to cause death. However, there is a greater distance to traverse before reaching the neck and tension is more likely to develop at the site of the anastomosis.

The unsightly presence of the stomach lying underneath the skin does not matter much among patients with an oesophagobronchial fistula, but female patients may find it undesirable. In such patients the retrosternal route can be used.

CASE REPORT.—

Case 5.—L. C. Y., a 69-year-old female, was admitted to hospital on 23 May, 1970, because of dysphagia. On examination a carcinoma of the upper oesophagus was found. Bronchoscopy revealed that the growth had penetrated the trachea. A Kirschner operation was carried out on 13 July. The stomach was placed behind the sternum and brought up to the neck. The patient's postoperative course was uneventful and she was discharged after having received a course of irradiation of 4560 rad (*Fig.* 5). Barium-swallow examination showed a slight hold-up at the level of the clavicle but the contrast medium cleared well (*Fig.* 6).

High Incidence of Leakage.—There seems to be a higher incidence of leakage at the site of the anastomosis in the neck when the stomach rather than the jejunum is used. Breakdown of the anastomosis usually occurs in the outer wall. It is possible that it is caused by the stomach, which after a few days gains its tone, producing tension at the suture line. This is supported by the fact that the breakdown in the anastomosis occurs where it is not anchored by sutures, as is the case of the inner part of the anastomosis.

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CLOSED LIVER INJURY: AN ASSESSMENT OF PROGNOSTIC FACTORS

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SUMMARY

The records of 65 patients with closed liver injuries were studied in order to determine which of 19 variables might be important in predicting the outcome. The statistical technique of multiple regression analysis was used. The presence of hypotension and of head injury were the most important prognostic factors; on the other hand, the number of associated injuries was not a significant factor. The major problem was the patient with the isolated severe liver injury.

PROGRESS in the management of any condition depends upon, first, our understanding of its usual course, secondly, the delineation of suitable discriminant prognostic factors (i.e., symptoms, signs, or special investigations) which can give information about the course the condition is likely to pursue in an individual instance, and, thirdly, having effective therapy available. Often in clinical practice the last has been forthcoming before the first two; debate then tends to centre around the deployment of therapy and may wax strong when the factors determining the clinical course are unknown. The problem is compounded by the multifactorial nature of so many clinical situations in which it is difficult to identify those factors which are of significance in determining what the clinician should do next. Although in the initial stages of the study of an heterogeneous clinical problem, detection of a small number of strong factors may be sufficient to permit radical modifications to natural history, once such situations have been exploited and exhausted further advance can only be predicated upon a rigorous analysis of *all* the factors acting on the individual patient and the assignment of the appropriate weights to those which are most practically significant.

Conventional analysis, as in most published series of medical data, has usually depended upon the determination of mortality for each subgroup specified by an individual criterion such as age, sex, or the number of associated injuries. Although useful, this method ignores the fact that all the subgroup criteria and other factors not so chosen may act concurrently. Multiple-regression analysis, now widely used in other fields, is one way of arriving at a better estimate of predicting factors in the clinical course.

We believe that the stage has been reached in closed liver injury where such a detailed analysis is necessary. The mortality of this injury in civilian life has probably fallen in recent years as therapy in general has improved, but it is well known that certain forms of trauma to the liver are highly lethal and the overall case mortality for closed injuries is about 30 per cent (Walt, 1969; Amerson and Stone, 1970). Furthermore, it is known that treatment of lesions of this type can be effective. What it is now important to determine are the factors which indicate an individual with a potentially treatable injury, which will be lethal unless early and effective treatment is deployed. The current study attempts such a multifactorial evaluation with the aim of the detection at a more remediable early stage of those patients whose subsequent course will be downhill to death or to serious, time-consuming, and anxiety-provoking complications. This method has recently been used to study the factors influencing the occurrence of wound infection (Bruun, 1970; Davidson, Clark, and Smith, 1971) and its application to other situations can be readily envisaged.

MATERIALS AND METHODS

The 65 patients with closed liver injuries admitted to Alfred Hospital, Melbourne, during the 11 years from 1959 to 1969 inclusive were studied. Four additional patients with iatrogenic but minor lacerations sustained during attempted resuscitation for post-infarction cardiac arrest have been excluded from this analysis. During the study period methods of assessment and therapy changed so that some procedures were applied only occasionally or with an uneven distribution in time. However, for the purpose of a multivariate analysis it was possible to identify 19 factors (*Table I*) which occurred sufficiently frequently for them to be useful in predicting outcome. The mortality—19 deaths among 65 patients—was sufficient to provide a predicted variable. The method of classification of the injury (*Table II*) was derived from that of Perry, Root, Hauser, and Keizer (1967). A fracture is defined as a single laceration greater than 10 cm. long or 3 cm. deep. A bursting injury is one in which there are stellate lacerations or severe disruption of the parenchyma.

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Table I.—THE 19 FACTORS USED TO PREDICT THE OUTCOME OF INJURY

1. Age
2. Sex
3. Severity of injury
4. Lobe injured (related to falciform ligament)
5. Blood-pressure on admission
6. Presence of abdominal rigidity
7. Number of associated injuries
8. Presence of chest injury
    - Grade 1: Fractured ribs
    - Grade 2: Pneumothorax ± haemothorax
    - Grade 3: flail chest, pericardial tamponade
9. Presence of gastro-intestinal tract injury
10. Presence of urogenital tract injury
11. Presence of splenic rupture
12. Presence of head injury
    - Grade 1: Unconscious on admission
    - Grade 2: Unconscious for longer than 24 hours; subdural haematoma
13. Number of major fractures, excluding ribs, hands, and feet
14. Number of units of blood transfused
15. Time between admission and operation
16. Use of non-absorbable pack
17. Type of operation
    - Grade 1: Exploration ± drainage
    - Grade 2: Suture ± absorbable haemostatics ± drainage
    - Grade 3: Resection
18. Use of prophylactic antibiotics
19. Occurrence of secondary haemorrhage

Table II.—TYPE OF INJURY IN 65 PATIENTS WITH CLOSED LIVER INJURY

Type of Injury	*No. of Injuries*
Subcapsular haematoma	4
Laceration(s)	30
Fracture	19
Burst	11
Avulsed porta hepatis	1

The information was coded for storage on magnetic tape. Correlation coefficients were calculated for each pair of variables and multiple-regression analysis was performed using a programme modified from that of Cooley and Lohnes (1962), with survival of the patient as the criterion to be predicted. The overall accuracy of prediction of the criterion is measured by the multiple-correlation coefficient. The square of this value gives the proportion of criterion variance which can be predicted from all the available predictors.

In addition to this analysis, the therapy and its relation to cause of death were non-statistically analysed in more detail.

RESULTS

Prediction of Death.—The correlation coefficients between the predictors and the survival of the patient are shown in *Table III*. Each of the factors listed makes a significant contribution to the outcome. For the remaining 10 factors (*Table I*) the correlations were not significant. Sixty-nine per cent of the variations in survival of the patients can be predicted by the factors studied; this is a highly significant proportion. The level of the blood-pressure on admission (*Table IV*) stands out as the most important determinant of severity of injury and ultimate death. This fact is of added importance in that, both in the present series and subsequently, patients whose fall in blood-pressure was profound but transient and initially responsive to quite a modest infusion of electrolyte or albumin solutions were subsequently found to have a severe or lethal injury.

Table III.—SIGNIFICANT PREDICTORS OF SURVIVAL

FACTOR	CORRELATION COEFFICIENT	SIGNIFICANCE
Admission blood-pressure (5)	0·4759	$P < 0·001$
Use of antibiotics (18)	0·4653	$P < 0·001$
Head injury (12)	−0·4560	$P < 0·001$
Presence of rigidity (6)	0·4419	$P < 0·001$
Severity of injury (3)	−0·4141	$P < 0·001$
Presence of urogenital tract injury (10)	−0·2769	$0·05 > P > 0·01$
Secondary haemorrhage (19)	−0·2625	$0·05 > P > 0·01$

The numbers in brackets refer to those of the list of factors in *Table I*. A negative correlation coefficient indicates that the presence of this predictor was associated with the death of the patient.

Also, as would be expected, a coexistent head injury often represents a lethal combination. In the current series the reasons for this association were: (i) the head injury itself may be lethal; (ii) the diagnosis of liver injury may be delayed in the presence of a head injury; (iii) the shock as a result of the liver injury may adversely affect the head injury.

Table IV.—SYSTOLIC BLOOD-PRESSURE ON ADMISSION TO HOSPITAL COMPARED WITH THE MORTALITY

Systolic blood-pressure	*No. of Patients*	*No. of Deaths*
Less than 50 mm. Hg	6	5
50–100 mm. Hg	38	13
Greater than 100 mm. Hg	21	1

Also self-evident was the predictive value of the grade of severity of the injury (*Table II*); in 8 deaths a massive solitary injury in a young person posed insoluble therapeutic problems. In addition to these major indicators of lethality, the presence of renal and liver rupture in the same patient was significant, as in the series of Walt (1969). Furthermore, secondary haemorrhage was a significant predictor of death. If this complication is prevented, e.g., by adequate excision of the wound, then a contribution to the survival of the patient has probably been made.

Prediction of Survival.—Somewhat surprisingly the presence of abdominal rigidity was a favourable sign. It was the only clinical feature included in the analysis as it was thought likely that it would have a smaller observer variation than tenderness or rebound tenderness. The explanation is not clear but may be a compound of three factors: (i) the elicitation of abdominal rigidity leads to early definitive treatment; (ii) patients with head injury did not display it; (iii) the very ill patient may also not have this sign. The administration of antibiotics is also favourably correlated with survival. However, it is probable that this association is spurious in that patients who died on the operating table did not get to the stage when prophylactic antibiotics would normally be administered.

Less Significant Factors in predicting Death or Survival.—One of the more valuable aspects of this analysis has been to show that several factors which are generally regarded as being important in determining the outcome of the injury are less significant than they have been thought to be. The most important of these is the number of associated injuries (*Table V*), which was not found to be a significant factor in predicting the death of the patient in the present series. This is in marked contrast to the published results of other authors who have almost universally found that the mortality rises with the number of associated injuries (Crosthwait, Allen, Murga, Beall, and De Bakey 1962; Amerson and Stone, 1970), while the predominant lethal factor in the present series was the technical problem posed by a severe, isolated liver injury in which the bleeding was unable to be controlled. The reports of Mikesky, Howard, and De Bakey (1956) and Kindling, Wilson, and Walt (1969) suggest also that the combination of liver and spleen injury is lethal. However, splenic rupture in this series did not have a significant effect on the mortality, agreeing with the finding of Little and Williams (1969). There was also no significant relation between the presence of gastro-intestinal injury and the death of the patient, and this conclusion is in accord with other authors' published results. Although the morbidity, especially septic complications, may be increased by the presence of bowel injuries there was no significant effect on the mortality. Pancreatic injuries, which by themselves carry a high mortality, were not influenced by and did not influence the outcome of a coexisting liver injury.

Table V.—NUMBER OF ASSOCIATED INJURIES COMPARED WITH THE MORTALITY

No. of Associated Injuries	*No. of Patients*	*No. of Deaths*
0	16	5
1	18	3
2	13	4
3	11	4
4	5	2
5	2	1

Although very commonly associated with liver rupture, injuries of the chest, at least in this series, did not have a significant effect on the outcome, which probably reflects the improvements in the care of patients with chest injuries, and particularly the use of intermittent positive-pressure respiration. The number of fractures present significantly increased ($P<0{\cdot}05$) the time between admission and operation, thus suggesting either difficulty in making the diagnosis in such instances or the possibility that mobilization of the appropriate team took longer when multi-system trauma was present.

As with secondary haemorrhage, the amount of blood transfused has been used as a retrospective index of outcome (Little and Williams, 1969; Amerson and Stone, 1970). In our series a significant influence was not observed, but this may represent inadequate recording when very massive transfusions were given in desperate circumstances usually associated with subsequent death.

Cause and Course to Death.—It would appear from the multivariate analysis that greater attention focused upon the patient who is initially hypotensive on admission and suspected of a large solitary liver lesion would reduce the mortality. The cause of death in the 19 fatal injuries confirms this view, for 10 patients died on the operating table and 2 within 6 hours of operation. Admittedly, 3 of these patients were apparently moribund on admission and 1 patient was found at operation to have total avulsion of all the structures in the porta. However, in 3 patients therapeutic delay which could have been avoided took place, and in 4 patients bleeding could not be controlled. It is conceivable that in some or all of these patients better preparedness could have been achieved through the knowledge that has been gained in recent years.

In addition to the ordinary clinical indications the availability of the gamma camera now permits the easy delineation of areas of tissue damage in the liver and spleen. Although scintiscanning was used only three times—each with positive results—between 1959 and 1969 it has been employed increasingly during the past 3 years (Dugdale, Rosengarten, and Dudley, 1973). It adds considerably to the more conventional techniques, although careful scrutiny of plain radiographs both for rib fractures and soft-tissue shadows may be helpful in about one-third of the patients (Little and Williams, 1969). In the later stages of management scanning may also have a place in detecting residual areas of necrosis which may presage the development of an abscess or post-traumatic haemobilia.

Operative techniques have changed as surgeons have gained increasing competence and confidence. Although before 1963 unabsorbable packs were used four times with 2 deaths, only 1 patient had such a pack in the ensuing 6 years. Suture was the commonest operation, but a lobectomy was undertaken three times. Two further patients should have had such a procedure, for both died of the consequences of extensive contusion.

Our recent experience since reviewing this series confirms the concept that the liver wound, whether open or closed, should be treated as any other by meticulous excision, haemostasis, and accurate, non-devascularizing, primary suture. In extensive bursting injuries these therapeutic goals can only be achieved by lobectomy. Both excision and lobectomy require good exposure. Often, as in the majority of these patients reviewed, a long abdominal incision is adequate. However, no hesitation should be felt in opening the chest either by lateral extension of an abdominal wound or as a primary procedure.

The problems of liver injury are now, we believe, clearly delineated. Although head injury as part of the damage profile of the civilian at risk will continue to claim some patients, the accurate interpretation of the physical signs and decisive treatment should save all except the most devastatingly injured patient.

Acknowledgements.—We are grateful to Dr. M. W. Johns for help with the statistical analysis and to the surgeons of the Alfred Hospital, Melbourne, who allowed access to their cases.

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THE COAGULUM PYELOLITHOTOMY

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SUMMARY

Coagulum pyelolithotomy is mainly indicated in cases of multiple stones, soft and crumbly stone or stones, small, mobile caliceal stones, and as an aid to fixing caliceal stone or stones in the calix prior to partial resection of the kidney or nephrolithotomy. Its main advantages are:—

1. Trauma to the kidney is minimized.
2. All the free stones in the pelvicaliceal system may be removed, thus reducing the incidence of so-called 'recurrent' stones.
3. Fragmentation of the stone during removal is avoided.
4. Surgical mobilization of the kidney is not necessary since it is sufficient to expose the pelvis.

A method of coagulum pyelolithotomy is described in detail and discussed. The operation has been performed in 22 cases with good results. Two cases are described in detail. It is suggested that this method could be utilized for common bile-duct stones.

THE number of cases with recurrent renal stones after pyelolithotomy and nephrolithotomy reported in the world literature is very high. However, it is very questionable whether these are always recurrent stones. In many cases this 'recurrence' is due to incomplete removal of renal stones during the operation. Oppenheimer (1940) reported incomplete removal of renal stones in 41·4 per cent of nephrolithotomies, in 32·4 per cent of pyelonephrolithotomies, and in 10·6 per cent of pyelolithotomies. Barney (1922) stated that there was incomplete removal of stones in 45 per cent of nephrolithotomies, and the author feels certain that the percentage of incomplete removal of stones is even higher, since postoperative radiographic checks fail to reveal all the stones which are left behind after operation. Several factors may be responsible for the impossibility of removing all the stones present at the time of operation:—

1. The shadow of smaller stones could be obscured by that of a bigger one on the radiograph.
2. Radiolucent stones and small radio-opaque stones may not be visible on the radiograph.
3. The interior of the renal pelvis cannot be completely surveyed through a pyelotomy incision, and the fact that a small stone may move from one calix to another in the course of the operation makes it difficult or impossible to locate the calculus.
4. A blood-clot may cover a small stone, which is then difficult to locate.

The technique of overdistending the renal pelvis with an isotonic saline solution with the ureter occluded has served well in washing out elusive stones, but this method leaves much to be desired. The same is true of carrying out routine radiographs on the operating table. Oppenheimer (1940) found that in a series of 63 cases radiographs taken on the operating table showed no evidence of any stones remaining in the kidney, yet a subsequent check revealed stones in 12·7 per cent of these cases.

Table I.—REVIEW OF COAGULUM PYELOLITHOTOMIES REPORTED IN THE WORLD LITERATURE

Author	*No. of Cases*
Dees (1943, 1944, 1946, 1955)	73
Harrison and Trichel (1949)	10
Hoffmann (1950)	1
Moore and Sweetser (1952)	7
Stoll (1959)	6
Singer (1962)	12
Total	109

From the above it is obvious that urologists are and always have been in search of more precise and certain methods for the operative removal of renal calculi. A significant contribution in this direction is contained in the original work of the American urologist, Dees. In 1943 he reported on a method for the removal of renal calculi with the help of a fibrin coagulum. Fibrinogen and thrombin solutions were injected into the renal pelvis. Within several minutes the mixture formed a firm clot which was then removed together with the incorporated stones. To date only 109 coagulum pyelolithotomies have been reported in the world literature (*Table I*).

It is obvious that this method has not gained the popularity that it deserves. There are two main reasons for this. First, no suitable commercial fibrinogen was available during the Second World War and post-war periods. Secondly, the method as described by Dees (1943) was somewhat complicated. Owing to many technical errors at different stages of the procedure, it proved difficult to produce a firm and elastic clot in the renal pelvis which would enmesh all the free stones and could be extracted completely and in one piece. Similar difficulties were experienced with the earlier cases in the present series. However, the method has since been simplified so that a suitable coagulum is now always obtained.

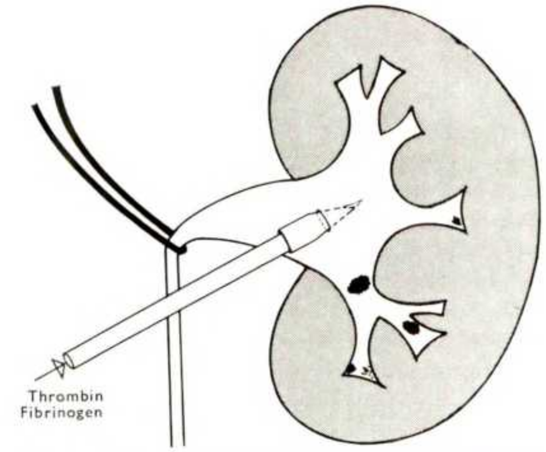

FIG. 1.—Injection of the fibrinogen and thrombin mixture into the renal pelvis with the help of a funnel-shaped catheter.

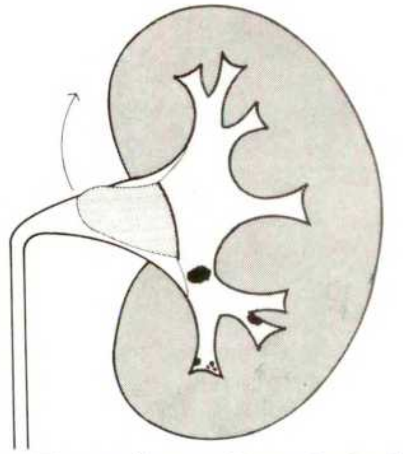

FIG. 2.—The protruding part of the coagulum is pulled with a movement slightly turning it towards the upper pole of the kidney.

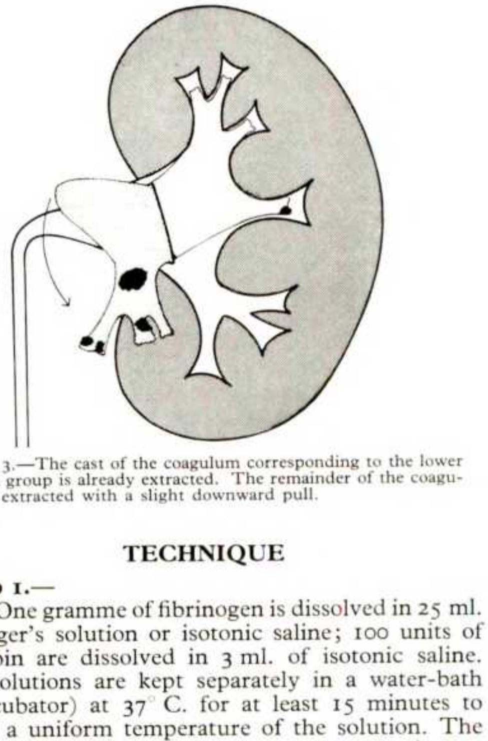

FIG. 3.—The cast of the coagulum corresponding to the lower caliceal group is already extracted. The remainder of the coagulum is extracted with a slight downward pull.

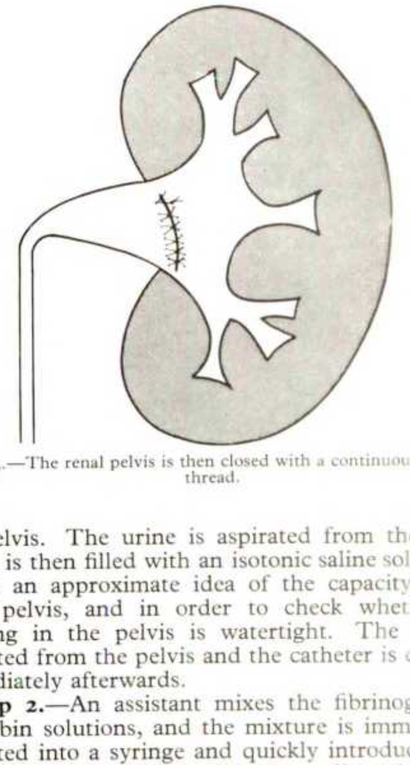

FIG. 4.—The renal pelvis is then closed with a continuous catgut thread.

TECHNIQUE

Step 1.—

a.—One gramme of fibrinogen is dissolved in 25 ml. of Ringer's solution or isotonic saline; 100 units of thrombin are dissolved in 3 ml. of isotonic saline. Both solutions are kept separately in a water-bath (or incubator) at 37° C. for at least 15 minutes to ensure a uniform temperature of the solution. The properties of the solutions are in no way altered, even if they have to be kept at 37° C. for a considerably longer period of time.

b.—In the meantime the renal pelvis is exposed. It is not necessary to mobilize any other part of the kidney. A small transverse incision is made in the pelvis. A catheter which is funnel-shaped at the tip is introduced into the renal pelvis so that it fits snugly into the aperture (*Fig.* 1). There is no need for a purse-string suture to ensure a watertight fit. The ureter has to be occluded with a rubber sling or a suitable soft clamp so as to keep the injected fluid in the pelvis. The urine is aspirated from the pelvis which is then filled with an isotonic saline solution to obtain an approximate idea of the capacity of the renal pelvis, and in order to check whether the opening in the pelvis is watertight. The fluid is aspirated from the pelvis and the catheter is clamped immediately afterwards.

Step 2.—An assistant mixes the fibrinogen and thrombin solutions, and the mixture is immediately aspirated into a syringe and quickly introduced into the renal pelvis until it is slightly overdistended. The catheter is then clamped to prevent any backflow. This entire procedure must be carried out rapidly, since coagulation begins within 30 seconds after the fibrinogen and thrombin solutions have been mixed. Normally the process of mixing the solutions, the aspiration of the mixture into a syringe, and its introduction into the renal pelvis takes less than 10 seconds. This is the most vital point in the entire operation, and it will therefore be described in detail.

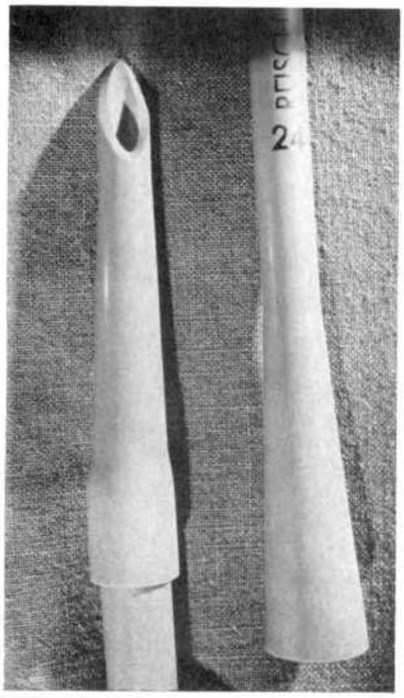
FIG. 5.—The funnel-shaped catheter used to introduce the fibrinogen and thrombin mixture into the renal pelvis.

A second assistant pours the warm solutions simultaneously into a prewarmed crucible on the instrument table. The operating urologist stirs the mixture. Stirring should be even and gentle, since the mixture, which is viscous, otherwise tends to become foamy and the enclosed bubbles subsequently diminish the tensile strength of the coagulum. The assistant then aspirates the mixture into a syringe. There is no need to attach a needle to the syringe; this saves time and prevents the aspiration of air through any leakage between the junction of the needle and the nozzle of the syringe. It is important to aspirate the mixture quickly but without air. If there are air-bubbles inside the syringe it takes many precious seconds before they rise to the surface of the viscous fluid, and it is impossible to wait for all the bubbles to come up since coagulation begins within 30 seconds. Particular care should be taken in handling the last 2 ml. of the mixture, because it is especially then that large quantities of air may very easily be aspirated. Meanwhile the first assistant opens the clamp on the catheter, applies a syringe, aspirates urine which might have gathered in the pelvis, and clamps the catheter to prevent the suction of air into the pelvis. The urologist then applies the syringe containing the coagulum mixture to the catheter with the help of a suitable connecting piece; the first assistant releases the clamp and the solution is quickly injected into the pelvis. The catheter is clamped again by the first assistant.

Step 3.—After 7 minutes the catheter is withdrawn (5 minutes would probably be sufficient to ensure the formation of a firm and elastic clot). The transverse pelvic incision is enlarged. Usually the distal part of the coagulum then pops out of the pelvis.

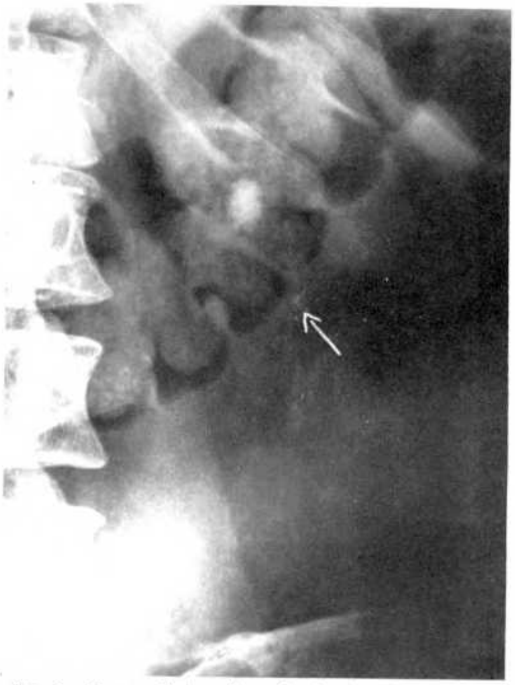
FIG. 6.—*Case* 1. Plain radiograph, showing a large stone in the area of the renal pelvis and a minute stone (indicated by the arrow) in the lower pole of the kidney.

Step 4.—The protruding part of the coagulum is very gently pulled at with a Desjardins's forceps with a movement slightly turning it towards the upper pole of the kidney (*Fig.* 2), so as first to extract that part of the coagulum which corresponds to the pelvis proper and to the lower caliceal group. Subsequently with a slight downward pull the remainder of the coagulum is extracted (*Fig.* 3). The cast which corresponds to the upper caliceal group may, of course, be extracted first, but this is more difficult since the upper caliceal group is usually longer than the lower one.

Step 5.—A ureteric catheter is passed through the incision towards the bladder to ascertain whether the the passage is free, and the pelvis is then closed with a continuous catgut thread to ensure a watertight closure (*Fig.* 4). Some urologists prefer to leave the pelvic incision partly open, but the present author sees no reason to do so. Once the passage to the bladder is free of obstruction it is advisable to close the pelvic incision so as to reduce the danger of urinary phlegmon and infection around the pelvis.

It is the author's practice to take radiographs of the coagulum containing the stones.

The funnel-shaped catheter which is used to apply the fibrinogen and thrombin solution into the renal pelvis is not available commercially. The author constructs one by cutting the funnel-shaped distal end of a Nélaton catheter and fixing it to the proximal end of another catheter which is 2–3 charrières wider (*Fig.* 5).

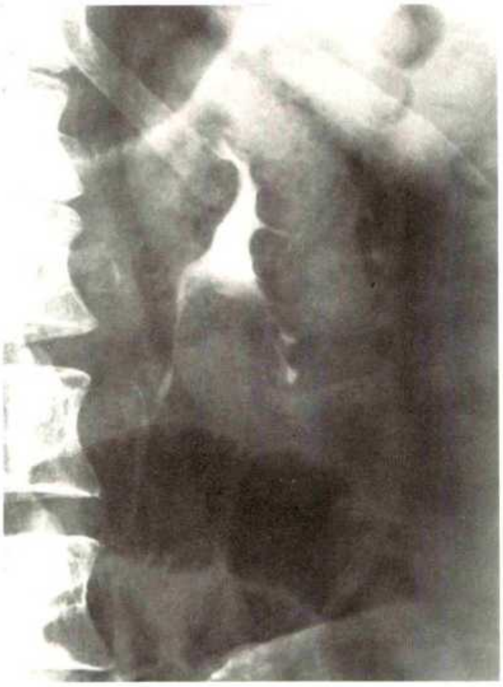

FIG. 7.—*Case* 1. Intravenous pyelogram.

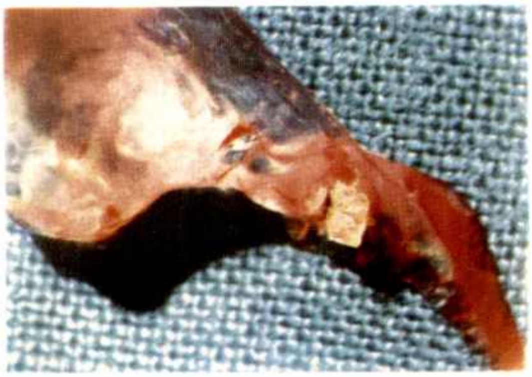

FIG. 9.—*Case* 1. Close-up of the coagulum corresponding to the lower calix, showing the crystalline stone.

PRESENT SERIES

The author has performed coagulum pyelolithotomy in 22 cases. In the first 11 cases Dees's (1943) method was employed and in the remaining cases the method was as described here. In 5 cases of the first group a firm coagulum was not produced owing to technical errors, such as an uneven mixture of the fibrinogen and thrombin solutions or leakage around the catheter. No such failures occurred when the new method was used. With the exception of those cases in which there was a technical breakdown all the free stones were removed. In fact, there were no complete technical breakdowns; in all 5 cases we did achieve a coagulum, although it was deficient in quality, and at least some stones were removed. Subsequently lavage of the renal pelvis failed to remove the remainder of the stones, which might in some cases have even been parenchymal stones.

In 9 of the 22 cases, apart from the stones which had been diagnosed, other stones were removed which had not been shown up during the preoperative radiographic diagnosis.

In 1 case of multiple stones in a parapelvic cyst communicating with the pelvis, the latter was filled with coagulum prior to the mobilization of the kidney. Stones were thus prevented from escaping into the pelvis and subsequently all the stones were removed by nephrotomy. In 1 case coagulum was used prior to lower-pole resection to block the escape route of a lower caliceal stone.

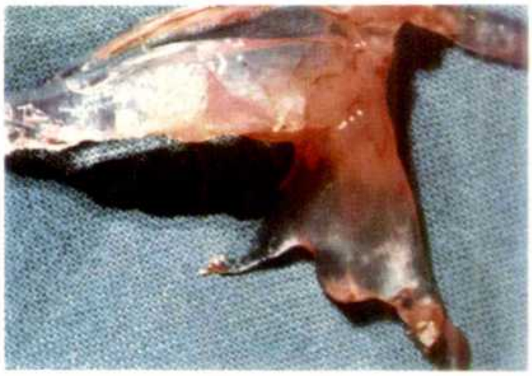

FIG. 8.—*Case* 1. The coagulum, showing the lower caliceal stone in the corresponding part of the coagulum.

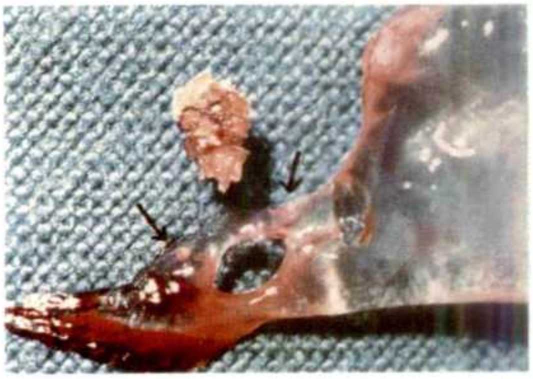

FIG. 10.—*Case* 1. The stone is removed from the coagulum revealing the thin ramifications of the coagulum which held the stone firmly. Two more tiny stones (indicated by arrows) can be recognized, which escaped radiographic detection because of their minute size.

A detailed analysis of the cases will be published at a later date; however, 2 cases are described here in detail to illustrate the effectiveness of coagulum pyelolithotomy.

CASE REPORTS

Case 1.—A 61-year-old patient was admitted to hospital with a diagnosis of a renal pelvic stone. On closer scrutiny the radiograph (*Fig.* 6) showed, apart from the large stone, a minute radio-opaque shadow in the lower caliceal group which might have been caused by a stone (cf. *Fig.* 7, which shows the intravenous pyelogram of the same kidney).

The large stone was removed through a pyelotomy incision with the help of stone forceps. Afterwards a fibrin coagulum was formed in the renal pelvis. The small lower caliceal stone which had been diagnosed on the radiograph was found in the corresponding part of the coagulum after its removal (*Fig.* 8). Close examination of the cast (*Fig.* 9) clearly showed the crystalline nature of the stone. It might well have been adherent to the caliceal wall, especially in the area where the surface of the stone was not covered by the coagulum. *Fig.* 10 shows the coagulum after the stone had been removed from it. Comparison with the size of the stone revealed that the ramifications of the coagulum holding the stone were extremely thin, and yet they were able to hold the stone firmly, thus making extraction possible. The coagulum was sufficiently firm not to tear even though it was very thin. Closer observation of the coagulum showed that in the vicinity of the stone, which itself was very small, there were two more tiny stones. These stones had escaped radiographic diagnosis owing to their minute size.

The operation was concluded in the usual manner. The patient was discharged after an uneventful postoperative period. The postoperative intravenous pyelogram failed to reveal any further stones.

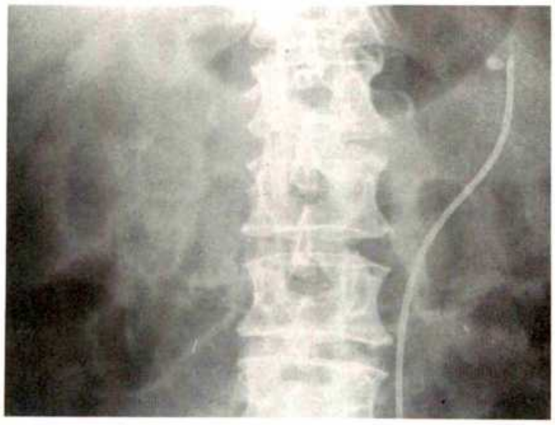

FIG. 11.—*Case* 2. Plain radiograph, showing a renal stone and a ureteric catheter on the left-hand side. No radio-opaque shadows are visible on the right-hand side.

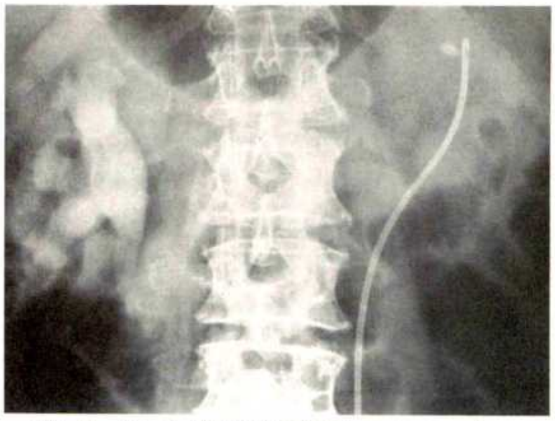

FIG. 12.—*Case* 2. Twenty-four-hour intravenous pyelogram, showing retention and stagnation of the contrast material in the renal pelvis on the right-hand side. Ureteric obstruction at the level of the third lumbar vertebra is also demonstrated.

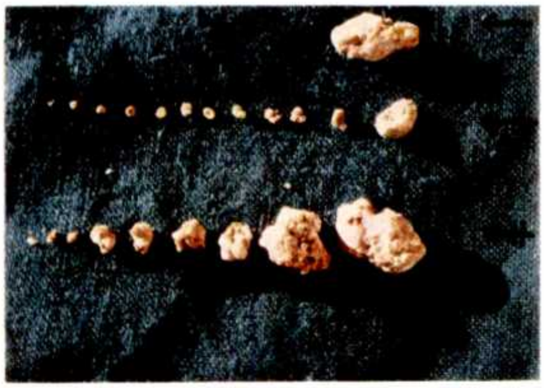

FIG. 13.—*Case* 2. The ureteric stone (←), the stones removed by ureteric lavage (←+), and the stones removed by coagulum pyelolithotomy (←++).

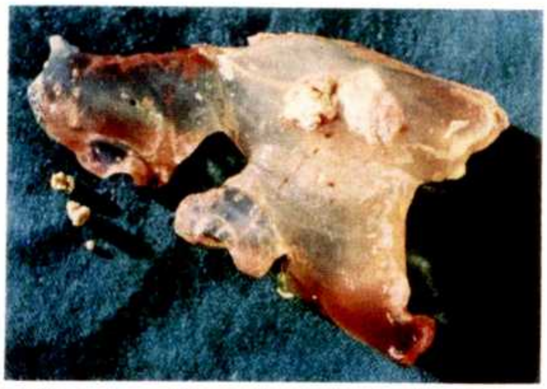

FIG. 14.—*Case* 2. The coagulum, showing the embedded stones.

Case 2.—A 55-year-old female patient was admitted to hospital in a poor general condition. She had not passed urine for about 8 days and her general practitioner had treated her with antispasmodics. On admission the urea-nitrogen was over 150 mg. per cent. The uric acid level in the serum was within the normal range at 5·1 mg. per cent. A plain radiograph showed a radio-opaque shadow near the vertebral column at the level of the second lumbar vertebra on the left-hand side. On the right-hand side no radio-opaque shadow was found which might have been attributed to ureteric calculus. On this side it was not possible to insert a ureteric catheter beyond 20 cm., nor was it possible to pass any contrast material beyond the obstruction. On the left-hand side the stone, which must have occupied the uppermost part of the ureter, was pushed back into the renal pelvis with the help of an 8 charrière ureteric catheter. The catheter was left in situ (*Fig.* 11). Subsequently the patient was treated with infusions, insulin, antibiotics, and strophantin until her general condition improved; her diabetes was regulated and the urea-nitrogen in the serum became normal. The infusion pyelogram obtained at this time on a 24-hour film showed considerable stagnation and indicated obstruction in the right ureter at the level of the third lumbar vertebra (*Fig.* 12).

The patient was operated on from the right-hand side. The radiolucent stone was removed by a ureterolithotomy incision (*Fig.* 13←). Through this incision the renal pelvis was lavaged and a number of small stones emerged with the irrigating fluid (*Fig.* 13⇷). It was then decided to perform a coagulum pyelolithotomy, assuming the presence of more stones in the renal pelvis. A Nélaton catheter was passed through the ureterotomy incision into the renal pelvis, where the coagulum was formed. A number of stones of varying sizes which had also escaped radiographic diagnosis were found in the coagulum after its removal (*Figs.* 13⇺, 14). Chemically they were uric acid stones.

The postoperative period passed without complications. The early postoperative intravenous pyelogram revealed a still slightly enlarged renal pelvis, but the calices showed no sign of stagnation (*Fig.* 15). The patient was discharged and advised to undergo a further operation on the other side after a period of 1 or 2 months.

DISCUSSION

The Solutions.—Dees (1955) suggested the use of a 4 per cent fibrinogen solution for the coagulum pyelolithotomy; the fibrinogen that he used was not available commercially. Stoll (1959) used fibrinogen manufactured by Behringwerke, but found that this product in a 4 per cent solution was not successful. He decided on a 3·84 per cent solution, which proved satisfactory. Klosterhalfen (1969) also had difficulties in obtaining a suitable coagulum and therefore decided to use a mixture of fibrinogen plus fresh blood-plasma with thrombocytes and thrombin plus a $CaCl_2$ solution. This seems to have proved satisfactory. The author has always used the fibrinogen manufactured by Behringwerke in the concentration suggested by Dees (1955) and has found it perfectly satisfactory. The early failures in the present series were due to the method being too complicated; since the simplified method has been used, as described in this paper, there have been no technical failures.

What happens to the Coagulum if it is left in the Kidney?—If part of the coagulum should remain in the kidney no harm is done. Dees (1943) showed that any coagulum kept in human urine at body temperature will dissolve within 6–24 hours, whereas a human blood-clot will have only partially disintegrated after 72 hours. Klosterhalfen (1969) found in a series of experiments involving 78 kidneys of rabbits that fibrin particles dissolved before encrustation could take place even in cases of chronic stone formation with urinary infections, alkaline urine, and hypercalcuria.

Partial Nephrectomy versus Coagulum Pyelolithotomy.—The main argument advanced in favour of partial nephrectomy (or pole resection) is that not only the stone itself but also its site of origin—the defective calix—is removed, thus reducing any possibility of stone recurrence. On closer examination, however, this assumption does not apply to all cases where pole resection is performed. Papathanassiasis and Swinney (1966) reported a series of 50 partial nephrectomies for calculi, of which 88 per cent were lower-pole resections. This is a similar figure to those reported by other authors. However, the frequent occurrence of calculi in the lower pole does not necessarily imply that the stones originated there. The stone nucleus might have developed in any part of the kidney and later have been deposited in the lower caliceal group owing to the effect of gravity. Of course, this explanation does not cover parenchymal stones.

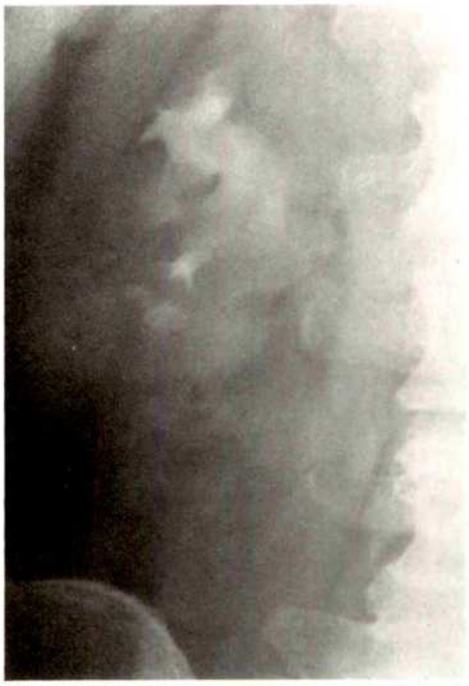

FIG. 15.—*Case* 2. Postoperative intravenous pyelogram.

Where the calix at the site of a stone shows extreme pathological/anatomical changes it is probably advisable to perform pole resection. However, it should be borne in mind that not all calices with gross pathological/anatomical changes necessarily form stones; this has been sufficiently well demonstrated by the many cases of pyelonephritis without nephrolithiasis. Therefore unless there is definite proof that the calix in which the stone has been found is responsible for its formation, coagulum pyelolithotomy rather than pole resection should be performed. Coagulum pyelolithotomy is much less traumatic and at the same time highly efficient, since it ensures complete removal of all the free stones, many of which may not even have previously been diagnosed. In many cases it proves to be technically difficult to remove a caliceal stone without inflicting gross injury to the kidney. In such cases nephrolithotomy or partial nephrectomy is often performed. The author would suggest performing coagulum pyelolithotomy first for the reasons mentioned above. Where the infundibulum of the calix is too narrow and the coagulum tears, leaving the part with the stone enmeshed inside the calix, partial nephrectomy or nephrolithotomy might still be performed. This procedure would have the additional advantage of the stone being fixed inside the calix so that it could not escape into the pelvis or another calix during the operation.

Suggestion for Common-duct Surgery.—The incidence of incomplete removal of stones in common-duct surgery, as reported by Paine and Firme (1957) and Catell (1957), varies from 2 to 28 per cent. Many other authors such as Glenn (1952), Hicken (1954), and Thomson (1956) have reported an incidence of 7–20 per cent. Common-duct stones, débris, and gravel might be removed as follows:—

a. Insert a Fogarty (1968) biliary balloon catheter through a small incision in the common duct in such a way that the balloon passes through the sphincter of Oddi.

b. Inflate the balloon and pull the catheter slightly so as to make the sphincter watertight. The hepatic ducts might be obstructed with the help of a soft clamp or one or two Fogarty catheters.

c. Inject a coagulum in a manner similar to that described for renal stones and extract it together with the enmeshed stones after deflating the balloon.

Intrahepatic calculi could be extracted in a similar fashion.

CONCLUSIONS

The indications for coagulum pyelolithotomy are as follows:—

1. Multiple stones and detritus in the renal pelvis.
2. Soft and crumbly stone.
3. Small mobile caliceal stones.
4. As an aid in fixing caliceal stone or stones prior to partial resection of the kidney or nephrolithotomy.

The advantages of this method are summarized below.

1. Trauma to the kidney is minimized. Every urologist has at one time or another experienced considerable difficulties in searching for an elusive stone. During his search he might injure not only the renal pelvis but also the calices and possibly even the renal parenchyma. Sometimes, owing to excessive bleeding a nephrectomy might have to be performed. Apart from this danger, it must be borne in mind that a traumatized kidney is more liable to form new stones. All of this may be avoided by the almost non-traumatic process of a coagulum pyelolithotomy.

2. Surgical mobilization of the kidney and subsequent nephropexy are not necessary since it is sufficient to expose the renal pelvis.

3. All the free stones within the renal pelvis are removed regardless of size, number, or position. Frequently additional stones are removed which for a variety of reasons had not been diagnosed and therefore not looked for. At a later date such stones would probably have been considered to be 'recurrent' stones. Sometimes it is even possible to remove stones which have been partly adherent to the mucosa. In the case of crystalline stones in particular the tough coagulum encloses that part of the stone which is not adherent to the mucosa so firmly that mucosal adherence constitutes no serious obstacle to extraction. Where the caliceal infundibulum is too narrow it is, of course, impossible to extract any stone. However, the width of the infundibulum as shown in an intravenous pyelogram does not correspond to the actual width. Once the renal pelvis is overdistended by the coagulum the width of the infundibulum increases considerably. This may be confirmed preoperatively with the help of an oxygen retrograde pyelogram, whereby the renal pelvis is distended by oxygen until the patient feels a slight pain in his kidney. Even when it is impossible to remove the coagulum with the stone enmeshed no harm is done, since partial resection may still be performed. In some cases it has been possible to remove stones which could not be dislodged even with extensive lavage of the renal pelvis.

4. In some cases it is advisable to fix a caliceal stone with the help of the coagulum prior to pole resection or nephrolithotomy. In this way the stone cannot get lost during further surgical mobilization and operation. This fixation is especially useful in the case of multiple caliceal stones, where the danger is greater because minute stones may escape unnoticed into the pelvis or into another calix.

5. Fragmentation of the stone during removal is avoided. Stone fragmentation happens more often than is realized. It occurs especially when the stone is soft and crumbly. However, even when the stone is fragmented the residual fragments may easily be removed with the help of the coagulum.

Acknowledgements.—I should like to express my gratitude for their active support to Dr. W. Becker, Head of the Urological Department, Municipal Hospital, Oldenburg, and Professor Dr. (med.) G. Karcher, Head of the Urological Clinic, Municipal Hospital, Offenbach.

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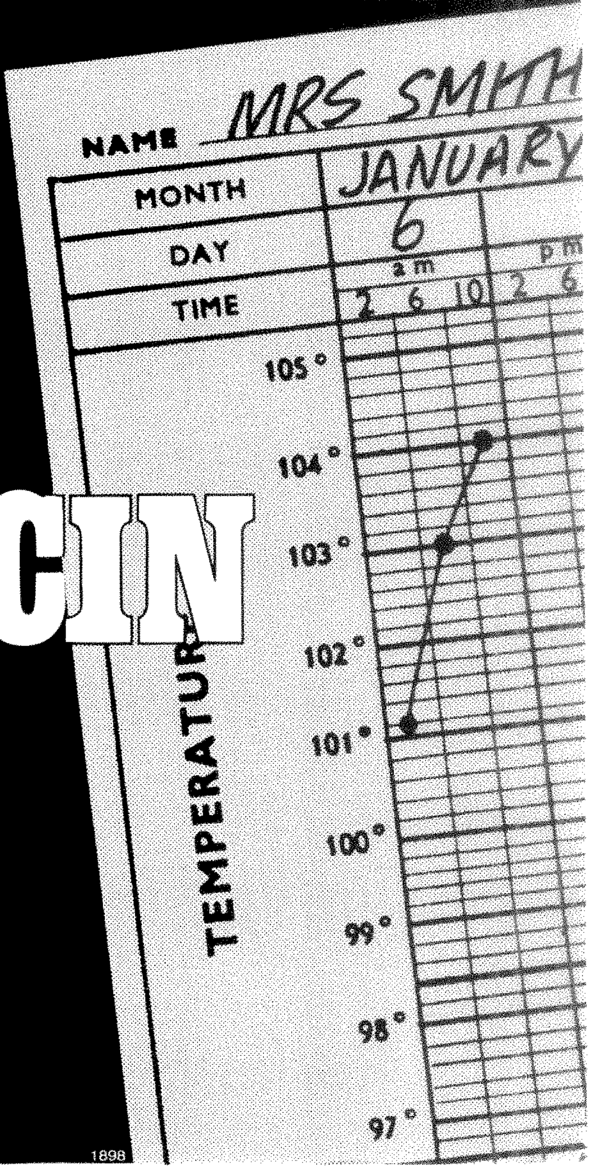

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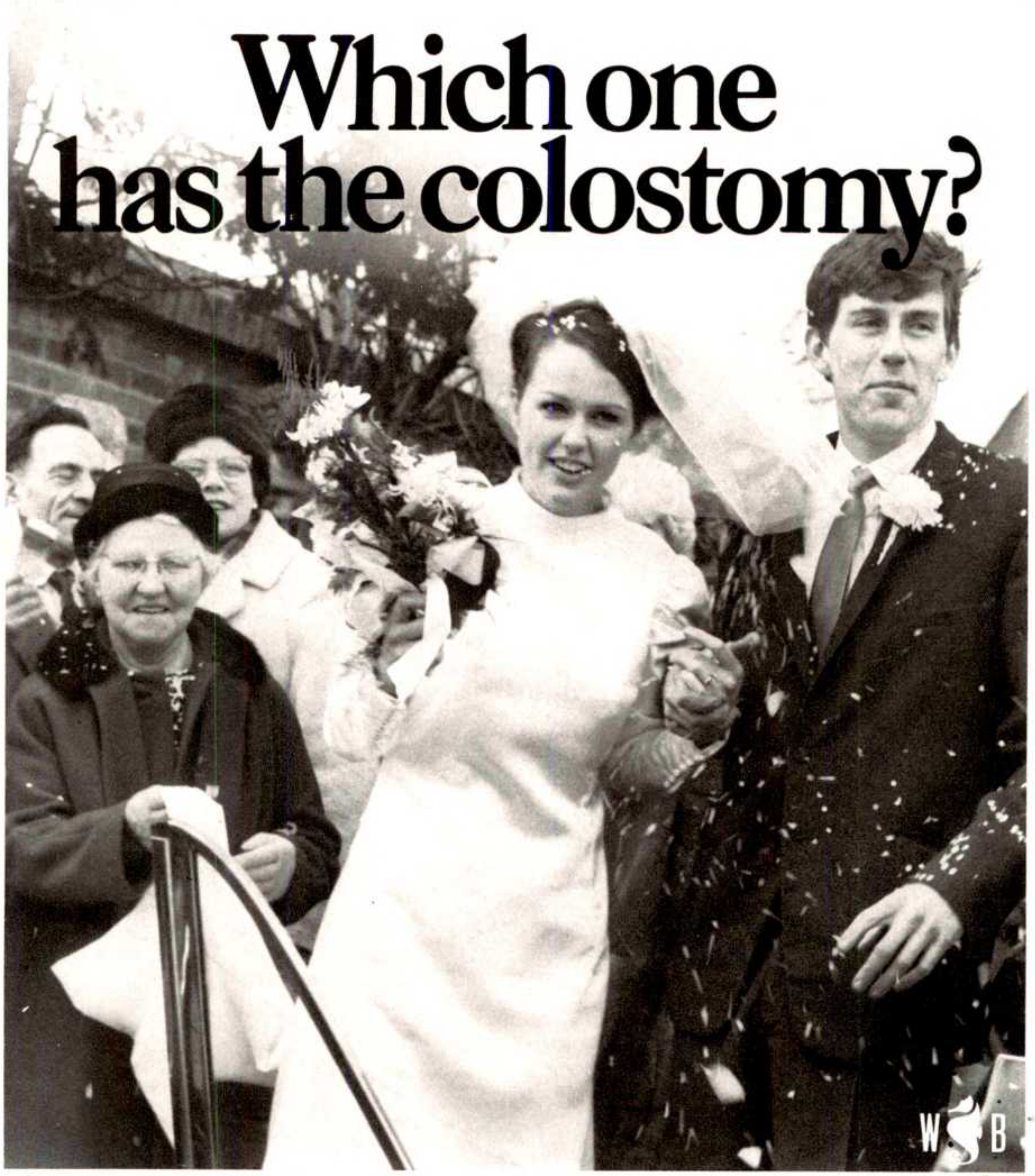

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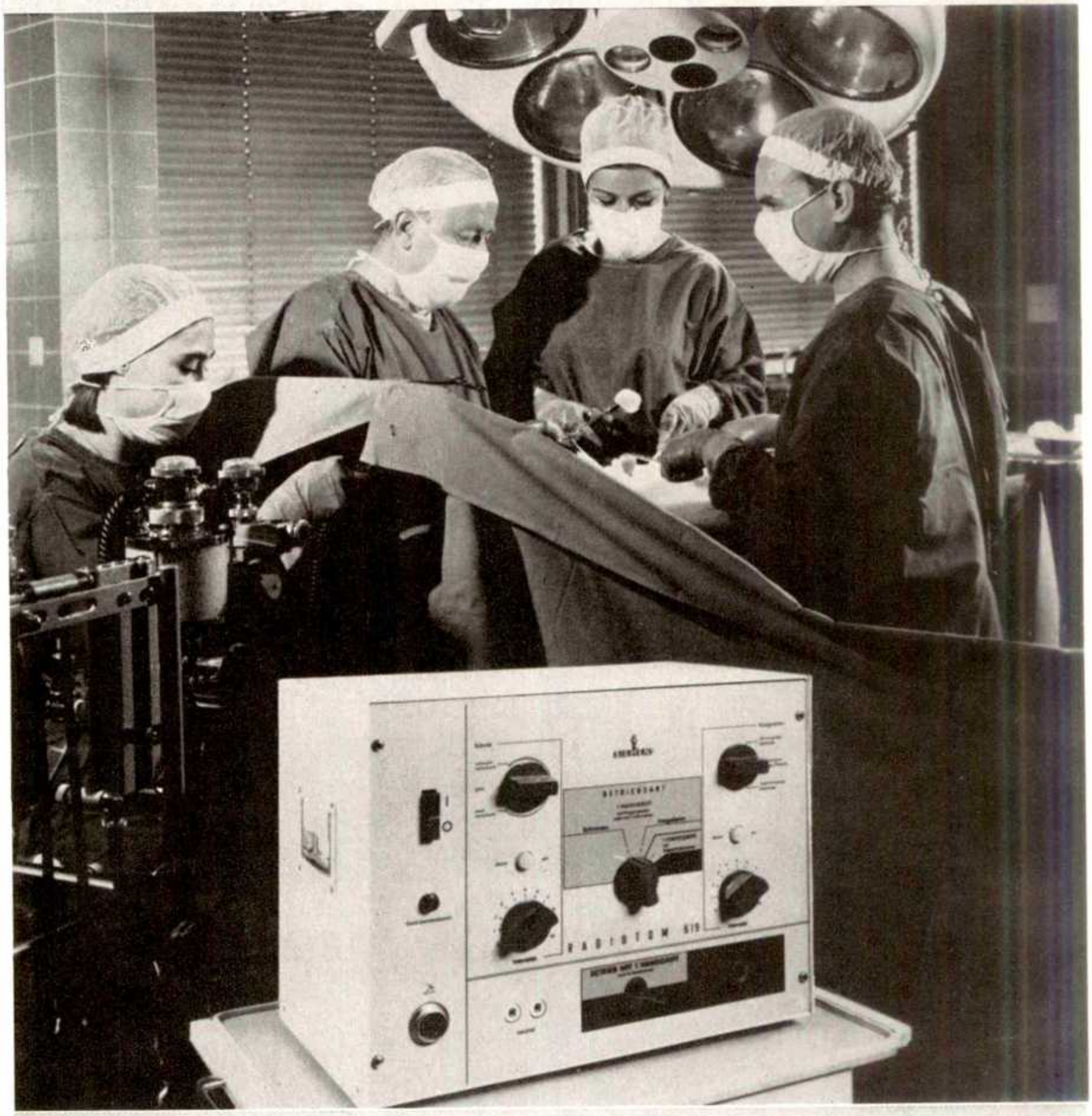

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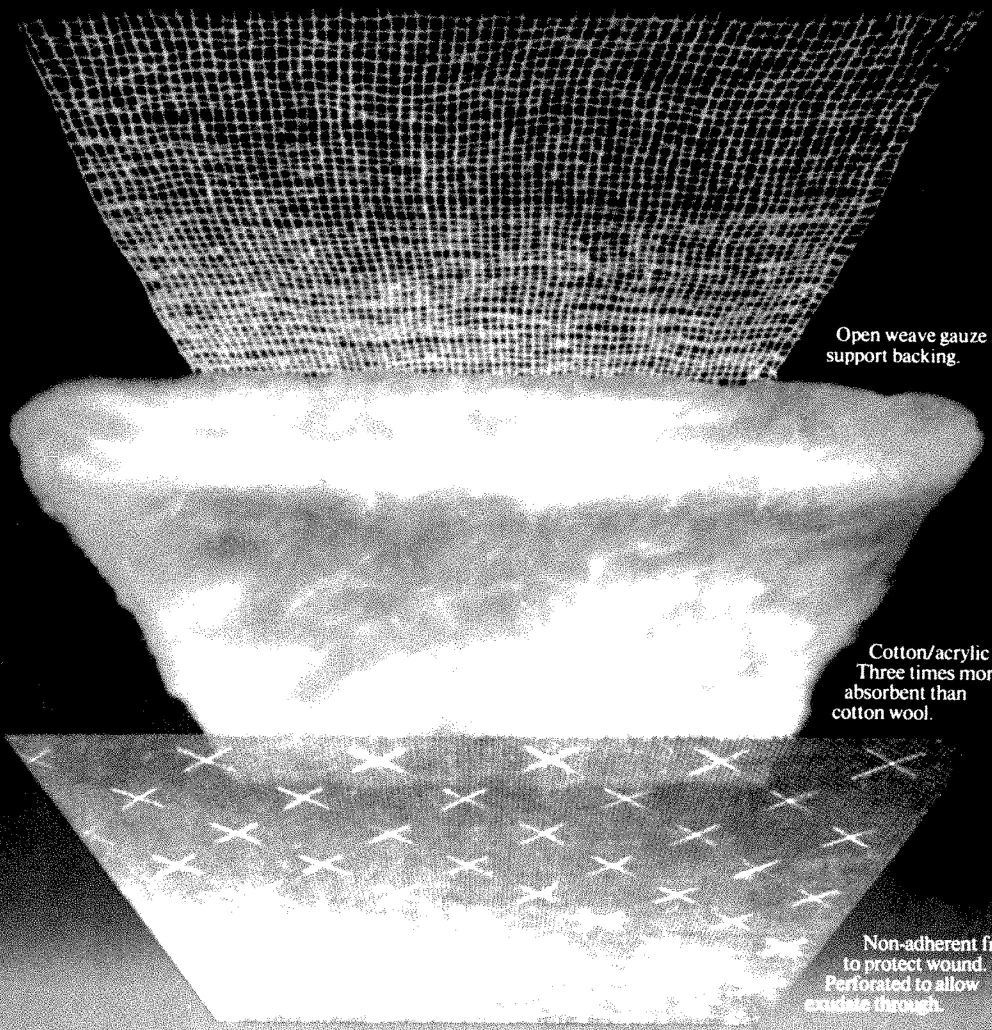
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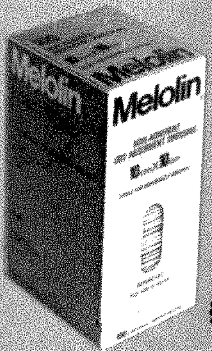


'FRUIT-STONE ILEUS'

BY PAUL C. WEAVER AND DAVID H. TRAPNELL
WESTMINSTER HOSPITAL, LONDON

SUMMARY

Three cases of 'fruit-stone ileus' are reported in which ingested plum stones were obstructed in their progress through the bowel by other disease. Over the succeeding months or years the stones enlarged and then began to cause symptoms. Radiological aids to diagnosis are discussed together with the surgical treatment.

'GALL-STONE ileus' is a well-known clinical diagnosis. In fact, it is inaptly named because the process is essentially one of simple mechanical obstruction by the calculus. This name is now so well established that we suggest it is reasonable to call the condition that is described here—intestinal obstruction produced by plum stones—by a similar misnomer, 'fruit-stone ileus'.

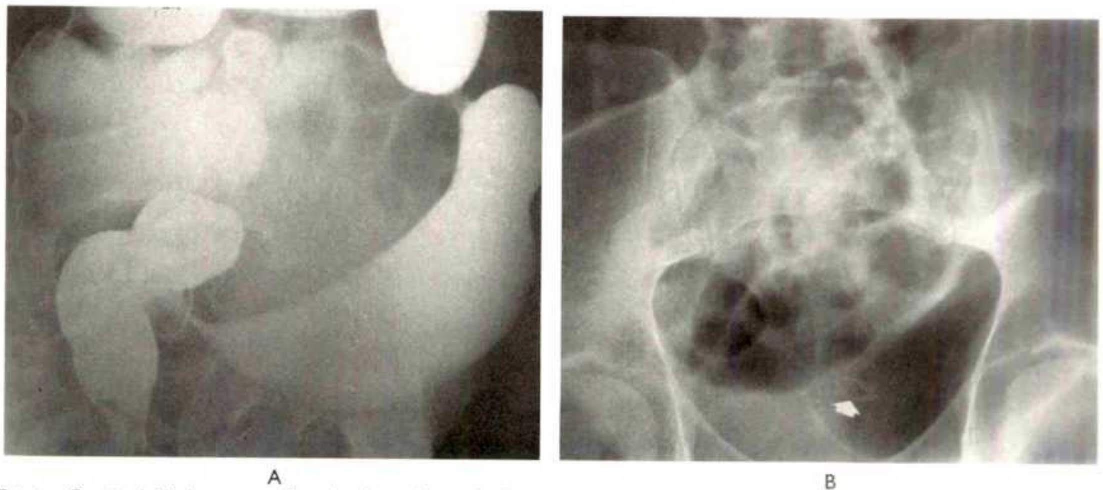


FIG. 1.—*Case* 1. A, Barium-enema film, showing strictures in the sigmoid colon. B, Plain radiograph, showing a calcified plum stone in a segment of gas-distended sigmoid colon.

Three cases are described to illustrate the 'silhouette' sign in the initial radiographic investigation and the presence of some pathological lesion within the intestinal tract which initially impeded progress of the fruit stones. In 2 patients the stones became coated by inorganic and organic material, permitting them to become large enough to produce intestinal obstruction. In the third case obstruction was caused by the plum stone itself when it impacted in a colonic stricture.

CASE REPORTS

Case 1.—Mr. L. L. C., aged 55 years, had a history of recurrent diarrhoea and blood in the faeces for 30 years. This had been diagnosed as chronic ulcerative colitis. Two years before admission to the Westminster Hospital the patient had been admitted to another hospital with an abscess in his right iliac fossa which was drained. A diagnosis of Crohn's disease had been made at that time and had been confirmed by barium studies of the small intestine in the following year. A barium-enema examination had shown multiple strictures in the colon (*Fig.* 1 A).

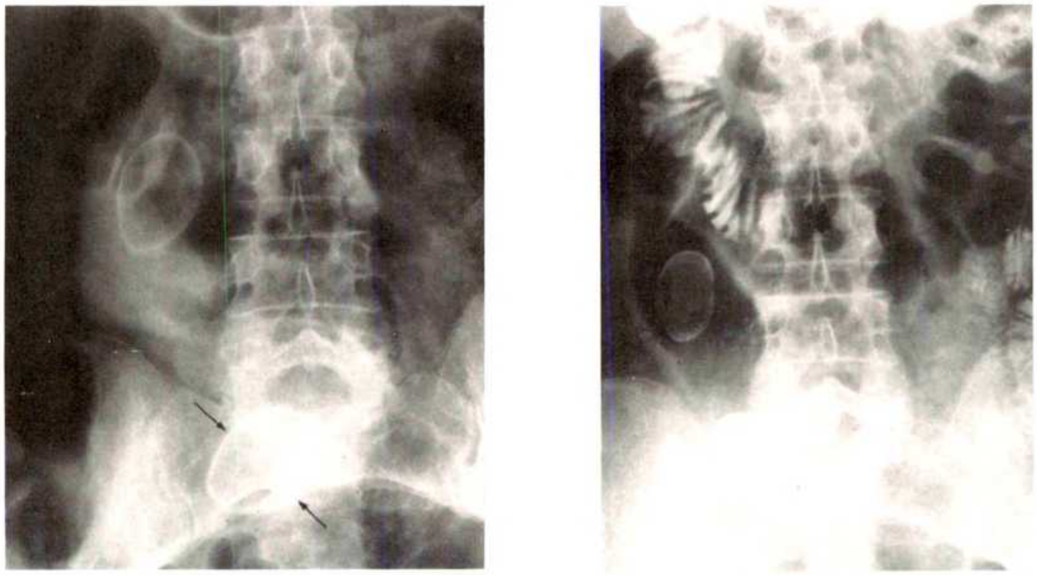
For the next year or so he had suffered from recurrent attacks of abdominal distension with pain, and alternating diarrhoea and constipation. Barium-enema examination again showed colonic strictures. During one of these attacks a plain radiograph of the abdomen revealed what looked like a calcified plum stone in the segment of gas-distended sigmoid colon (*Fig.* 1 B).

The patient said that he had eaten no plums or prunes recently. Later radiographs showed the opacity unchanged. A subsequent operation 5 months later to remove part of the left colon and its strictures proved the presence of a plum stone trapped in a length of sigmoid colon between two strictures. Histological examination of the excised colon showed changes typical of Crohn's disease.

Case 2.—Mrs. F. B., aged 62 years, was investigated for attacks of abdominal pain in 1965 at another hospital in London. She was told that there were two radio-opaque foreign bodies which appeared to be in a loop of dilated small bowel. An operation was offered but was declined. From that time she had minor intermittent attacks of colicky abdominal pain and was subsequently admitted to Queen Mary's Hospital, Roehampton, in August, 1970, as a surgical emergency with severe colicky abdominal pain and vomiting. She had had an appendicectomy at the age of 16, a laparotomy for adhesions at the age of 18, and a hysterectomy at the age of 32 years.

On examination there were three lower abdominal scars. The abdomen was distended. Plain radiographs of the abdomen showed a dilated loop of small bowel and three calcified foreign bodies. The patient's symptoms settled on conservative treatment and she again refused operation.

A Gastrografin meal confirmed that the foreign bodies were in the lumen of the bowel with the help of the 'silhouette' sign (*Fig.* 2 A, B). The films also indicated that the lesions were impacting at a narrowed segment within the ileum. The patient agreed to operation 9 days later when three large black stones were found lying in a distended loop of small intestine. This loop was occluded at its distal end by dense adhesions. There was also a fistula between the two ends of the loop (*Fig.* 2 C). The stones proved to be plum stones with numerous layers of faecal material around them, the outermost parts being calcified. The patient made a satisfactory and uneventful recovery.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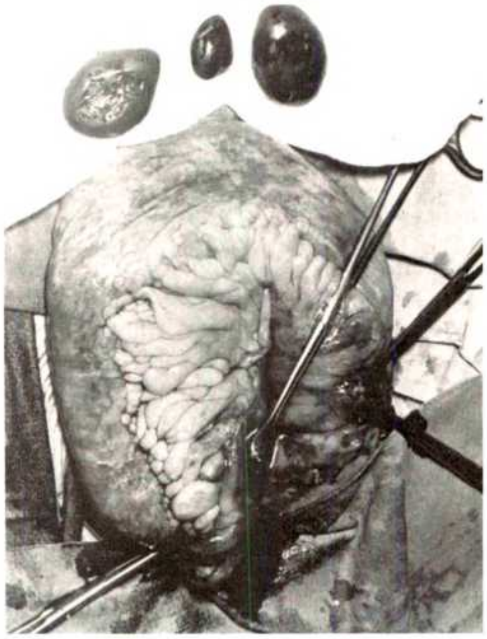
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FIG. 2.—*Case* 2. A, Gastrografin-meal film, showing two foreign bodies within a distended loop of bowel. Gastrografin surrounds them and makes them less distinct. B, Plain radiograph, showing the foreign bodies without surrounding Gastrografin. The upper stone is surrounded by air and is therefore more sharply defined. The lower stone is surrounded by fluid and overlies part of the sacrum making it less distinct. The thick wall of the distended loop of intestine is well shown. C, Operative photograph, showing the obstructed loop of bowel with the three coated plum stones removed. Instruments mark the site of the fistula.

Case 3.—Mrs. A. W., aged 85 years, was admitted as a surgical emergency in March, 1971, to Queen Mary's Hospital, Roehampton, with a history of abdominal pain and vomiting for 2 weeks. Two years earlier she had had an attack of colicky abdominal pain which had settled without treatment. A plain radiograph of the abdomen at that time had shown an oval opacity, which looked like a plum stone, near the left sacro-iliac joint (*Fig.* 3 A). There had been no evidence of intestinal obstruction at that time.

On examination on the present occasion the patient was a frail, elderly woman with a distended abdomen which was tender and quiet. Abdominal radiographs showed the presence of multiple fluid levels in the small intestine and also two laminated foreign bodies (*Fig.* 3 B). Laparotomy was carried out and the terminal ileum was found to be obstructed by two large black smooth stones which could not pass along the lumen because they were held back by a pedunculated polyp (*Fig.* 3 C). The bowel wall over the larger stone had perforated and there was generalized peritonitis. The segment of ileum containing the polyp, stone, and perforation was excised. The patient deteriorated and died from intraperitoneal sepsis and congestive cardiac failure.

The stones were found to have a nucleus of fruit stone around which there were layers of inorganic and faecal material. Histological examination showed that the polyp was a pedunculated angioma.

DISCUSSION

Each of our 3 cases had intermittent attacks of intestinal obstruction caused by radio-opaque foreign bodies within the bowel lumen impacting against a pathological form of mechanical obstruction. When considering such a diagnosis it is obviously important to be certain that the foreign body lies within the lumen of the bowel. The 3 cases described here show how this can be proved radiologically by the 'silhouette' sign, as described by Melhem, Habbal, and Imad (1970), who applied it to the localization of urinary-tract calculi. They point out that when a radio-opaque calculus lies within a hollow viscus it is clearly seen in the radiograph. However, when the viscus is filled with contrast medium the opacity becomes less clearly defined or if the contrast medium is sufficiently opaque it 'disappears' and the whole lumen becomes evenly radio-opaque (*Figs.* 1 A, 2 A, B). On the other hand, if the foreign body is lying outside the viscus containing contrast medium it will remain visible through it and the edges of the opacity produced by the lesion will remain sharply defined.

In the present cases the downward passage of the fruit stone in the gut was blocked by some mechanical obstruction: in the first case by a stricture due to Crohn's disease, in the second case by adhesions following appendicectomy, and in the third case by a polyp. These cases illustrate that fruit stones may be held up by a narrowed segment of bowel where they may become the centre of an enterolith by being coated with layers of organic or inorganic material. When large enough the enterolith may cause obstruction or perforation of the bowel. Where intraluminal foreign bodies are removed it is worth looking carefully for the site of gut narrowing which should also be removed to prevent a recurrence of the problem.

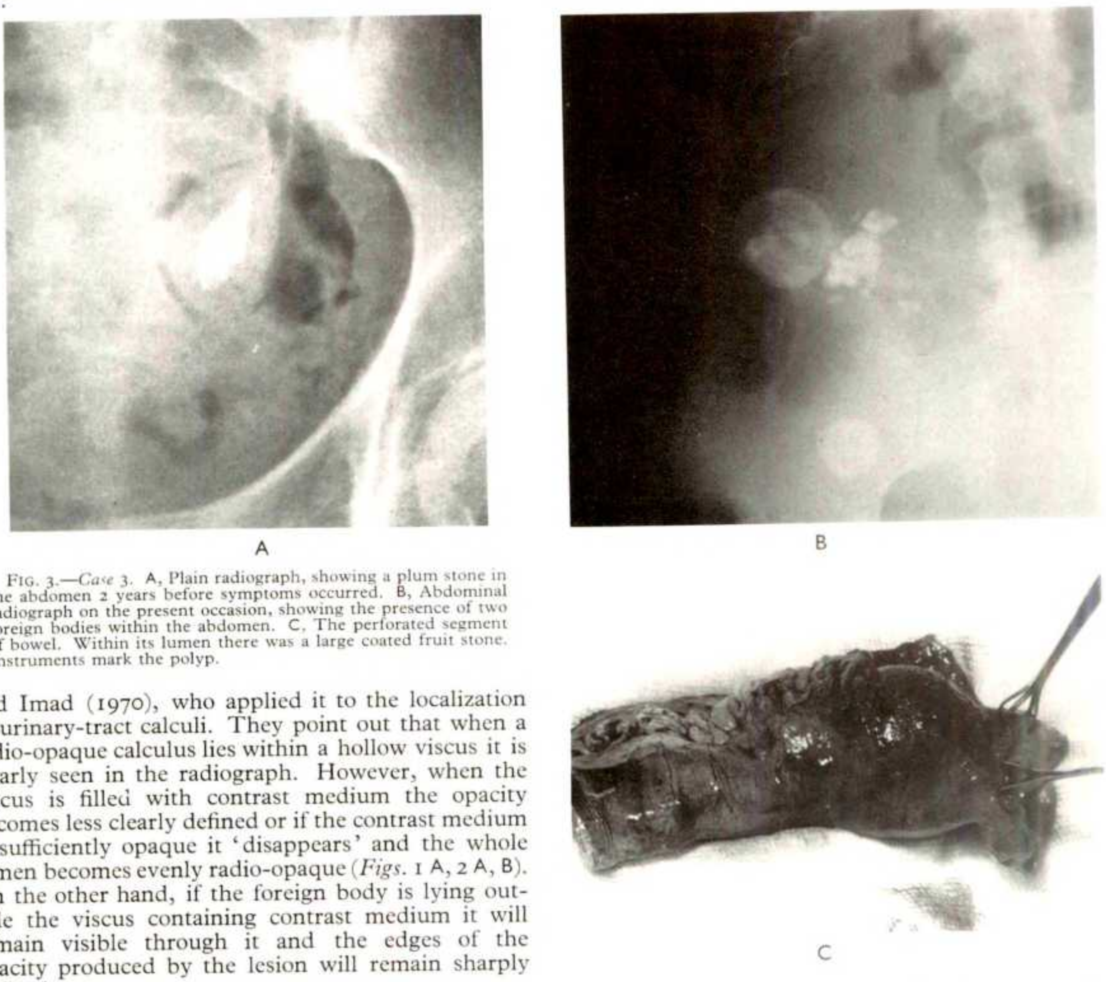

FIG. 3.—*Case* 3. A, Plain radiograph, showing a plum stone in the abdomen 2 years before symptoms occurred. B, Abdominal radiograph on the present occasion, showing the presence of two foreign bodies within the abdomen. C, The perforated segment of bowel. Within its lumen there was a large coated fruit stone. Instruments mark the polyp.

Acknowledgements.—We are indebted to Professor Harold Ellis and Mr. A. G. Rutter, under whose care these patients were admitted, for permission to publish details of these cases, to the Department of Medical Photography, Westminster Hospital, for the preparation of the photographs, and to Miss R. Kitson for typing the manuscript.

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SHORT NOTES OF RARE OR OBSCURE CASES

GLOVE-POWDER GRANULOMA OF THE TESTIS AFTER SURGERY

BY J. I. PUGH AND PAUL STRINGER
ST. ALBANS CITY HOSPITAL, ST. ALBANS, HERTFORDSHIRE

SUMMARY

A case of epididymitis and periorchitis due to talc granulomatosis 11 years after operation for hydrocele is reported. The pathology of the lesions caused by the inadvertent contamination of tissues during surgical operations is reviewed with particular reference to the testis.

THE contamination of operation wounds by dusting powder (either *Lycopodium* or magnesium silicate) from the surgeons' gloves with the reaction of tissue granulomata has been the subject of numerous studies both clinically and experimentally. The widespread recognition of talc granulomata, particularly within the peritoneal cavity, prompted the adoption of starch powder, but similar changes have now been described following the use of this agent. These may occur at other sites outside the abdomen, such as the skin, soft tissue, and viscera, and give rise to clinical and histological problems, as the present case illustrates.

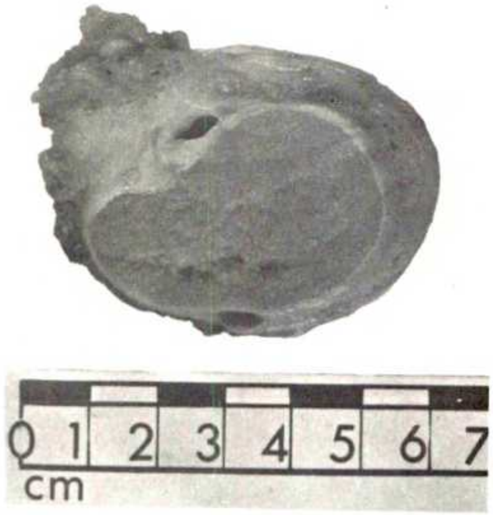

FIG. 1.—Bisected left testis showing periorchitis and a white mass in the head of the epididymis.

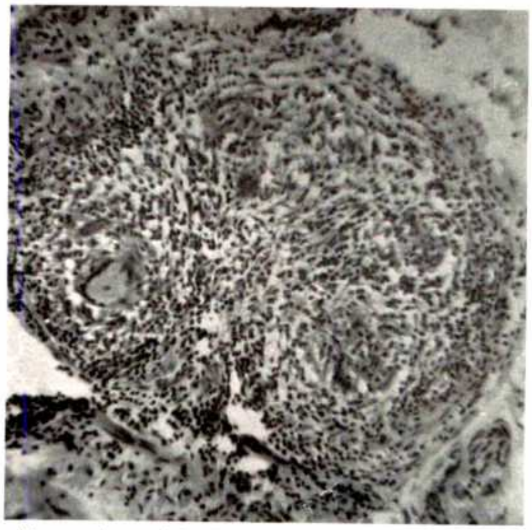

FIG. 2.—A rounded cell nest in the epididymis composed of foreign-body giant cells, epithelioid histiocytes, and lymphocytes. H. and E. (× 54.)

CASE REPORT

F. P., aged 71 years, underwent left orchidectomy for the removal of a craggy testis in October, 1970. He presented with one episode of haematuria when the enlarged testis was noted. As he gave a history of the removal of a left kidney for hypernephroma by Mr. M. R. Williams at the Isle of Thanet Hospital in October, 1969, a preoperative diagnosis of metastatic deposit in the testis was contemplated. It was not until after the specimen had been examined microscopically that the patient admitted on questioning that an operation for radical cure of a left hydrocele had been done in 1958. Also, in May, 1967, a similar operation had been performed for a right hydrocele, and at the same time a herniorrhapy had been carried out. All these operations had been done in Thanet by Mr. Williams who kindly confirmed the patient's story. The patient made an uninterrupted recovery from the present operation. He remained free of trouble until September, 1971, when after a second episode of haematuria a space-occupying lesion was demonstrated in the lower mid-zone of the single remaining kidney by an excretory urogram. Further investigations are now proceeding at another hospital.

PATHOLOGY.—The testis measured 5 × 4 × 4 cm. and weighed 55 g. and had been removed with a stump of spermatic cord. The bisected testis was noted to be normal but there was a thick layer of connective tissue applied to the tunica albuginea. Replacing the head of the epididymis was a hard, white, poorly defined lump, 2 cm. in diameter (*Fig.* 1).

Microscopic examination of haematoxylin-and-eosin-stained paraffin sections showed a dense fibrous reaction within the head of the epididymis, at the base of the spermatic cord, and around the tunica albuginea. Amongst the fibrous tissue were rounded nests of cells, 0·5 mm. in diameter, which were confluent in places. They consisted of foreign-body giant cells with both central and peripheral nuclei surrounded by epithelioid histiocytes and lymphocytes. Only rarely was a small focus of fibrinoid necrosis seen. The seminiferous tubules were normal for a man of 71 years apart from a very occasional granuloma found between superficially placed tubules.

Examination of the same section by polarized light revealed a multitude of needle- or irregularly shaped optically active crystals, up to 20 μ long, lying mainly amongst collagen fibres but also within giant cells (*Figs.* 2, 3). In general it was noted that the fully developed granulomata contained scanty optically active crystals.

At this point a histological diagnosis of glove-powder granuloma was considered and two further sets of examinations were employed to confirm the diagnosis. First, the nature of the optically active material was investigated and, secondly, other forms of granuloma were excluded. For the latter Ziehl-Neelsen preparations were examined for tubercle bacilli, and a search for lipid was made by the use of the periodic acid-Schiff and long Ziehl-Neelsen techniques, as described by Phillips (1961). These investigations proved negative. In order to identify positively the birefringent material a spodagram was used (Wolman, 1970). In this technique the dewaxed unstained paraffin sections were incinerated to about 600° C. and after cooling a cover-slip was placed over the residue. Examination of this preparation by polarized light showed the needle-shaped and amorphous material to be present to the same extent as before, thus establishing their nature as silica or talc. Resistance to exposure to 50 per cent hydrochloric acid for 1 hour was further proof of identification.

CLINICAL APPRAISAL

The appearance of nodules within tissues, particularly the peritoneum, after surgical intervention presents the clinical problem of either recurrent or newly acquired disease, and in respect of malignant neoplasms the possibility of metastasis. The occurrence of granulomata following the use of various glove powders is now well recognized, and the literature concerning these lesions mostly pertains to the peritoneum (Antopol, 1933; German, 1943; McAdams, 1956; Hyden and McClellan, 1959; Myers, Deaver, and Brown, 1960; Blair and Blumenthal, 1964; McNaught, 1964; Bates, 1965; Cox, 1970).

The direct implantation of glove powder into the tunica vaginalis is illustrated in 2 case reports. Antopol (1933) records the case of a 35-year-old Spaniard who developed a mass in the epididymis with a persistent sinus 2 months after operation for traumatic hydrocele. Orchidectomy was performed and microscopic pathology revealed a tuberculous type of lesion due to spores of *Lycopodium*. Cox (1970) also reports the case of a 6-year-old boy whose testis was explored for suspected torsion. Epididymo-orchitis was found and the scrotum was closed. A mass developed during the following month and, assuming a diagnostic error, the testis was excised. The mass was a starch granuloma.

In the case reported here it was reasonable to postulate secondary deposits of a renal adenopapillary carcinoma, spreading by extension or embolism along the left spermatic vein. The apparent enlargement of the testis was not associated with the previous operation for hydrocele, which would necessarily entail the opening of the tunica vaginalis. It is not necessary, however, for the scrotum to be incised to produce testicular foreign-body granulomata. Saxén and Saxén (1965) report an example (*Case* 13) of the transmission of starch powder from the abdominal cavity to the testis after laparotomy for ruptured liver in a boy aged 4 years. Two months later an olive-sized nodule was found in the testis when removed. Microscopic examination showed a starch granuloma within the tunica vaginalis. Presumably, although it is not actually stated, the processus vaginalis was patent. Crystalline talc has also been shown to spread by lymphatics and to give rise to granulomatous lesions in regional lymph-nodes (Shattock, 1917). Starch particles also spread in this manner and cause lymphadenitis (Neely and Davies, 1971). The powder is either a contaminant from the surface of the gloves (Lee and Lehman, 1947) or from punctures, which are often unrecognized (Weed and Groves, 1972). Butterfield (1970), analysing 100 operations, found a total of 190 separate punctures and confirms the findings of Shouldice and Martin (1959) and Russell, Roque, and Miller (1966) that there is at least one defective glove after operations lasting 1 hour. The recognition of this complication and the importance of washing fresh gloves are emphasized (Taft, Lasersohn, and Hill, 1970).

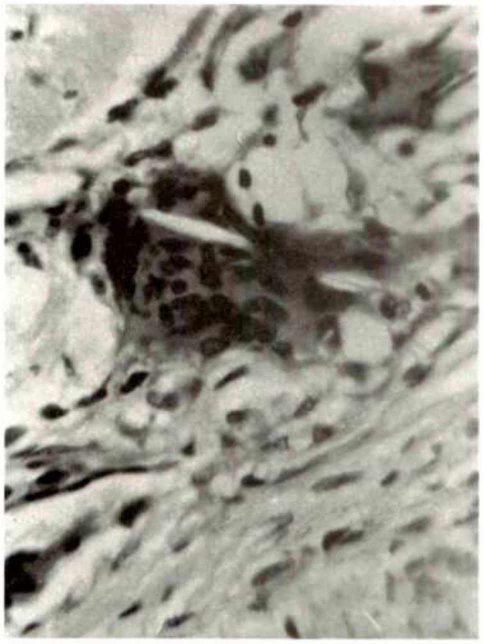

FIG. 3.—A foreign-body giant cell containing birefringent talc crystals in a fibrous tissue reaction. H. and E. (× 240.)

The recognition of glove-powder granulomatosis is primarily for the histologist, but without knowledge of previous operations the microscopical appearances could easily be confused with sarcoidosis, tuberculosis, syphilis, granulomatous orchitis, sperm granuloma, malignant lymphoma, and miscellaneous inflammatory lesions simulating malignancy (Morgan, 1964). This is because the mixture of cellular elements is so variable. The key to microscopic diagnosis is the examination of sections by strong polarized light, for the foreign bodies may be quite inconspicuous by ordinary light microscopy. Foreign bodies that are not in proximity to the cells comprising the granuloma should be ignored, for they may be derived from either the surgeon's or the pathologist's gloves whilst handling the specimen.

Lee, Collins, and Largen (1952) state that no matter how benign the powder may be and no matter how quickly absorbed, it is, for the duration of its presence in tissue, a foreign body. Furthermore, the longer the granules remain unabsorbed the more advanced the foreign-body reaction will be and the less chance there is that it will be reversible. When a complicating factor such as an infection is added to the foreign-body reaction of the tissues the process is exaggerated and the extent of permanent scar tissue is proportionately increased. The amount of the contaminant powder is another factor in the pathogenesis and, as would be expected, the larger the contamination the greater is the lesion. The variation in response is reflected in the clinical manifestation after contamination by starch powder. The time lapse may be between 2 weeks and 4 years (Cox, 1970) but most appear within a few weeks or months (Saxén and Saxén, 1965). Mackey and Gibson (1948) describe florid granulomata developing within 2 weeks of implantation of talc, and Walker (1948) has shown that a siliceous granuloma can produce a firm peritoneal adhesion in 7 weeks. However, talc may also remain dormant in tissues and 45 years may pass before a lesion appears (Roberts, 1947). In the example reported here over 11 years elapsed between the two operations within the scrotum. Neely and Davies (1971) consider that the condition is more common than is usually realized, particularly within the peritoneum. That starch powder is preferable to talc is borne out by Myllarniemi (1967), who found a foreign-body reaction in 61 per cent of patients after abdominal surgery, for which talc was responsible in 31 per cent and starch in 1 per cent of cases. Nevertheless the comparative rarity of starch granulomata despite the wide use of glove powder and the possibilities of contamination suggests that the response is due to hypersensitivity or an allergi reaction. No such response was evident in the presen case and no such experimental confirmation ha been hitherto adduced (MacQuiddy and Tollman 1948; Lee and others, 1952; Bates, 1965).

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NEURILEMMOMA PRESENTING AS A LUMP IN THE BREAST

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As far as is known a neurilemmoma growing in the breast tissue has not previously been reported. Such a case is described here.

CASE REPORT

The patient was a 43-year-old housewife and mother of 4 children. One child had been breast-fed for a month, the second child had not been breast-fed because a breast abscess had developed, and after the births of the other 2 children breast-feeding had been suppressed.

Nine years prior to admission the patient had been on a contraceptive pill for 1½ years. In 1965 she had had a hysterotomy for a termination of pregnancy. She also had curettement of the uterus and dilatation and cauterization of the cervix in 1966 for a cervical erosion. Sh had had a variety of complaints recently including depression and, 6 months prior to admission, a mycoplasm pneumonia.

The patient presented with a lump in the right breas which she had noticed for 1½ weeks whilst she was havin a period. It was not tender and the patient thought tha it might have become larger during the time that she ha waited for an out-patient appointment.

On examination she had a firm lump, 2 × 1 cm., o rubbery consistency and regular outline in the uppe outer quadrant of the right breast. This was mobile an not tender. There were no axillary or supraclavicula nodes palpable, no stigmata of neurofibromatosis, an no other abnormal physical signs. She had not noticed any discharge from the nipple. Clinically, it was considered that the lesion was a fibro-adenoma of the breast and that it should be removed.

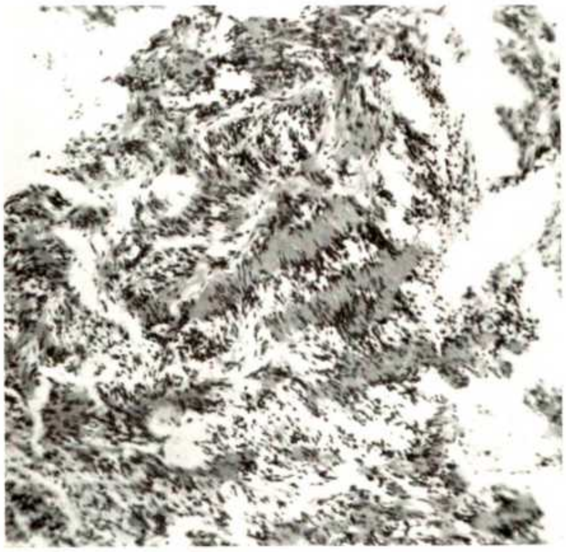

FIG. 1.—Characteristic nuclear palisading in Antoni A areas. H. and E. (× 75.)

OPERATION.—At operation a freely mobile lump was removed from deep in the breast. It did not have the appearances of a fibro-adenoma in that it seemed myxomatous and there was an area of yellow material at one end that looked like hard, dense fat. This was subjected to a frozen section, the report of which was inconclusive. However, it was felt that there were no grounds for advocating a mastectomy until the paraffin section had been seen. The wound was closed with silk sutures and the patient returned to the ward. Subsequently the wound healed satisfactorily and the patient was discharged a few days later. Postoperatively she has remained well.

HISTOLOGY.—Paraffin sections of the tumour showed a typical neurilemmoma. Both the main histological features of Antoni A areas (highly cellular with a dark-staining cytoplasm) and Antoni B areas (pale cells with an irregular outline lying in a watery matrix) were present. Within the Antoni A areas there were groups of cells showing the characteristic palisaded nuclei (*Fig.* 1).

DISCUSSION

Solitary neurilemmomas or Schwannomas may arise from any nerve that has a sheath. They are thought to be tumours of the Schwann cells which comprise the nerve-sheath, although there has been some attempt to cast doubt upon this theory (Penfield, 1932).

Neurilemmomas may be intracranial or peripheral. The commonest form of intracranial neurilemmoma is the acoustic neuroma. Peripherally the commonest sites are on the flexor aspect of the principal nerves of the limbs, in the posterior mediastinum, and in the stomach (Stout, 1935). However, although various sites have been described we can find no evidence of one presenting as a lump in breast. In several series (Willis, 1967) it has been noted that whatever the site females are more frequently affected than males.

The tumour itself is not locally invasive and, depending upon the site, it should be possible to enucleate it completely without damaging the underlying nerve. Local recurrence only occurs if enucleation has not been complete.

Acknowledgements.—Our thanks are due to Mr. Peter Lord and Dr. David Spencer for allowing us to report on this case, to Professor Noel F. Gowing for his second opinion on these sections, and to Mr. Martin Casling for the photography.

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HORSESHOE KIDNEY AND ABDOMINAL AORTIC ANEURYSM

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SUMMARY

A case of horseshoe kidney and an abdominal aortic aneurysm is presented. The 32 previously described cases are reviewed and the diagnosis and management are discussed. The major factors influencing the operative approach to an aortic aneurysm associated with a horseshoe kidney concern the site of origin of the renal arteries, their number, and the portion of the kidney which each supplies.

THE association between a horseshoe kidney and an abdominal aortic aneurysm has previously been reported and 32 cases are documented in the world literature. A further case is described here and the previous 32 cases are reviewed.

CASE REPORT

Mr. J. S., a 65-year-old man, presented with a 4-month history of aching midlumbar backache and abdominal pulsation. On examination he was found to be normotensive and to have a large abdominal aortic aneurysm.

INVESTIGATIONS.—A radiograph of the abdomen confirmed calcification in the abdominal aneurysm. An intravenous pyelogram (*Fig.* 1) showed calcification in the right kidney and malrotation of both sets of calices, suggestive of a horseshoe kidney. The blood-urea was 33 mg. per cent.

OPERATION.—On 17 Sept., 1970, a laparotomy was performed via a long midline incision which confirmed the preoperative diagnosis. The main bulk of the horseshoe kidney with its convexity caudad lay on the left side. The tissue bridging the aorta was 2·5 cm. in thickness and 5 cm. in depth, the right half of the kidney being small. There were three separate renal arteries, renal veins, and ureters (*Fig.* 2). The distribution to the left and right halves of the kidney was essentially normal, with the ureters descending anteriorly to the isthmus. The isthmus was tethered by its vascular supply with the central artery arising from the posterior aspect of the abdominal aorta at its bifurcation and the central vein descending across the aortic bifurcation and entering the right common iliac vein. The central ureter lay behind the right common iliac vein. To gain access to the proximal and normal-looking aorta it was necessary to retract the kidney by dividing the central artery, vein, and ureter (*Fig.* 3).

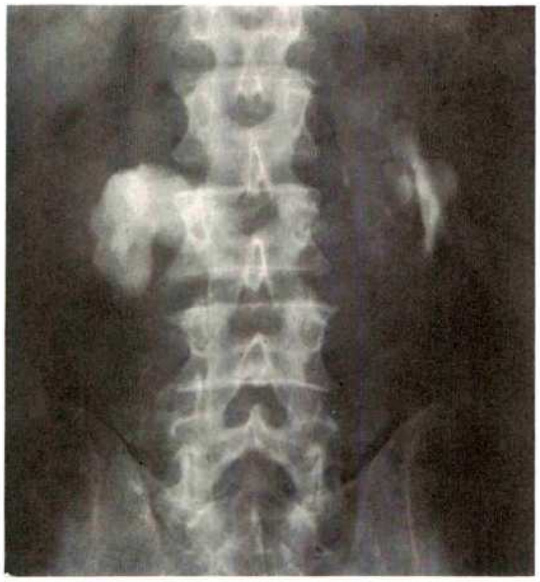
FIG. 1.—The intravenous pyelogram, showing rotation of the pelvis and calcification in the right kidney.

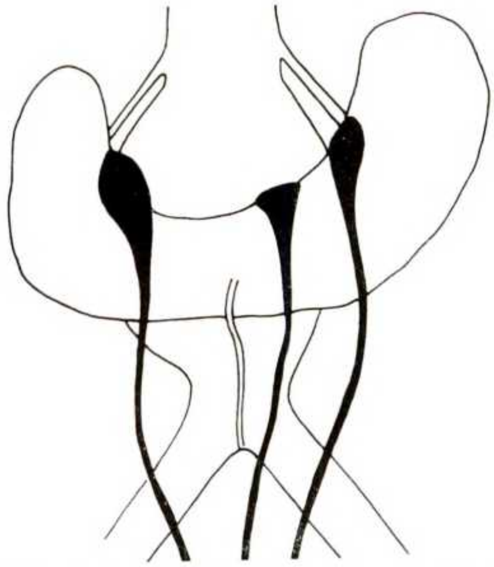
FIG. 2.—Diagrammatic representation of the anatomical configuration in the present case. For the sake of clarity, the veins have been omitted. The ureters are depicted in black.

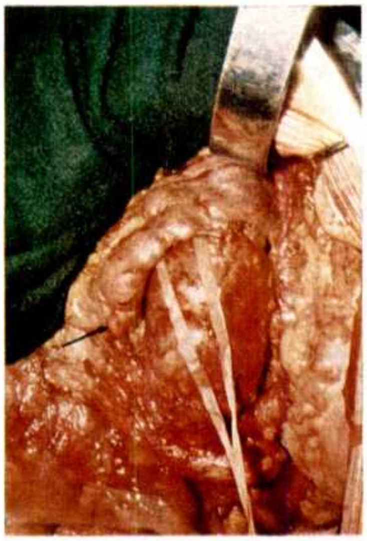
FIG. 3.—Peroperative photograph. The isthmus of the horseshoe kidney is retracted proximally after division of the central artery and ureter. The right ureter is arrowed.

The artery was clamped initially and this produced only a minimal area of cyanosis. The aneurysm lay distal to the main renal arteries and aneurysmectomy was performed with a 16-mm. woven Dacron graft, 2 cm. distal to the renal vessels.

The patient made an uneventful postoperative recovery and was discharged home on the twelfth postoperative day, with a blood-urea of 54 mg. per cent. He remains well 2 years later.

DISCUSSION

The association between horseshoe kidney and abdominal aortic aneurysm was first recorded by Julian in 1956, who found that the aneurysm was non-resectable because it supplied multiple small vessels to the kidney.

A horseshoe kidney is a congenital abnormality that occurs between the 4th and 8th weeks of foetal life, with a frequency ranging from 1 in 400–1000 births. There is an early midline fusion of the metanephric blastema that prevents rotation and migration of the kidneys. The isthmus joining the two renal masses may vary from a thin fibrous band to functioning renal tissue. Ninety per cent of cases have their convexity caudad with the isthmus lying at L.V.3 or 4, but this may vary from L.V.1 to the pelvic brim. In 60 per cent of cases the vasculature is anomalous with the arteries arising at various sites on the aorta in segmental distribution from the iliac vessels to the mesenteric vessels.

It is the anomalous distribution of the blood-vessels that provides the major surgical complication in dealing with the association of abdominal aortic aneurysm and horseshoe kidney. Lacombe, Vaysse, Andreassian, and Desmonts (1970) described four groups of arterial distribution, each requiring a different management:—

Group I: Normal vascular distribution. Twelve cases (37·5 per cent) have been reported. In each case resection was carried out and in 3 cases it was necessary to divide the isthmus.

Group II: One or two main arteries arising from the aneurysm. The management of the 11 cases (34·5 per cent) in this group is shown in *Table I*.

Table I.—THE MANAGEMENT OF ABDOMINAL AORTIC ANEURYSM ASSOCIATED WITH HORSESHOE KIDNEY IN CASES IN WHICH ONE OR TWO MAIN ARTERIES ARISE FROM THE ANEURYSM (GROUP II)

Author	*Management of Aneurysm*
Falor and Rufflo (1964)	(i) Not resected. Right renal artery from aneurysm. (ii) Aneurysm wrapped in Mersiline polyester. One single anterior renal artery from aneurysm.
Lynn and Bruce (1965)	Resection of aneurysm and left heminephrectomy. Left renal artery from aneurysm.
Cohn, Stoney, and Wylie (1969)	Resected. Renal artery reimplanted into graft.
Scott, DeBakey, and Mani (1969)	Resected. Renal artery reimplanted into graft.
Trabattoni, Miele, and Losapio (1969)	Not resected. Both arteries from aneurysm.
Hoofer (1970)	Resected. The left renal artery was reimplanted.
Lacombe, Vaysse, Andreassian, and Desmonts (1970)	(i) Resected with ligation of two smaller vessels to the lower poles. (ii) Resected. There were two normal arteries plus two vessels from the aneurysm that were reimplanted.
Marable and Thomford (1970)	Resected with ligation of two smaller vessels to the lower poles.
Davis, Hardin, Hardy, and Neely (1971)	Resected. Left renal artery was reimplanted.

Since 1969, 5 cases have been recorded where a reimplantation of a major renal artery has been performed successfully. Prior to that the aneurysm has been considered inoperable except on one occasion (Lynn and Bruce, 1965), when a left heminephrectomy was performed.

Group III: One or more arteries supplying the isthmus from the aneurysm. Seven cases (22 per cent) have been recorded, including the present case. In 4 cases it was found necessary to divide the isthmus. One patient died—the only operative death in the series. In each case the artery to the isthmus was divided after prior assessment of its distribution. If after clamping the vessel cyanosis occurred the isthmus was divided. Division of the renal tissue results in an increased risk of infection to the Dacron graft. Whenever this manœuvre is performed, a culture should be taken from the cut surface of the kidney.

Group IV: Vessels from the aneurysm are too numerous to consider resection. Two cases (6 per cent) have been described.

It becomes obvious that the major factors influencing the operative approach to an aortic aneurysm associated with a horseshoe kidney concern the site of origin of the renal arteries, their number, and the portion of the kidney which each supplies.

Preoperative intravenous pyelography is necessary to demonstrate the renal pattern and the distribution of the calices. Prior knowledge of an abnormal renal pelvis is essential if division of a thick isthmus is required, as leakage of urine will compromise the graft.

Preoperative aortography, whether by the high translumbar route (Scott, DeBakey, and Mani, 1969; Press, 1970) or by the left axillary artery (Marable and Thomford, 1970), may delineate the aneurysm and the renal arteries. Minken and Rob (1967) and Cox and Machado (1968) both performed operative aortography. Demonstration radiologically is probably better and the risks of leakage from the aneurysmal wall or disruption of a mural plaque do not arise.

In cases where division of the isthmus or sacrifice of renal vessels may have to be performed the distribution of the arterial supply may be demonstrated preoperatively by selective angiography (Press, 1970) or renal scanning with ^{203}Hg (Allen and Riley, 1963). If this problem presents at operation, as in the case described here, temporary clamping of the involved renal vessel will produce an area of cyanosis related to its distribution.

In the event of reimplantation of a major renal vessel some form of local cooling or perfusion may be required. Szilagyi, Smith, and Whitcomb (1959) commented that if the left renal artery is involved this may be successfully anastomosed to the splenic artery.

In the whole series of 32 cases the resection rate was 82 per cent with a mortality-rate of 4 per cent.

Acknowledgements.—We should like to thank Mr. R. Ruddick for his help in preparing the photographs and Miss I. Love for her secretarial assistance.

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SUBMANDIBULAR DUCT LITHIASIS ASSOCIATED WITH A MIXED SALIVARY GLAND TUMOUR

A CASE REPORT

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SUMMARY

A case of submandibular gland pleomorphic adenoma in association with duct lithiasis is presented. These are probably incidental findings, but it is possible that they may be causally related.

EXAMINATION of the recent English literature has revealed no reported case of pleomorphic adenoma associated with duct lithiasis. Such a case is presented here and the possible aetiological factors are discussed.

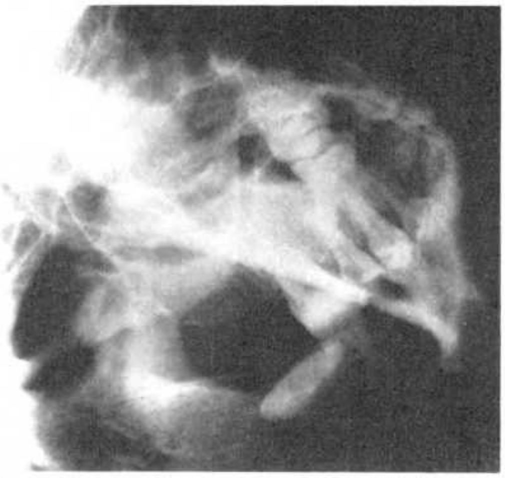

FIG. 1.—Oblique radiograph of the mandible, showing a large radio-opaque calculus in the left submandibular duct.

CASE REPORT

M. M., a Bantu female aged 43 years, was admitted to the General Hospital, Johannesburg, in February, 1971, with a 1-year history of a painful tender swelling in the area of the left submandibular gland. The mass had slowly been increasing in size and was more tender and painful during mastication. There had been a recent weight-loss of about 4 kg. Systematic and past history revealed nothing of significance.

On examination the patient was found to be a fit middle-aged female with a discrete oval swelling measuring 2·5 × 3 cm. in the position of the left submandibular gland. The surface of the mass was slightly lobulated and the gland was mildly tender. No cervical lymphadenopathy was detected. Palpation of the floor of the mouth revealed a 1-cm. calculus in the posterior part of the left submandibular duct. This was confirmed radiographically (*Fig.* 1). The lungs were clinically and radiologically normal.

A diagnosis of sialitis secondary to duct lithiasis was made. Under general anaesthesia and endotracheal intubation a longitudinal mucosal incision was made over the calculus, which was removed. The wound was not sutured. A mild cellulitis at the operative site was treated with antibiotics and it settled after 3 days. The gland remained tender and swollen for 7 days and then diminished slightly in size and became non-tender. The patient was discharged on the fifteenth postoperative day. Over the next 9 weeks the gland remained the same size and without tenderness.

The patient was readmitted in May, 1971, for complete removal of the left submandibular gland. This was

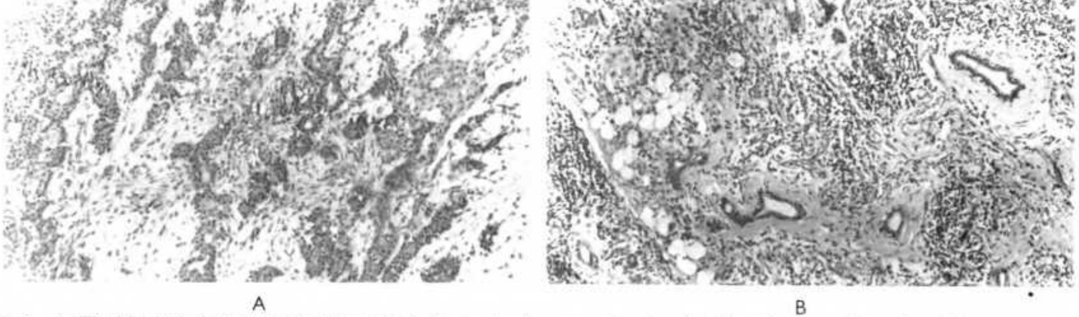

FIG. 2.—A, The histological appearances of the mixed salivary-gland tumour, showing glandular elements and cartilage-like stromal change. B, A representative area showing chronic sialitis. H. and E. (× 42.)

done under general anaesthesia using a submandibular incision.

Pathological examination revealed a gland weighing 24·5 g. A partly encapsulated tumour measuring 3·0 × 3·5 × 2·2 cm. was found in the superficial part of the gland.

On histological section the features of a typical mixed salivary tumour were seen (*Fig.* 2 A). The deep part of the gland showed periductal fibrosis, fatty infiltration, atrophy of the parenchymal tissue, and a chronic inflammatory infiltration, the features being those of a chronic sialitis (*Fig.* 2 B).

The patient made an uneventful postoperative recovery and was discharged from hospital on the seventh postoperative day.

DISCUSSION

Two relatively rare conditions—submandibular gland pleomorphic adenoma and duct lithiasis—have been found to be present simultaneously in one patient. This raises the question whether these could be causally related or whether this association is incidental. Evans and Cruickshank (1970) feel that there is at present no definite correlation between salivary-gland tumours and duct lithiasis, and urge that clinicians should make a deliberate note of conditions and disorders that may be associated with salivary-gland tumours.

The question exists as to whether the tumour is secondary to the stone or the stone is secondary to the tumour. The former proposal seems unlikely, and although the latter is a possibility, it is more likely that they are both incidental findings in this patient.

Formation of a stone in the duct of a gland containing a tumour might arise by desquamation of part of the tumour into the duct to act as a nidus for stone formation. A decreased rate of secretion in the duct owing to the presence of the tumour may result in stasis and stone formation. Stewart (1968) reported the development of a squamous carcinoma in a gland that was chronically infected as a result of the presence of a calculus. Shanon (1965), in a case report, showed the presence of a squamous carcinoma of the submandibular duct in association with a stone.

Phleboliths are commonly seen in soft-tissue cavernous haemangiomata and when these occur in or near a salivary gland they should not be confused with lithiasis (Hopkins, 1969).

Acknowledgements.—Our thanks are due to Mr. C. G. Bremner, under whose care this patient was admitted, to the Superintendent of the Johannesburg Hospital, and to the Director of the South African Institute for Medical Research for permission to publish this report.

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PRIMARY ADENOCARCINOMA ARISING IN A VITELLO-INTESTINAL DUCT REMNANT AT THE UMBILICUS

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Summary

A case is presented of a primary adenocarcinoma which arose from a vitello-intestinal duct remnant at the umbilicus in a 46-year-old woman. The incidence, diagnosis, and management of these unusual tumours are reviewed.

A primary adenocarcinoma arising at the umbilicus is very rare. A case is presented of one such tumour which appeared to develop in a vitello-intestinal (omphalomesenteric) duct remnant.

CASE REPORT

Mrs. V. S., a 46-year-old housewife, was referred to the Out-patients' Department of Hillingdon Hospital, Uxbridge, in August, 1967, because of a mucopurulent umbilical discharge of 6 weeks' duration. She had no other symptoms but admitted to some menorrhagia on direct questioning. Micturition was normal. For the previous 10 years she had noticed an occasional slight gelatinous discharge from the umbilicus but this had always cleared up spontaneously after a few days. Examination of the anterior abdominal wall revealed a normal-looking umbilicus which was discharging small amounts of pus. Above the umbilicus there was a round, tender, subcutaneous swelling approximately 6 cm. in diameter; the overlying skin was inflamed but intact. The only other abnormality found on examination was a large fibroid uterus. A diagnosis of an infected umbilical cyst was made and the patient was admitted to hospital. Under general anaesthesia the swelling above the umbilicus was incised and a large amount of mucopurulent discharge was obtained; a bacteriological swab from this showed a growth of anaerobic non-haemolytic streptococci. The inflammation and discharge rapidly settled and the patient was allowed home after a few days.

The possibility of this lesion being a metastatic deposit was considered and a chest radiograph, barium-meal, follow-through, and barium-enema examinations, and sigmoidoscopy were performed at the follow-up clinic but these were all normal.

Eight months later the patient returned with a discharging sinus above the umbilicus, but there was no evidence of an underlying swelling. There was a moderate amount of brown mucoid discharge tinged with blood from both the sinus and umbilicus. The patient only

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agreed to admission 3 months later (September, 1968) by which time she had developed a fungating tumour 4 cm. above the umbilicus (*Fig.* 1). This was a firm, non-tender, oval mass measuring 4 cm. vertically and 5 cm. horizontally. The surface was heaped up irregularly and was constantly secreting mucus; the mass was not infiltrating locally and there was no surrounding induration or inflammation. Neither the axillary nor the inguinal lymph-nodes were palpable. The umbilicus was again apparently normal to inspection and palpation, with only an occasional slight discharge. Repeated investigations were all normal apart from an iron-deficiency anaemia with a haemoglobin of 8·3 g. Surgery was performed on 9 Oct., 1968, after a preoperative blood transfusion.

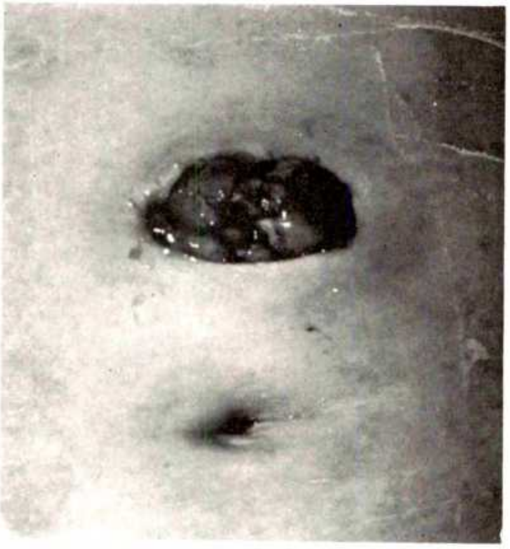

FIG. 1.—Preoperative view of the anterior abdominal wall, showing a supra-umbilical tumour.

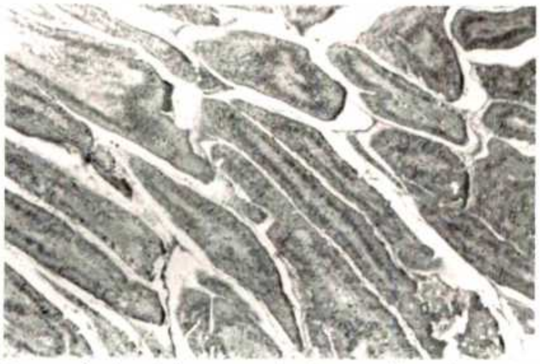

FIG. 2.—Section of the tumour, showing a papillary adenocarcinoma of low-grade malignancy. H. and E. (× 11.)

OPERATIVE PROCEDURES.—Cystoscopy revealed a normal bladder. On pelvic examination the cervix was normal but the uterus was enlarged to the size of a 16-week pregnancy. A cervical smear and then curettage of the uterus were carried out. Laparotomy performed through a lower left paramedian incision revealed no evidence of an intra-abdominal tumour. The presence of a large fibroid uterus was confirmed. The omentum was attached to the parietal peritoneum beneath the umbilicus but there was no evidence of spread of tumour into the abdominal cavity. There was no Meckel's diverticulum or vitello-intestinal duct remnant in the abdomen. The fundus of the bladder felt normal and there was no swelling or tumour along the line of the urachus running up to the umbilicus. All the other viscera were normal and the incision was therefore closed. Excision biopsy of the supra-umbilical lesion was then performed via a transverse elliptical incision. The tumour was surrounded by a well-defined fibrous capsule which ran downwards as a patent, narrow, fibrous duct towards the umbilicus. The umbilicus was not excised at this stage.

The histological reports were as follows: cervical smear, normal; uterine curettings, hypoplastic endometrium showing secretory changes with no evidence of malignancy; abdominal-wall tumour, a columnar-cell, papillary, mucus-producing tumour showing evidence of low-grade malignancy (*Figs.* 2, 3).

The patient's postoperative progress was satisfactory but she declined to have a radical excision of the umbilicus which was advised. Over a period of several weeks she began to have an increasingly heavy discharge of mucus from the umbilicus and finally agreed to further surgery which was performed on 10 Jan., 1969. A wide transverse elliptical incision with a 12-cm. clearance on either side of the umbilicus was made and this block of tissue containing the umbilicus, subcutaneous tissues, muscle, sheath, and peritoneum was excised *en masse*. The peritoneum was closed and a Mayo repair using silk was performed on the rectus sheath. The patient's postoperative course was again satisfactory. The specimen showed a solid core of neoplastic tissue, 3 cm. thick, extending down beneath the umbilicus through the rectus sheath but not spreading through the peritoneum. Histology of the specimen showed identical appearances to the previous biopsy.

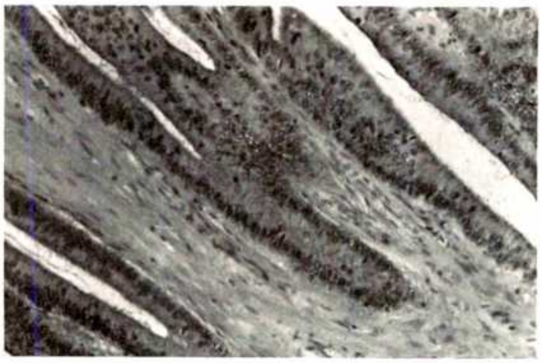

FIG. 3.—Section of the tumour, showing a well-differentiated, columnar-cell adenocarcinoma. H. and E. (× 53.)

In February, 1970, the patient underwent an abdominal hysterectomy for her fibroid uterus. A general examination of the abdomen was again normal at this time. She has remained in good health since her last operation with no evidence of local spread or distant recurrence of her tumour.

DISCUSSION

The embryological remnants found in the region of the umbilicus are derived from the vitello-intestinal (omphalomesenteric) system or the urachus. The anatomy and incidence of these uncommon anomalies have been reviewed by Cullen (1916), Begg (1931), Trimingham and McDonald (1945), and Moore (1956).

An adenocarcinoma occurring at the umbilicus is nearly always a metastasis from an intra-abdominal tumour. In a review of 112 tumours of the umbilicus Steck and Helwig (1965) found 64 benign and 48 malignant lesions; 40 of the malignant lesions were secondary deposits, 36 being adenocarcinomas. There were 7 definite primary tumours of the umbilicus (4 malignant melanomas, 2 basal-cell carcinomas, and 1 myosarcoma), whilst the remaining case, a 37-year-old male, presented with an umbilical discharge and tumour which proved on excision to be an adenocarcinoma resembling an intestinal epithelium. This patient died after 2 months with multiple tumour nodules throughout the abdomen. No other primary tumour was demonstrated and this fact together with the presence of a Meckel's diverticulum suggested that the tumour could have arisen in a cutaneous remnant of the vitello-intestinal duct. Steck and Helwig (1965) also studied 40 patients with cutaneous vitello-intestinal anomalies, 48 with urachal remnants at the umbilicus, and 28 with umbilical endometriosis and failed to detect any tendency to neoplastic change in these uncommon conditions. Thus, they confirmed the findings of Beurey, Rousselot, Vadot, and Barbier (1961), O'Leary and O'Leary (1964), and Willis (1967) that primary adenocarcinoma of the umbilicus is excessively rare.

In the case reported here the 10-year history of umbilical discharge suggests a previous underlying umbilical abnormality. The absence of any other tumour indicates that the lesion is a primary. Furthermore, the long-term survival of the patient is unlike the behaviour of patients with umbilical secondary deposits in whom the average survival time was only 11 months in the series reported by Steck and Helwig (1965).

A primary adenocarcinoma at the umbilicus can only arise from a pre-existing endometrioma or an embryological remnant. A pre-existing endometrioma can be excluded in this patient on clinical grounds since there had been no pain or bleeding from the umbilicus and the discharge was not related to menstruation. The histology (*Figs.* 2, 3) of the tumour showed it to be a columnar-cell, papillary, mucus-producing adenocarcinoma of low-grade malignancy—a picture which is consistent with a vitello-intestinal duct origin. However, since the majority of urachal tumours resemble intestinal tumours histologically (Mostofi, Thomson, and Dean, 1955; Nadjmi, Whitehead, McKiel, Graf, and Callahan, 1968; Grogono and Shepheard, 1969) this does not help in the differentiation of the tissue of origin, which will depend more on the anatomical and clinical features of the case.

The urachus runs downwards in the extraperitoneal space from the umbilicus to the apex of the bladder. Urachal tumours are usually found at the apex of the bladder, 75 per cent occur in males (Nadjmi and others, 1968), and the initial symptom is commonly related to micturition. A suprapubic mass is palpable in 80 per cent of cases at the time of presentation (Grogono and Shepheard, 1969). The tumour spreads in the retropubic space and despite radical surgery the prognosis is poor, with a 5-year survival rate of 8 per cent (Nadjmi and others, 1968). Begg (1931) discussed several urachal tumours found below the umbilicus but admitted that the diagnosis of such a tumour actually situated at the umbilicus is difficult to confirm. Willis (1962) stated that there has been no proved case of a urachal tumour at the umbilicus, but Pettorelli Lalatta (1966) reported a possible case.

Theoretically, urachal tumours might occur at any point up to the umbilicus but not above, as occurred in the present case. The features in this patient thus favour the diagnosis of a primary adenocarcinoma arising in a vitello-intestinal remnant. From the few reports of similar cases (Cullen, 1916; Williams, 1946; Steck and Helwig, 1965; Boscaino and Gambardella, 1968) it is difficult to determine the normal clinical course of such tumours. The present patient had a well-differentiated, slow-growing tumour and she is symptom-free 5½ years after the onset of symptoms (4 years after final surgery). These features are different from those in the possible case reported by Steck and Helwig (1965) in which there was rapid dissemination of the tumour and early death.

The management of an umbilical neoplasm is surgical excision. In the unlikely event that the tumour is a primary lesion, radical local surgery is indicated. If the tumour is a metastatic deposit the prognosis is poor but palliation is achieved. However, since the occasional long-term survivor has been reported in this situation (Steck and Helwig, 1965) an aggressive attitude to both the primary tumour and the umbilical secondary should be adopted.

Acknowledgement.—I would like to thank Mr. C. G. Scorer for permission to report this case and his helpful advice in the preparation of the manuscript.

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REVIEWS AND NOTICES OF BOOKS

Hamilton Bailey's Emergency Surgery. Ninth edition. Edited by T. J. McNair, M.D., F.R.C.S. (Edin.), F.R.C.S. (Eng.), Royal Infirmary of Edinburgh. 9¾ × 6½ in. Pp. 998, with 1155 illustrations. 1972. Bristol: John Wright & Sons Ltd. £12 50.

There can be no doubt about the continued popularity of this book, which is specifically designed to help the less experienced surgeon—a category that we all fit into for a time. Since the first edition which appeared in 1930–1 there have been vast changes in surgical practice and in the prevalence of different emergencies; therefore the present edition, like its predecessors, contains important new material. However, the charm of the book does not lie in the fact that it has been brought up to date but in the retention of Hamilton Bailey's style of teaching which by a combination of vivid English and liberal illustrations confers on the reader not only facts but a judgement which reflects the combined experience of the contributors. The language may seem archaic at times, for example, 'Unless Nature is overcoming the obstruction as announced by . . .', but it impresses itself on the mind. The illustrations, sometimes realistic, sometimes diagrammatic, and often a combination of photograph and diagram, are all memorable. 'Strangulated gangrenous small bowel' is not just a phenomenon, it is 'a warning to those who procrastinate'.

The book comprises sections on the treatment of shock, electrolyte imbalance, infection, respiratory failure, cardiac arrest, and injuries to major vessels, nerves, and tendons. This is followed by sections dealing with emergencies on a regional basis: head, neck and spine, ear, nose, and throat, thorax, abdomen, genito-urinary tract, and extremities. There is a final section on emergency conditions peculiar to the tropics. The present edition contains excellent new sections by Professor H. A. F. Dudley on the resuscitation, assessment, and treatment of the severely injured which reflect experience in the Vietnam War. Sections on burns and cardiorespiratory emergencies have been completely rewritten and many other areas have been brought up to date. It may be doubted whether any book is truly indispensable, but certainly those who have to get up at night and operate will do well to be familiar with this book.

The Scientific Fundamentals of Surgery. By J. Gwynne Brockis, Ch.M., F.R.C.S., F.R.A.C.S., University of Western Australia. 8¼ × 5½ in. Pp. 719 + x. Illustrated. 1972. London: The Butterworth Group. £10.

This is a remarkable book in that it contains a tremendous mass of information collected together by one man. With the vast expansion of physiology and biochemistry this is a great achievement. Some of the chapters, such as those on the biology of ageing and on pain, are fascinating essays which are a pleasure to read. Other chapters are composed of masses of data grouped together in a rather uncoordinated fashion. The single authorship has the advantage over multiple-author volumes in that there is no repetition, but it does suffer in this case from some serious omissions. The most noticeable of these concern the spleen and lymphatic system, and there is little about cardiac function and its control—matters which are so important to the surgeon.

In the preface the author states that the book is designed to help surgeons to apply the basic sciences to their surgical thinking; at the same time it sets out to provide extensive bibliographies and reference lists to help those working in surgical laboratories; the needs of doctors taking a training in surgery and facing examinations have also been kept in mind. In these respects the book hardly achieves its aims, for in the subjects which are adequately dealt with it tends to be too detailed for the surgeon in training, while the research worker will still have to refer to the original papers. In spite of these comments the information provided is up to date and there is much in the book which will be of immense value to surgeons who wish to keep in touch with progress in the basic research on which their clinical practice depends, and for this the book is to be recommended.

Scar Tissue—Its Use and Abuse. By J. J. Longacre, M.D., Ph.D., Ohio. 10 × 7 in. Pp. 170 + xv. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $18.50.

This is an important book. It deals with a problem which confronts every surgeon and causes anxiety and disappointment to the surgeon and patient alike, and comes from the pen of an experienced surgeon, who has tenaciously studied the problem of scar tissue for more than 30 years and has involved his colleagues in the laboratory to assist him in interpreting his clinical observations. Histological and chemical research has supported Longacre's clinical concepts; they are novel, and in this book he sets them down and backs them with a wealth of photographic records which are most convincing and cover a follow-up period of more than 20 years.

The role of collagen in wound healing and scar formation is the thesis of the book. The orientation of collagen in the normal dermis is described; it is principally along the crease lines of the skin and secondarily perpendicular to the crease lines. The crease lines are at right-angles to the direction of pull of the main muscle mass exerting tension on the skin. The mechanism of production of collagen from the fibroblast is discussed, including its chemical composition and the factors necessary for its production. The writer then turns to the effect of wounds and wound healing on the production of collagen, concluding that in hypertrophic scars there is excessive production in lines of tension and in the direction of stresses produced by muscle movement as, for example, across a joint. He makes the point that even after a prolonged period of postoperative immobilization these stresses will promote excess collagen formation, leading to hypertrophic scars and contracture as soon as movement commences, and that the greater the effort made the more the scar hypertrophies.

In contrast to the linear arrangement of collagen along the lines of tension in hypertrophic scars, the author asserts that in keloids there is lack of orientation of collagen and overflow of it into the surrounding tissues. He regards this as 'consistent with the disorganization characteristic of that twilight zone approaching neoplasia'.

The surgical application of these findings is to change the lines of stress in a hypertrophic scar by multiple Z-plasties and to apply skin-grafts and skin-flaps whenever possible, with their crease lines corresponding to the crease lines at the recipient site. He recommends that the Z-plasties should be contained within the hypertrophic scar itself; if normal skin is included new tensions set up in it may provoke hypertrophy in just these parts of the operation field. He maintains that hypertrophic scars even 3–4 cm. thick can be transposed safely providing dissection is carried down to the fascia and the vascular supply to the subcutaneous fat is uninjured.

The rapid and permanent improvement in the scar which he notes after this procedure is analysed by the collagen chemist, Professor Helen Berry. She succeeds, in describing her biochemical studies, in making this highly complicated subject relatively easy for the uninitiated. She stresses the normally concurrent processes of collagen synthesis and degradation in healing wounds and the failure of the remodelling process in hypertrophic scars. Most important, she notes the greatly increased urinary excretion of the collagen-degradation products—hydroxyproline and hydroxylysine—after multiple Z-plasties confined within the hypertrophic scar.

The value of directional placement of skin-grafts is equally convincing, as judged by the illustrations. It is a pity that the work has not so far included a study of the possible influence on the cosmetic result of the tension at which grafts are sewn into place to resurface defects. Such a study would seem a natural continuation of the present work.

The book also includes a full chapter on the biophysics and pathology of radiation. One concludes, although the author says so only by implication, that he regards irradiation as useless and potentially harmful in scars, and that its use should be restricted to the treatment of malignancy.

The temptation to excise and suture a hypertrophic scar will always remain, and occasional successes from this simple procedure will continue to encourage, and maybe rightly so, but the weight of evidence which the author has brought to support his new concept of treatment is indisputable and surgeons will do well to heed the advice given in dealing with these difficult problems. Longacre has shown that it works.

Peptide Transport in Bacteria and Mammalian Gut. A Ciba Foundation Symposium. 9 × 6½ in. Pp. 161 + vii. Illustrated. 1972. Amsterdam: Elsevier Excerpta Medica. £2·40.

THIS volume contains the papers read at a Ciba Foundation Symposium held in 1971 (not 1972 as stated in the book), together with verbatim records of the discussion. The central theme was the relatively recent recognition that peptides do not all have to be broken into their amino-acid components before they can be absorbed. The phenomenon of peptide absorption has been observed in bacteria and in mammals. Several of the reports are concerned with the mechanisms by which such direct absorption can occur and with the controversy as to just where—in or on the cell—the subsequent breakdown to amino-acids takes place. One chapter draws from studies of genetic errors of metabolism, such as Hartnup disease, to illustrate the relevance to disease, but the rest are concerned with biochemical and physiological studies.

Physiologie des Kreislaufs, Volume 1. By E. BAUEREISEN, Wurzburg. 9¾ × 6½ in. Pp. 505 + xiv. Illustrated. 1971. Berlin: Springer-Verlag. DM.148.

ONE is aware of a gap existing between clinical medical science and the theoretical basic sciences such as pathology and physiology. In this book, which is volume 1 of a series dealing with the circulation, one is astonished by the exactness with which the velocity of the blood-stream, the resistance in the vessels, and the elasticity modules of the vessel walls can now be measured.

Old laws such as the famous law of Poiseuil are still important but electromagnetic measurements and clearances of radioactive substances must complete the investigations in the physiology laboratory. For the clinician the effect of the autonomous nervous system and pharmacological substances such as vasoconstricting and vasodilatating drugs deserves careful attention; one may gain the impression that many of the drugs produced by industry are not as valuable as the manufacturers suggest. Needless to say, every vascular clinic needs a modern physiologist and a mathematician as advisers.

This book belongs among the best on modern medicine.

The Principles of Transurethral Resection and Haemostasis. By J. P. MITCHELL, T.D., M.S., F.R.C.S., F.R.C.S.E., Bristol. 9¼ × 6⅜ in. Pp. 276, with 124 illustrations. 1972. Bristol: John Wright & Sons Ltd. £6.

THERE can be no doubt that with modern methods of illumination and diathermy equipment the loop resectoscope represents the most versatile instrument in dealing with many varieties of bladder-outflow obstruction and selected bladder tumours. The technique of perurethral resection, however, is sophisticated and any description which aids in its accomplishment is to be welcomed. Hitherto, the British literature has remained sparse in this respect, but during the past year two useful additions have been made. These may essentially be regarded as complementary, and the emphasis laid in the present account on the need for scrupulous haemostasis stems from the author's profound knowledge of the principles of surgical diathermy and his personal modification of the instrument. These attributes are modestly proclaimed and a wealth of useful practical and clinical information is included which greatly enhances the value of the book to the urological trainee. There is also a great deal of practical common sense which may help even the established urologist in the selection of suitable cases and, despite its price, the volume should find a place in the library of every urological department.

Core Textbook of Surgery. Edited by RICHARD H. EGDAHL, M.D., Boston, J. A. MANNICK, M.D., Boston, and LESTER F. WILLIAMS, jun., M.D., Boston. 9¾ × 7 in. Pp. 484 + xii. 1972. New York. Grune & Stratton Inc. Hardback, $13.50; paperback, $8.75.

THIS textbook of surgery has been written by 25 members of the staff of the Boston University School of Medicine. and is for medical students, surgical house-officers, nurses, and 'other allied health personnel'. The aim was to produce a book that contained the essential facts of surgery without the technical operative details that are unnecessary for the undergraduate. It is intended to be used in conjunction with standard reference textbooks and not to supplant them. The editors have integrated the work of the contributors in an exemplary fashion.

There are two parts: 'general' and 'organ systems' (though it is not clear why urology, orthopaedics, and paediatric surgery are included under 'general'). The general section has excellent chapters on pre- and post-operative care, in which principles are discussed and also very practical details are included which house-officers will find useful. There is a good chapter on anaesthesia, which reflects the increasing importance of clinical measurement. The chapter on advanced cancer is clearly set out, and staging, treatment, and care, including the care of the dying patient, are discussed. The chapter on immunology is lucid and relevant.

The organ systems section covers a wide field, including cardiothoracic, vascular, and gynaecological surgery and the subjects are presented clearly and briefly. As might be expected from Dr. Egdahl, the chapter on surgical endocrinology is particularly good, although the pituitary gland is not included.

One pleasing feature is the annotated bibliography of key papers (some of them British) that follows each chapter. There are no diagrams or photographs. The index is adequate.

The soft-cover edition (at $8.75) will be a very useful part of the student's library throughout his surgical course, but the book is too long and detailed for nurses and 'other allied health personnel'.

Embryology for Surgeons. By STEPHEN WOOD GRAY, A.B., M.A., Ph.D., Atlanta, and JOHN ELIAS SKANDALAKIS, M.D., M.S., Ph.D., F.A.C.S., Atlanta. 10 × 7¼ in. Pp. 918+xv. Illustrated. 1972. London: W. B. Saunders Co. Ltd. £15·30.

DEVELOPMENT from the fertilized egg to the newborn baby with its millions of cells and complex tissues and organs is such a remarkable feat of biological programming that it is hardly surprising that so many potential individuals fail to get born. In their excellent introductory chapter the authors demonstrate the striking probability that only some 30 per cent of fertilized human eggs will develop into normal babies; of the remainder, about 69 per cent fail to implant in the uterus or become absorbed or otherwise lost at some stage in pregnancy. This may well be of some comfort to the ecologist and, indeed, one school of thought has suggested that such embryonic mortality is not so much sheer waste as a biologically determined method of population control. The authors, however, are mainly concerned with the small number, perhaps 1 per cent of all fertilized eggs, which gives rise to babies with recognizable congenital defects presenting surgical problems.

The remainder of the book is devoted to a systematic account of congenital anomalies of the various organ systems as they are seen in the foetus or after birth. The incidence, diagnosis, and treatment of the various conditions are described, as well as their morphology and embryogenesis; the inclusion of scholarly historical notes is most welcome. Each section begins with a clear and well-illustrated account of normal development and contains a good bibliography.

The embryologist may regret that this book does not deal with the interesting and relatively common defects of the face and palate, or with abnormalities of the limbs and the organs of special sense; presumably these topics are regarded as falling within the province of the specialist rather than the general surgeon. Within its terms of reference, however, the book is a mine of information on congenital conditions. It should be of great value to surgeons; its lucid style and systematic method of arrangement make it particularly suitable as a work of reference. It will also be much appreciated by those who teach human embryology, and who wish, very properly, to enliven anatomical detail by clinical illustration.

Operative Surgery. Principles and Techniques. Edited by PAUL F. NORA, M.D., Ph.D., Chicago. 11 × 8½ in. Pp. 1106+xvii. Illustrated. 1972. London: Henry Kimpton. £26 10.

THE editor of this book and his 72 eminent contributors have produced a comprehensive one-volume operative surgery textbook. The only contributor not working in the United States is Richard S. Handley, who gives a characteristically lucid account of modified radical mastectomy. The book, though bulky, is very readable, and is clearly set out in two parts, with some references at the end of each chapter. The four largest sections—alimentary and para-alimentary, thoracic, and vascular surgery with principles and fluid dynamics—form two-thirds of the volume. Urology is allotted one-tenth, and there are chapters on the extremities, head and neck, paediatric surgery, and the breast, with small sections on abdominal hysterectomy and burns.

There is perhaps more detailed discussion and description in the text than in some popular British books on operative surgery. The line drawings of the operative techniques are excellent.

This book should find a place in every hospital library, and will be of great value to the isolated surgeon. It is a convenient detailed reference book to operative surgery, and reflects current practice in the United States.

Mammakarzinom Diagnose und Differentialdiagnose. By HANS-KLAUS ZINSER, Koln-Lindenthal. 9 × 6 in. Pp. 134+xviii. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.29.70.

WHILE the frequency of breast carcinoma is not declining a booklet containing a more or less complete inventory of diagnostic resources must be welcomed by everyone who is interested in the subject. Hints are given to the patients on how to detect tumours themselves. Mammography and galactography are valuable diagnostic assets and thermography of the breast might prove to be as important but biopsy is indispensable in most cases.

The size of the tumour is much more important for the prognosis than the localization; the idea that a carcinoma in the medial quadrants of the breast is more unfavourable is outdated. Laboratory chemical tests include enzyme determinations for metastases of the liver, while the sex chromatin in the carcinomatous cells might be of special interest. The differential diagnosis receives adequate attention. One may cherish the hope that this book will contribute to better achievements in the still disappointing results in treatment of breast cancer.

Homoiostase. Wiederherstellung und Aufrechterhaltung. Edited by Professor Dr. R. FREY, Mainz, Dr. F. KERN, St. Gallen, and Professor Dr. O. MAYRHOFER, Wien. 9 × 6 in. Pp. 192+ix. Illustrated. 1972. Berlin: Springer-Verlag. DM.68.

THIS small monograph, No. 60 in the series 'Anaesthesiology and Resuscitation', records the proceedings of a symposium held in October, 1970, at Mainz. It is brightly called 'Maintenance of Homoeostasis', but in fact deals with what von Bauer has named 'thanatogenesis'. By this is meant the complex alterations in homoeostasis caused more by the complications than by the primary disease itself, and having an obstinate tendency to run their own independent but lethal course. The three systems mainly concerned are the circulation, respiration, and acid–base balance, and each is separately analysed and discussed. There is a considerable number of contributions, each covering a few pages. This implies that the subject-matter is given in a very condensed form, while taking a considerable basic knowledge on the part of the reader for granted. Those carrying Wright's *Applied Physiology* in their intellectual baggage will not have too much trouble in following the discourse. They will be helped by the illustrations, consisting exclusively of diagrams, which are very clear and most informative. The book seems best suited for those beginning work in an intensive-care unit. It may serve as a frame around which the required amount of theoretical knowledge can be conveniently built up, and this will be aided by the selected references at the end of each paper.

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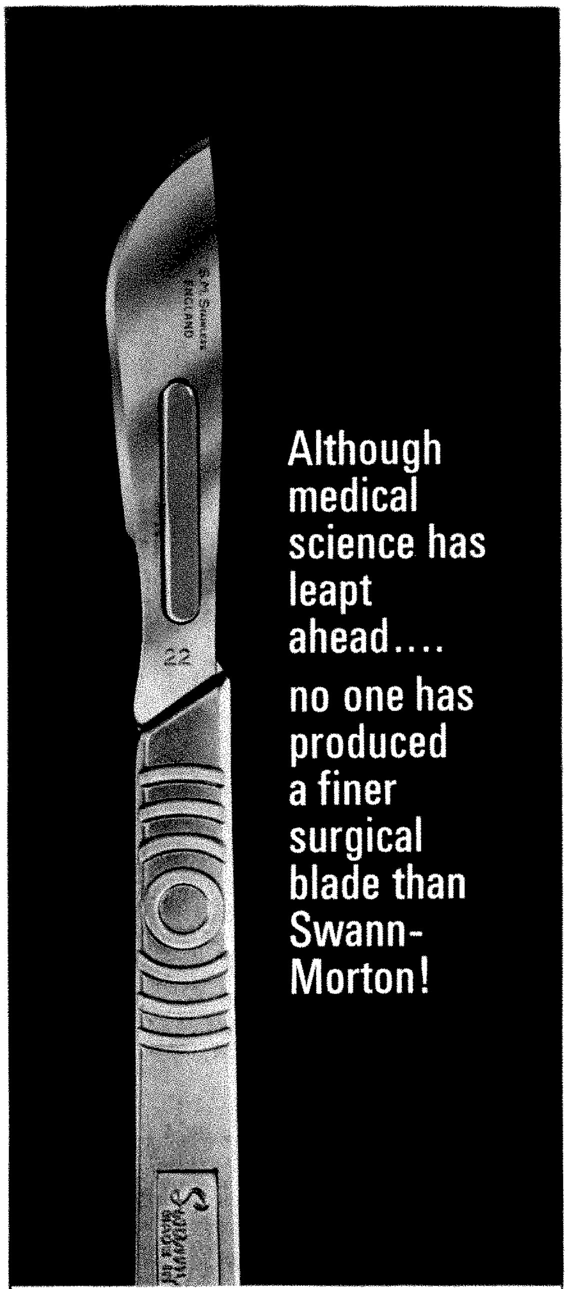

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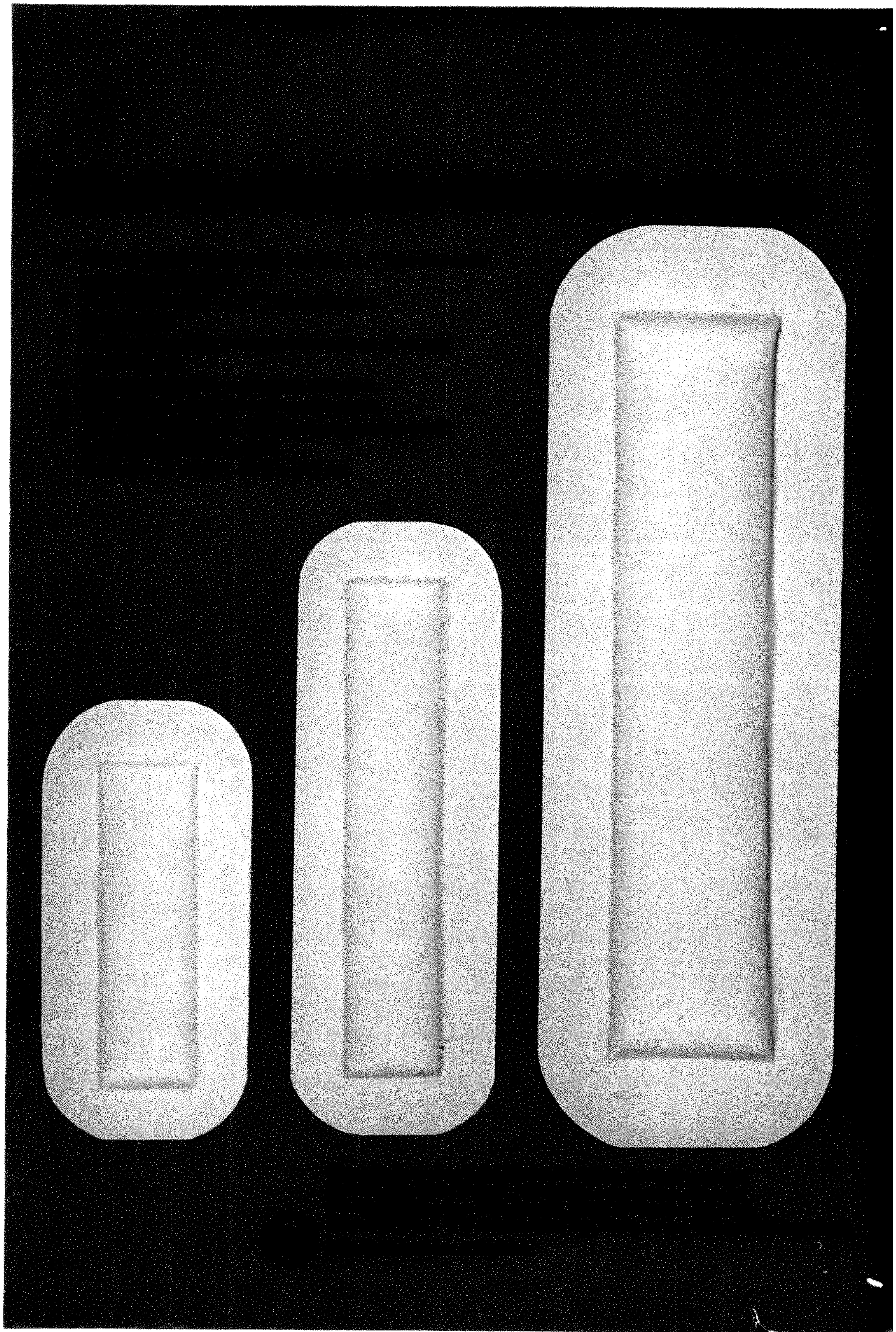

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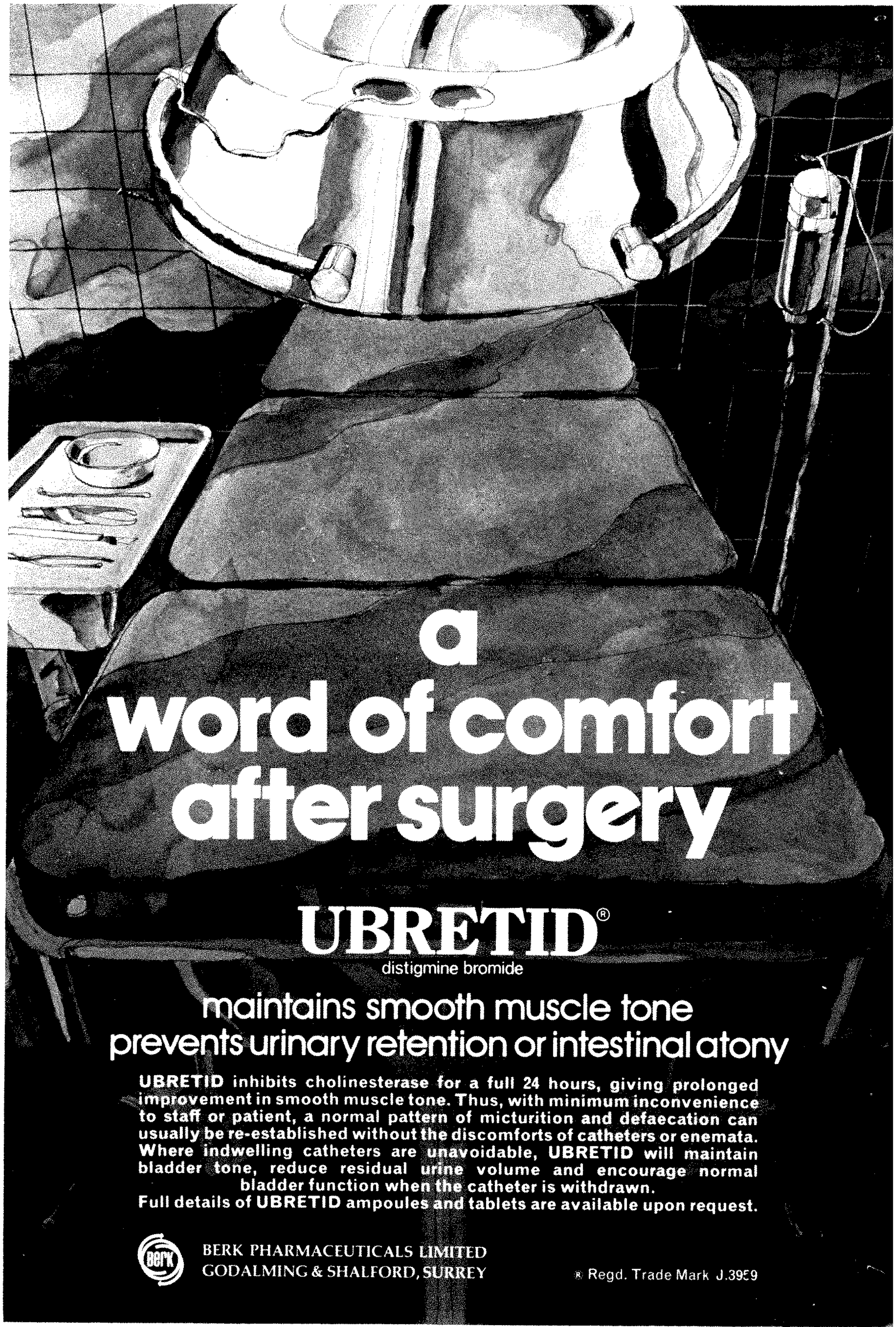

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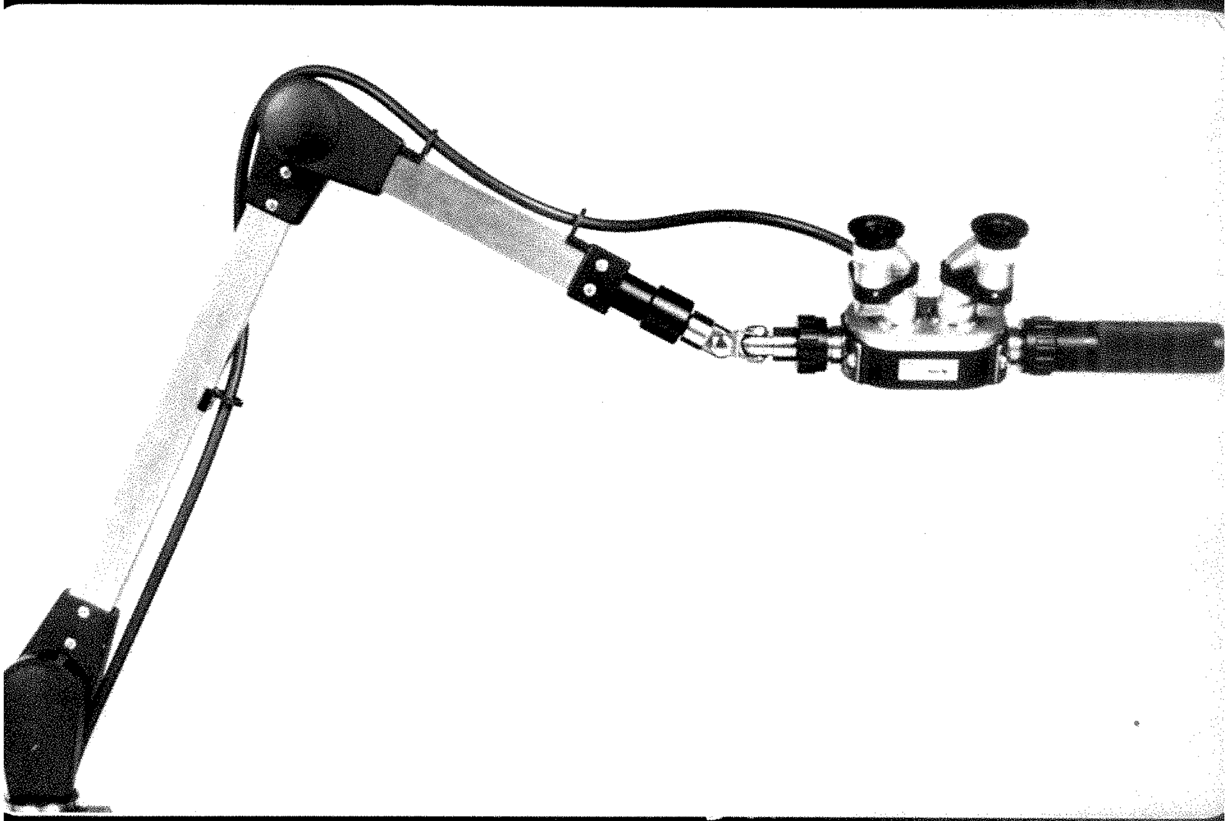

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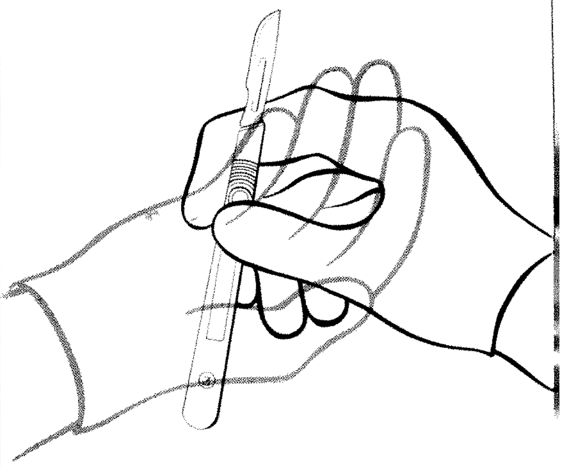

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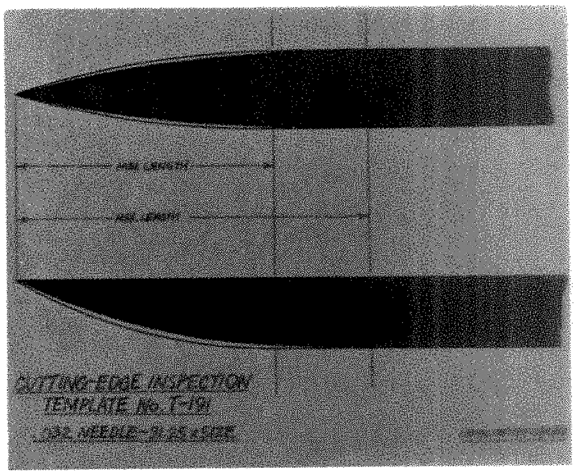

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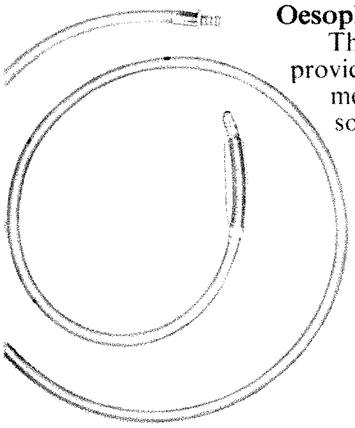

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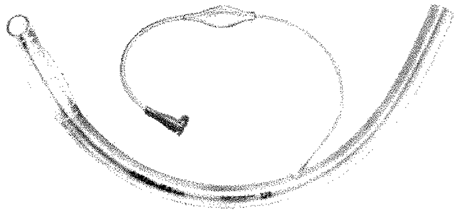

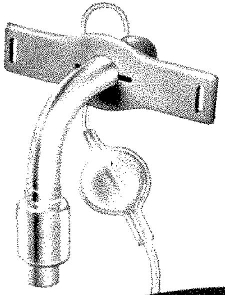

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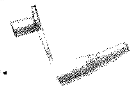

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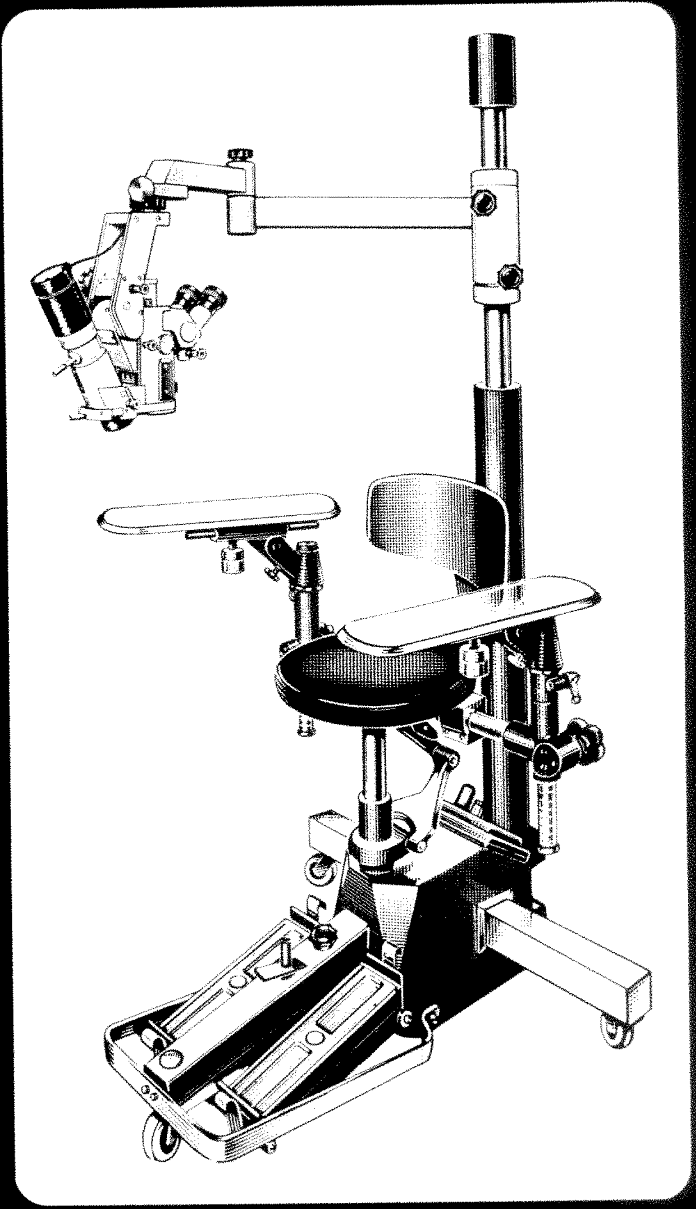

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2. Symposium : The Synergy of Trimethoprim and Sulphonamides. *S Afr med J,* (1970), **44**, Supplement (August) 12.
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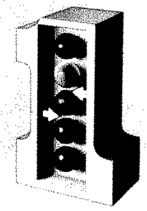

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THE
BRITISH JOURNAL OF SURGERY

Vol. 60 APRIL, 1973 No. 4

ORIGINAL PAPERS

THE EFFECTS OF EARLY EXPERIMENTAL CRYPTORCHIDISM AND SUBSEQUENT ORCHIDOPEXY ON THE MATURATION OF THE GUINEA-PIG TESTICLE

BY P. M. ATKINSON
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SUMMARY

A histological study of experimental cryptorchidism in the immature guinea-pig and the results of subsequent orchidopexy are described.

Arrest of development of a testis was produced by delaying its descent into the scrotum. Subsequent orchidopexy at ages up to and beyond puberty allowed development to continue to active spermatogenesis.

The poor results following orchidopexy for natural cryptorchidism in man are discussed in relation to this experimental work and the existence of a primary testicular abnormality is suggested. The superficial inguinal pouch ectopic testicle and the retractile testicle are also discussed.

THE naturally occurring cryptorchid testicle of man has been the subject of extensive histological study (Robinson and Engle, 1954; Sohval, 1954). Its progress following surgical treatment has been studied to a lesser extent. The underlying cause of cryptorchidism and the reason for the poor fertility results following its surgical correction remain essentially unknown. It is still unclear whether a testicle is undescended because it is abnormal or is abnormal because it is undescended.

The situation might be clarified by comparing the results following surgical treatment of experimental cryptorchidism in animals with those found after orchidopexy for natural cryptorchidism in man. It may be suspected that the cause of naturally occurring cryptorchidism is due to a primary abnormality of the testicle itself. If this is true the abnormal testicle would behave differently from the experimental testicle which is initially normal. A discrepancy in their behaviour might be anticipated following reversion to a normal scrotal environment. However, if there is a primary environmental cause preventing natural testicular descent then both experimental cryptorchid and natural cryptorchid testicles should behave similarly when subsequently placed within a normal scrotal environment. The experimental work reported here is presented to test this hypothesis.

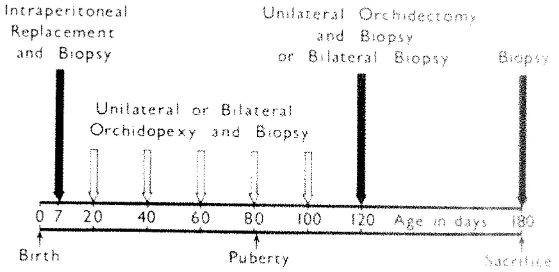
Intraperitoneal Replacement and Biopsy
Unilateral Orchidectomy and Biopsy or Bilateral Biopsy
Biopsy
Unilateral or Bilateral Orchidopexy and Biopsy
0
7
20
40
60
80
100
120
Age in days
180
Birth
Puberty
Sacrifice

FIG. 1.—Age at which operative procedures were performed.

Previous studies have shown the effect of artificial cryptorchidism and subsequent orchidopexy in the experimental animal (Moore, 1924; Wangensteen, 1927; Nelson, 1951; Shirai, Matsushita, Kagayama, Ichijo, and Takeuchi, 1966). In those series, however, the animals were mature and the testicles had already reached a scrotal position prior to their replacement within the peritoneal cavity. In this study young animals were used in order to mimic the natural cryptorchid state as closely as possible. Normal young male guinea-pigs were used. Their testicles were found to lie within the inguinal canals at the age of 7 days and had not therefore experienced a scrotal environment by the time of their experimental replacement into the peritoneal cavity. Subsequent orchidopexy of the experimentally cryptorchid testicles was then performed at different ages from 20 days until after puberty (*Fig.* 1).

MATERIALS AND METHODS

Two groups of normal male Hartley-strain guinea-pigs were used. At the age of 7 days one group was made either unilaterally or bilaterally cryptorchid and the other group acted as controls for the first group. All the animals were returned to their mothers or foster mothers after operation and were not weaned until 30 days of age (Valenstein, Riss, and Young, 1955). General anaesthesia with intraperitoneal Nembutal was used for each operative procedure throughout the project.

Intraperitoneal Replacement of the Testicle.—When the guinea-pigs were 7 days old either one or both testicles were mobilized through a lower abdominal incision. The testicle was found to lie within a peritoneal sac and had not yet completed its descent to the scrotum. After biopsy the testicle was placed within the peritoneal cavity and a silk suture closed the inguinal ring to minimize the possibility of later testicular prolapse.

The control animals also had a lower abdominal incision and mobilization of one or both testicles. The testicle was placed in the scrotum after a biopsy had been taken. A loose silk suture was placed at the inguinal ring to prevent prolapse of the abdominal contents.

Orchidopexy.—Either unilateral or bilateral orchidopexy was performed at 20, 40, 60, 80, or 100 days. The peritoneal cavity was opened through a midline abdominal incision. The retained testicle was drawn from the peritoneal cavity, through the inguinal ring, into the scrotum by forceps inserted through a separate scrotal incision. A biopsy was taken and if there was a tendency for the retained testicle to prolapse from its intraperitoneal position it was noted at this stage. The control group of animals underwent a similar operation, with mobilization and biopsy of their already scrotal testicles.

Table III.—AVERAGE RESULTS OF THE SPERMATOGENIC INDEX AND TUBULE COUNT PER HIGH-POWER FIELD

TIME OF TESTICULAR BIOPSY	OPERATION	HISTOLOGY	AGE AT ORCHIDOPEXY (d.)					COMBINED AVERAGE RESULTS FOR CONSECUTIVE COMPARISON
			20	40	60	80	100	
At intraperitoneal replacement (7 d.)	O	S.I.	1	1	1	1	1	1
	C	S.I.	1	1	1	1	1	1
	O	T.C.	37	40	42	40	43	40·4
	C	T.C.	45	35	50	42	41	42·6
At orchidopexy (20–100 d.)	O	S.I.	1	1·14	1	1·14	1	1·1
	C	S.I.	1·33	2·3	2·5	3·5	4·6	2·9
	O	T.C.	30·2	18·6	31·8	27	30	27·5
	C	T.C.	24·8	10·6	9·5	7·7	6·6	11·8
At postpubertal age (120 d.)	O	S.I.	3·4	4·6	4	1·5	1·6	3·0
	C	S.I.	3·7	4·7	4	3·8	4·8	4·2
	O	T.C.	6·2	6·4	6·7	12·3	13	8·9
	C	T.C.	8·1	6·5	7·0	5·6	7	6·8
At sacrifice (180 d.)	O	S.I.	4·3	4·3	3·8	4	4	4·1
	C	S.I.	3·8	4·6	3	4	5	4·1
	O	T.C.	6	6·7	7·4	7	7·7	7·0
	C	T.C.	7·5	6·1	8·8	7·4	5·8	7·1

O, Orchidopexy. C, Control. S.I., Spermatogenic index. T.C., Tubule count.

Contralateral Orchidectomy and Biopsy.—At the postpubertal age of 120 days the animals which had undergone bilateral orchidopexy had testicular biopsies taken through bilateral scrotal incisions. The unilateral cases had a biopsy of the surgically treated or control testicle, and orchidectomy of the contralateral scrotal testicle. The orchidectomy was performed at this stage as part of a concurrent study of plasma-testosterone levels following surgical treatment of experimental cryptorchidism.

Table I.—CRITERIA BY WHICH THE SPERMATOGENIC INDEX WAS ASSESSED

SPERMATOGENIC INDEX	HISTOLOGICAL FINDINGS
1	No evidence of active spermatogenesis. Presence or absence of spermatogonia
2	Presence of primary spermatocytes
3	Presence of primary and secondary, or secondary spermatocytes
4	Evidence of spermatid production. Immature spermatids
5	Complete spermatogenesis with mature spermatids or spermatozoa

Table II.—NUMBER OF TESTICLES USED FOR THE ORCHIDOPEXY AND CONTROL PROCEDURES

	AGE AT OPERATION (d.)					
	20	40	60	80	100	Total
Number of orchidopexy testicles analysed	6	7 (1)	6	7 (1)	6	32 (2)
Number of control testicles analysed	6	7	4	7	5	29

Numbers in brackets relate to testicles which were discarded from further study because of premature prolapse from their intraperitoneal position.

Sacrifice at 180 Days.—All the animals were sacrificed in young adult life under anaesthesia by cardiac puncture exsanguination. The testicles were removed for histological analysis.

Histology and Measurements.—Testicular biopsy specimens were fixed in Bouin's fluid and stored in 70 per cent ethanol. Sections were cut at 5 μ thickness and stained with haematoxylin and eosin. The biopsies which had been taken at four stages in the animal's life were studied from two histological aspects.

Tubule Count.—A count was performed of the number of seminiferous tubules seen in one high-power microscope field of 0·52-mm. diameter. A part of each section was selected where as many of the tubules as possible were cut transversely. Tubules at the periphery of the field were counted only if more than half of a tubular cross-section was included within that microscope field.

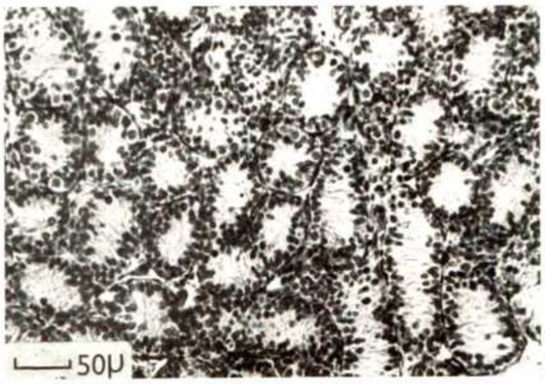

FIG. 2.—Guinea-pig testicular biopsy at 7 days of age, showing immature seminiferous tubules.

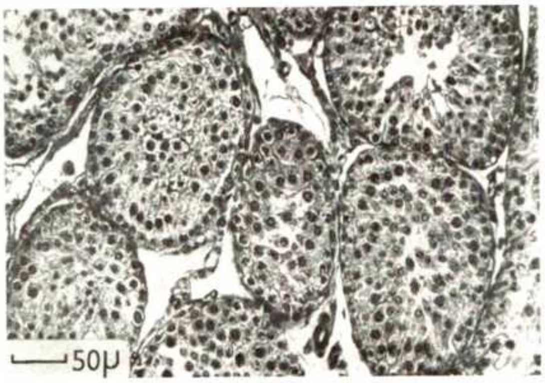

FIG. 4.—Biopsy of a control testicle at 60 days of age, showing spermatogenesis developing with enlargement of the tubules.

Spermatogenic Index—In order to assess the degree of spermatogenesis reached by the testicular biopsies the histological appearances were classified into five groups. The groups were numbered from 1 to 5 and the number was called the 'spermatogenic index'. The individual groups indicate the broad stages of spermatogenesis and are explained in *Table I*. In some cases the spermatogenesis was patchy. It was then necessary to judge which was the prominent stage of development and assign the appropriate index.

RESULTS

The number of testicles which were studied after unilateral, bilateral, and control procedures is shown in *Table II*. The testicles of animals which had undergone unilateral orchidopexy and of those which had had bilateral orchidopexy gave comparable results and have been grouped together for this study. The mean results of the two aspects of testicular histology are shown in *Table III*.

Tubule Counts.—The highest tubule counts were seen at the age of 7 days when all the animals had tightly packed immature tubules (*Fig.* 2). The average tubule number per high-power field (h.p.f.) for all the animals at this age was 41·5.

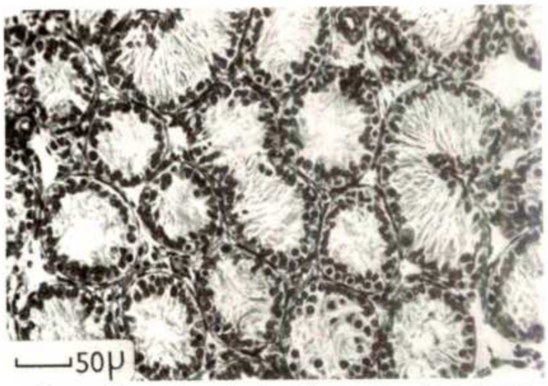

FIG. 3.—Biopsy of a retained testicle at 60 days of age, showing no evidence of active spermatogenesis but some tubule enlargement.

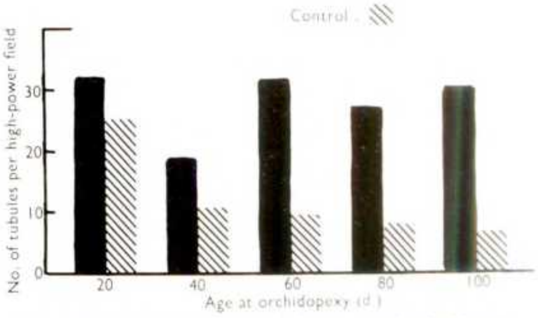

FIG. 5.—Tubule count per h.p.f. shown by testicular biopsies at the time of orchidopexy or the equivalent control operation.

Biopsies of the intraperitoneal testicles at orchidopexy showed that by 20 days of age the tubule count had fallen from 41·5 to 28 per h.p.f. There was then no further change during their intraperitoneal retention (*Fig.* 3), even when retained until 100 days of age.

The control testicles showed a gradual tubule development (*Fig.* 4) which was completed by 100 days of age (*Fig.* 5). As the tubules enlarge, the number of tubules seen in each high-power field diminishes.

At 120 days of age the tubule count of all the control testicles and those testicles which had had an orchidopexy at 20, 40, or 60 days (*Fig.* 6) was similar and low. Although the testicles which had undergone orchidopexy at 80 or 100 days also showed a decrease in tubule count at 120 days, this was much less marked than that of the control or early orchidopexy animals.

At 180 days of age all the control and orchidopexy animals had a similar low tubule count. Even the testicles which had been intra-abdominal until 80 or

100 days old had completed their tubular development by this age.

Consecutive Comparison of Tubule Counts.—Each animal had testicular biopsies at four stages in its life: in infancy, at orchidopexy, postpuberty, and at sacrifice in young adult life. Average tubule counts of surgically treated and control animals were taken for each stage. A consecutive comparison could then be made by representing the results diagrammatically (*Fig.* 7). The orchidopexy age was variable but had a mean age of 60 days. It can be seen from *Fig.* 7 that intraperitoneal replacement delays tubule development and subsequent orchidopexy allows the development to continue to normality by the time of sacrifice at 180 days.

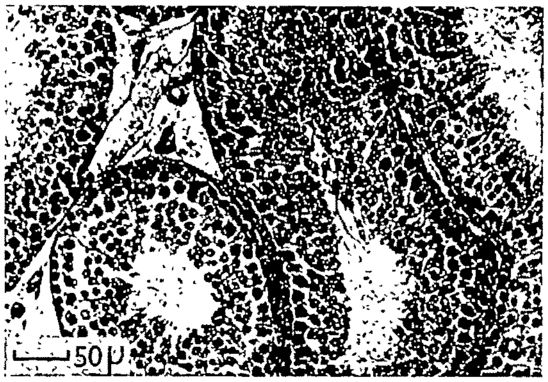

FIG. 6.—Testicular biopsy at 120 days of age, after orchidopexy at 60 days, showing complete spermatogenesis.

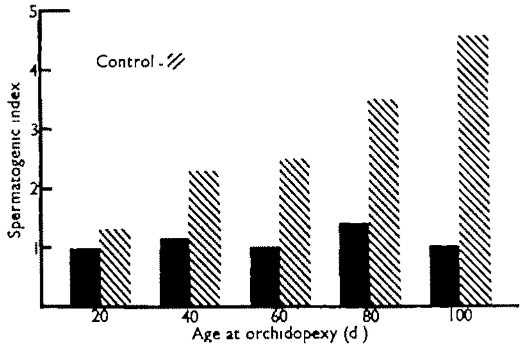

FIG. 8.—Spermatogenic index of testicular biopsies taken at the time of orchidopexy or the equivalent control operation.

Spermatogenic Index.—It was not surprising that all the testicular biopsies taken at 7 days of age showed no evidence of active spermatogenesis. They were given a spermatogenic index of 1.

At orchidopexy there was almost no evidence of active spermatogenesis in those testicles which had been replaced within the peritoneal cavity for periods of time up to 100 days of age. Two unilaterally cryptorchid animals were noticed to have prolapsed their testicles by the time of orchidopexy. Their testicular histology showed some evidence of active spermatogenesis at orchidopexy and they were therefore excluded from further study. In contrast to the cryptorchid animals the control animals demonstrated a gradual development of active spermatogenesis with increasing age (*Fig.* 8).

At 120 days of age all the control testicles and also the testicles which had had an orchidopexy at 20, 40 or 60 days showed a high spermatogenic index. The testicles which had been retained within the peritoneal cavity until 80 or 100 days of age showed some evidence of spermatogenesis but much less than that of the control animals.

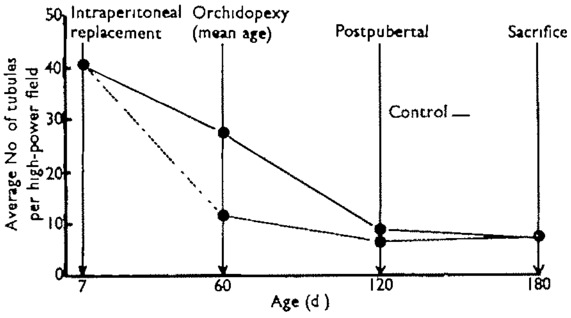

FIG. 7.—Consecutive comparison of average tubule counts per h.p.f. There is an inverse relationship between tubule number per h.p.f. and tubule diameter.

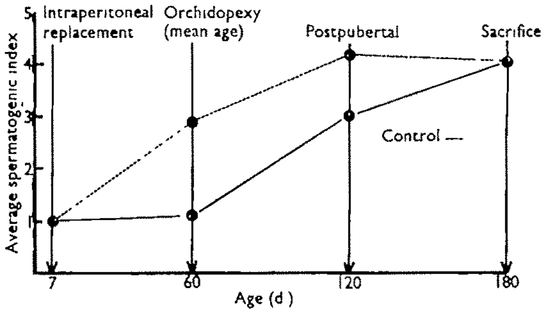

FIG 9.—Consecutive comparison of average spermatogenic index.

By the age of 180 days animals which had undergone a late orchidopexy had developed a high spermatogenic index, which was comparable to that of the control and early orchidopexy cases.

Consecutive Comparison of the Spermatogenic Index.—As shown for the tubule counts, the spermatogenic index of orchidopexy and control animals may be compared at the four stages in their lives when a testicular biopsy was taken. The results are best demonstrated in diagrammatic form (*Fig.* 9) and show that intraperitoneal retention of a testicle prevented active spermatogenesis. Subsequent orchidopexy allowed it to continue and at 180 days there was equally active spermatogenesis of both the treated cryptorchid and control testicles.

The results of the two aspects of testicular histology studied were subjected to statistical analysis. A significant difference was found in the results of both the spermatogenic index and the tubule count of the test group when compared with the control group at orchidopexy ($P < 0.005$). By the age of 180 days there was no significant difference in the results of the two groups of animals.

DISCUSSION

Normal development of the young guinea-pig testicle may be experimentally arrested by placing the animal's gonad within its peritoneal cavity. In this study the testicle was made cryptorchid before it had reached its natural scrotal position. The arrest of development persisted for as long as the intraperitoneal environment was maintained. The testicle was then able to continue normal development after orchidopexy, even if it had been retained within the peritoneal cavity beyond the age of puberty.

The two aspects of testicular histology which were used to monitor the fate of the testicle showed a close relationship. Counting the number of tubules per high-power field was found to be simpler than direct measurement of tubule diameters. The term 'spermatogenic index' has been used to express the stages of active spermatogenic development. It was necessary to compare the delay of spermatogenesis produced by the temporary retention of a testicle with that of the normally developing control testicle. A multistage index appeared more satisfactory in this particular situation than the tubular fertility index used by Mack, Scott, Ferguson-Smith, and Lennox (1961).

It may be seen from *Fig*. 9 that the spermatogenic index for both the treated cryptorchid and control animals was equal at 180 days of age. The fact that the index was less than 5 might be explained by the number of operations performed on each testicle.

John Hunter (1786) thought that the cause of cryptorchidism was an abnormality of the testicle itself. Astley Cooper (1841) and Bland-Sutton (1910) agreed with Hunter, but Curling (1843) said that the undescended testicle was normal and it was the mechanism for descent that was at fault. Wangensteen (1927) believed that the undescended testicle owed its imperfection to its abnormal position. Griffiths (1892–3) showed that experimental cryptorchidism in the dog caused arrest of spermatogenesis. Subsequent articles (Moore, 1924; Wangensteen, 1927; Nelson, 1951; Shirai and others, 1966) have shown that experimental replacement of a *mature* testicle within the peritoneal cavity is followed by recovery upon subsequent replacement into the scrotum. Nelson's experiments also suggested that prolonged retention of the mature testicle would prevent a return to normal. In contrast to previous work the present experiments have attempted to mimic more closely the natural cryptorchid state and its surgical correction. It is not *recovery* that has been studied but the ability of a cryptorchid testicle to continue normal development after it has been placed in the favourable scrotal environment for the first time.

The present work was confined to observation of the immature testicle and its development up to and just beyond puberty. Puberty is a gradual phenomenon in the guinea-pig as in other species. Accessory sex structures show a growth spurt around 35 days (Phoenix, 1970) and puberty is said to be complete at 81 days. This was shown by Webster and Young (1951) to be the mean age for the first appearance of a fertile ejaculate. Prolonged retention of the testicle into adult life was not studied. It seems possible that if short periods of retention of a normal testicle produce temporary arrest of spermatogenesis, then prolonged retention, as shown by Nelson (1951), might well cause permanent damage.

It has been shown in this study that the experimentally cryptorchid testicle, whose initial normality is accepted, achieves normal development after orchidopexy. However, it is known that the natural cryptorchid testicle of man often does not achieve normal development after surgical treatment. Kiesewetter, Schull, and Fetterman (1969) studied a series of prepubertal patients who had bilateral cryptorchid testicles operated upon individually at different prepubertal ages. They found that 70 per cent of the testicles which were operated upon first showed slight or no improvement when compared histologically with the cryptorchid partner at the second operation. Scott's (1962) review of the literature showed that following prepubertal surgical treatment one-quarter of unilateral and one-half of bilateral cryptorchid patients were not fertile. Scorer and Farrington's (1971) review of previous series of bilateral cases confirmed the poor results found by Scott (1962). It is unlikely that the poor results are due to peroperative trauma. Hecker and Hienz (1967) indicated that the risk of infertility caused by operative injury was about 1 per cent. It would therefore seem likely that the natural cryptorchid testicle of man is initially abnormal. This initial abnormality, as well as causing infertility, might also be an important aetiological factor in the failure of descent of the testicle.

A discussion of this experimental work would not be complete without mentioning both the superficial inguinal pouch ectopic testicle and the retractile testicle in relation to it. The superficial inguinal pouch ectopic testicle and the experimental testicle used in this study are comparable. Browne (1938) considered the superficial inguinal pouch ectopic testicle to be a different entity from that of the true undescended testicle. He stated that the superficial inguinal pouch ectopic testicle had been prevented from entering the scrotum by a fibrous barrier. This was caused by an abnormal attachment of the membranous layer of superficial fascia to the pubic bone. This theory was supported by Hand (1955), McNab (1955), and Jones (1958). Mack and others (1961) indicated that the proportion of seminiferous tubules containing germ cells at the time of orchidopexy was greater in ectopic testicles than in true undescended testicles. The present study has shown that arrest of development of an initially normal guinea-pig testicle will occur if it is prevented by mechanical means from descending. It has also shown that the development continues normally after surgical treatment. An ectopic testicle lying in the superficial inguinal pouch is often well developed with a cord of normal length and is not usually associated with an inguinal hernia. The true undescended testicle has remained on the natural line of testicular descent but has a short cord. It frequently has an abnormal appearance and is often associated with an indirect hernial sac. These factors would suggest that whereas the superficial inguinal pouch ectopic testicle may be quite normal initially, the true undescended testicle is probably not an initially normal testicle. So far, no comparison has been made between the subsequent fertility results of the two groups.

It is generally accepted that the retractile testicle will achieve a stable scrotal position at puberty without treatment. However, it has been suggested that although scrotal the previously retractile testicle may not have normal function because of its prepubertal residence within the superficial inguinal pouch. If it is assumed that the retractile testicle is initially normal but has an overactive cremasteric muscle, then the only cause for concern is the possibility that the temporary environment of the superficial inguinal pouch will cause permanent testicular damage before scrotal entry is maintained at puberty. The present animal experiments have demonstrated that a normal testicle will continue normal development after entry into the scrotum, in spite of abdominal retention beyond puberty. It is therefore likely that the retractile testicle, which is retained within the less harsh environment of the superficial inguinal pouch, will mature normally when permanent residence within the scrotum is gained at puberty. Operation would seem unjustifiable in these cases, provided that the diagnosis of retractile testicle is certain.

Acknowledgements.—I would like to thank the Joint Standing Research Committee of St. Mary's Hospital, London, for its financial support, and also Mr. H. H. Nixon and Mr. C. W. Jamieson for their helpful criticism.

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THE EFFECT OF UNILATERAL EXPERIMENTAL CRYPTORCHIDISM AND SUBSEQUENT ORCHIDOPEXY UPON MATURATION OF THE CONTRALATERAL SCROTAL TESTICLE OF THE GUINEA-PIG

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SUMMARY

A study of the contralateral scrotal testicle of the guinea-pig before and after the surgical treatment of unilateral experimental cryptorchidism is described.

The contralateral scrotal testicle of the guinea-pig has been found to mature quite normally without any evidence of incomplete development. In man, however, the contralateral scrotal testicle of unilaterally cryptorchid patients often shows incomplete development. The difference in results suggests that in man the unilateral cryptorchid state may be associated with a bilateral testicular abnormality. This bilateral abnormality might be the cause of poor fertility and, if severe, might also be the cause of failure of descent of the cryptorchid testicle.

SOME impairment of fertility is shown by two-thirds of postpubertal patients who have an untreated unilaterally cryptorchid testicle (Scott, 1962). If prepubertal surgical treatment had been performed in these unilaterally cryptorchid patients 25 per cent of them would have been infertile subsequently. The fertility of a young man who has had a unilateral orchidectomy for conditions other than cryptorchidism is normal. These figures would suggest that in man the descended partner of a unilaterally cryptorchid testicle is not entirely normal in spermatogenic function.

Raboch and Zahor (1956) and Hecker, Hienz, Daum, and Hollmann (1967) noticed that there was incomplete maturation of the contralateral scrotal testicle in unilateral cryptorchid patients when compared with the expected normal histology for a given age. However, this incomplete maturation was less pronounced than that shown by the cryptorchid testicle.

In order to investigate the subject further a study was made of the effects of experimental unilateral cryptorchidism and subsequent orchidopexy upon the contralateral scrotal testicle of guinea-pigs. This study was performed during a concurrent investigation of the histological effects of surgical treatment upon the experimentally cryptorchid testicle (Atkinson, 1973).

MATERIALS AND METHODS

Procedure.—Twenty-eight immature male Hartley-strain guinea-pigs were made experimentally unilaterally cryptorchid at the age of 7 days. Intraperitoneal Nembutal anaesthesia was used for this and subsequent procedures. Unilateral orchidopexy and biopsy were performed at 20, 40, 60, 80, or 100 days. A biopsy of the contralateral scrotal testicle was taken at the time of orchidopexy, and a biopsy was taken from both testicles at the age of 120 days (*Fig.* 1).

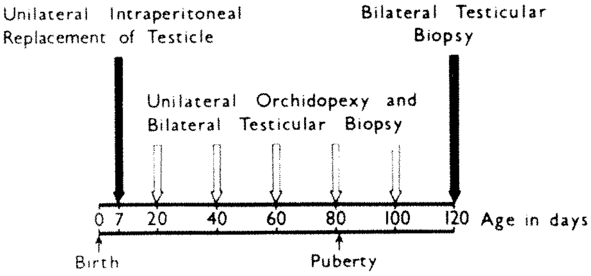
Unilateral Intraperitoneal Replacement of Testicle
Bilateral Testicular Biopsy
Unilateral Orchidopexy and Bilateral Testicular Biopsy
0
7
20
40
60
80
100
120
Age in days
Birth
Puberty

FIG. 1.—Age at which operative procedures were performed.

Table I.—AVERAGE QUANTITATIVE RESULTS OF THE TWO ASPECTS OF TESTICULAR HISTOLOGY OF THE CONTRALATERAL SCROTAL TESTICLE

TIME OF TESTICULAR BIOPSY	ORCHIDOPEXY ANIMALS		CONTROL ANIMALS	
	Tubule Counts (per High-power Field)	Spermatogenic Index	Tubule Counts (per High-power Field)	Spermatogenic Index
At intraperitoneal replacement of the opposite testicle (7 days of age)	41	1	41	1
At orchidopexy or control operation of the opposite testicle (20–100 days of age)	12·1	3·4	13·4	3·6
At postpubertal age (120 days of age)	4·9	4·9	5·1	4·7

In a similar number of animals a control procedure was used in which both the testicles remained scrotal. Testicular biopsies were taken at the age at which orchidopexy was performed in the test group of animals and at the postpubertal age of 120 days. Puberty in the guinea-pig was said to be complete by 81 days of age (Webster and Young, 1951).

Histology.—Biopsy specimens from the body of the testicle were fixed in Bouin's fluid and stored in 70 per cent ethanol. Sections were cut at 5 μ thickness and stained with haematoxylin and eosin.

The histology was studied from two aspects. First, the number of tubules per high-power microscope field of 0·52 mm. diameter was counted. Secondly, the degree of active spermatogenesis reached by the tissue was assessed by the use of the spermatogenic index. If there were spermatozoa or mature spermatids present the testicular tissue was considered to have a spermatogenic index of 5. Immature spermatids indicated an index of 4, the presence of secondary spermatocytes an index of 3, and primary spermatocytes only, an index of 2. If there were only spermatogonia present an index of 1 was afforded.

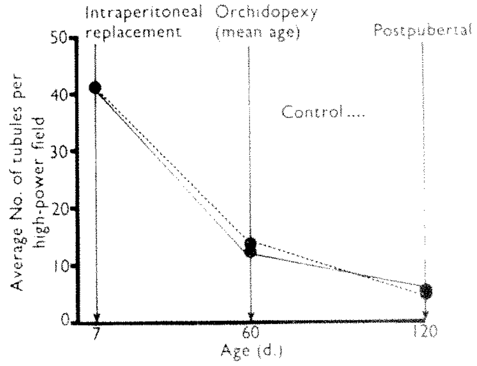

FIG. 2.—Consecutive comparison of average tubule counts per high-power field of contralateral scrotal testicles. Tubule counts per high-power field and tubule diameters have an inverse relationship.

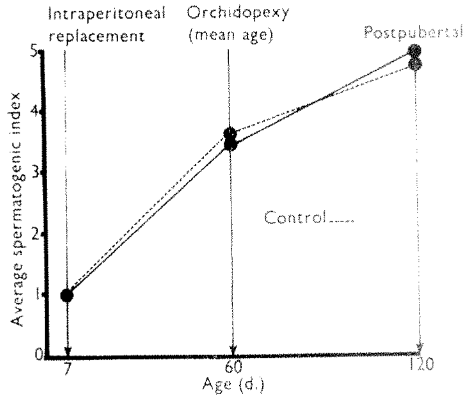

FIG. 3.—Consecutive comparison of average spermatogenic indices of contralateral scrotal testicles.

RESULTS

The study was made on the contralateral scrotal testicle of 28 guinea-pigs and a similar number of animals was used as controls. The results of studying the two aspects of testicular histology are shown in *Table I*.

Tubule Count.—The tubule count of the contralateral scrotal testicle of the animals undergoing orchidopexy and the contralateral scrotal testicle of the control animals for any given age was similar. As the tubules matured and enlarged the number of tubules seen in one high-power field clearly fell. At 120 days of age the tubule count of the contralateral scrotal testicle of both the animals which had undergone orchidopexy and the control animals was the same, and less than that seen at orchidopexy age (*Fig.* 2).

Spermatogenic Index.—At the orchidopexy age the average spermatogenic index of the contralateral testicle of both groups of animals was similar. There was no delay in development of the contralateral scrotal testicle in either group. At 120 days the average spermatogenic index of the contralateral scrotal testicle of both groups was 4·8 (*Fig.* 3).

The results of the two aspects of testicular histology studied were subjected to statistical analysis. No significant difference was found in the results of both the spermatogenic index and tubule count of the test group when compared with the control group at the age of orchidopexy and also at 120 days of age.

DISCUSSION

The contralateral scrotal testicle of unilaterally cryptorchid patients may show some evidence of incomplete maturation on histological analysis. It is not known why this abnormality should occur. There are two main possibilities to be considered. First, it may be that the testicles are both unequally affected by the same basic defect. This might explain why there is a poor fertility rate in patients with unilateral cryptorchidism who have not had the benefit of surgical treatment. It might also be postulated that if this basic defect was severe enough on one side it might prevent that testicle from responding to (or producing) the stimulus for its descent to take place. Secondly, and less likely, there is the possibility that the delayed maturity of the scrotal partner is produced in some way by hormonal influence. This might be promoted by the presence of an undescended testicle and coincidentally affect its scrotal partner.

It has been shown here that development of the contralateral scrotal testicle of the guinea-pig is not altered in any way by the presence of a cryptorchid testicle. It has also been shown that the contralateral scrotal testicle continues its development to full active spermatogenesis following surgical treatment of its cryptorchid partner. The only relevant previous experimental work is that of Shirai, Matsushita, Kagayama, Ichijo, and Takeuchi (1966). This was concerned with the observation of the contralateral scrotal testicle of experimentally cryptorchid dogs before and after surgical treatment. Their work was performed on an unstated number of mature dogs and they found that following intraperitoneal replacement of a *mature* testicle the contralateral scrotal testicle degenerated. Subsequent orchidopexy, however, allowed the contralateral scrotal testicle to resume some degree of spermatogenesis, but it was far below normal.

The reason why our results differ is not entire clear. The present work has used the immatu guinea-pig testicle which was placed within tl peritoneal cavity before it had ever experienced scrotal environment. This was done by design, as seemed to approach the situation of natural cryp orchidism more closely than did the intraperitone replacement of a mature testicle. This work h observed not the ability to recover but the ability achieve normal active spermatogenesis for the fir time. Shirai and others (1966) studied the recovery spermatogenesis after degeneration had occurred the mature testicle. They concluded that suppress spermatogenesis in the scrotal testicle of unilater cryptorchidism was induced in some way by tl degenerative changes in the cryptorchid testicle.

These guinea-pig experiments have shown that experimental situation, in which there was o cryptorchid testicle, allowed the contralateral scrot testicle to develop normally. This would suggest th the cryptorchid testicle did not induce a hormon effect to act upon the scrotal testicle.

It is suggested that this work gives support to t concept that there may be an inherent testicul abnormality in unilaterally cryptorchid patien which is often bilateral. This abnormality may be t cause of the poor results following surgical treatme in man. It is possible that if severe enough it may al be the cause of failure of descent of the cryptorch testicle. If the superficial inguinal pouch ectop testicle is excluded, the varying degree of no descent might indicate the severity of this bas abnormality. The underlying cause or nature of t basic abnormality remains unknown.

Acknowledgements.—I would like to thank t Joint Standing Research Committee of St. Mar Hospital, London, for its financial support, and al Mr. H. H. Nixon and Mr. C. W. Jamieson for th helpful criticism.

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SINCIPITAL ENCEPHALOMENINGOCELES

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SUMMARY

A definition of cranial encephalomeningocele is presented together with a classification of the types of sincipital encephalomeningocele and a review of their frequency throughout the world. A series of 30 cases encountered in Burma is described, including the personal details, clinical presentation, diagnostic procedures, general management, operative treatment, and the observations at operation. The aetiology and pathogenesis of sincipital encephalomeningocele are discussed with reference to the literature, to the embryogenesis of the skull and brain, and consideration of the observations made in this series of cases.

ENCEPHALOMENINGOCELES are congenital herniations of cerebral tissue through the skull. They are usually composed of a meningeal sac containing brain tissue, cerebrospinal fluid, or both and are enclosed externally by skin and soft tissues. They pass through congenital defects in the skull and are usually continuous with their intracranial counterparts. Guthrie and Dott (1927), however, suggested that perhaps these lesions are not true herniations as the displaced tissues were present before the skull was developed and were not, therefore, originally intracranial.

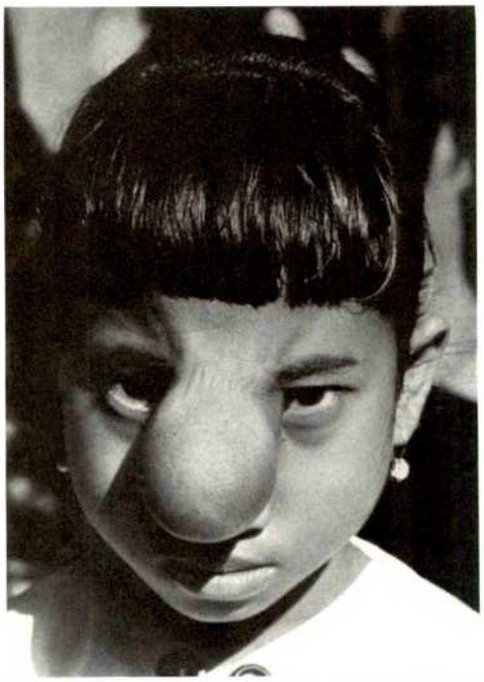


FIG. 1.—A nasofrontal encephalomeningocele, passing between the nasal and frontal bones and appearing in the midline at the root of the nose.

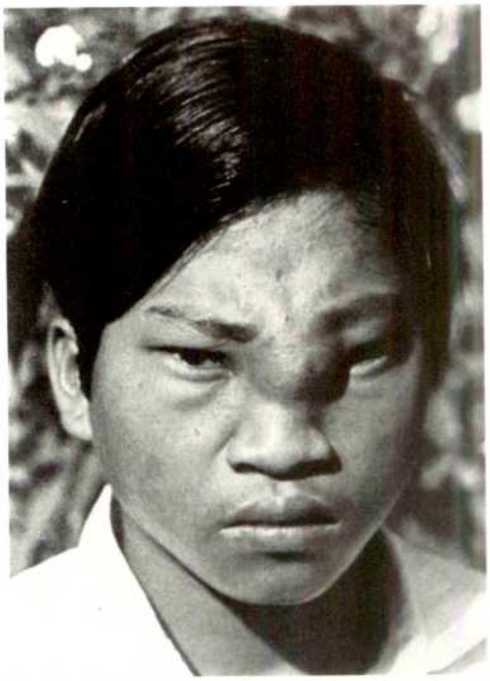


FIG. 2.—A left naso-ethmoidal encephalomeningocele, passing between the ethmoid, frontal, and nasal bones to appear on the side of the nose at the cartilaginous and bony junction.

They can occur anywhere in the midline sagittal axis of the cranium from the occiput to the nasofrontal region and only rarely appear lateral to this line. Mood (1938) stated that they are usually found at the sites of the fontanelles (occipital, frontal, sphenoidal, mastoid) or at the cribriform plate of the ethmoid, the foramen caecum, the foramen magnum, or occurring through a suture line.

Cranial encephalomeningoceles are encountered much less frequently than spinal encephalomeningoceles. Matson (1969) reported that in a 20-year period at the Harvard Clinic, 1390 spinal lesions were seen but only 265 cranial lesions. Gisselsson (1947) estimated the incidence of cranial encephaloceles as 1 in every 3500–4000 births and, of these, 15–20 per cent were anterior encephaloceles, while Lampert (1924) assessed the incidence of cranial encephaloceles at 2–3 per 10,000 births. In the Western world occipital encephalomeningoceles are the commonest variety, whilst in certain countries in the East anterior encephaloceles are more frequent. Of Matson's (1969) 265 patients, 14 had nasal encephaloceles, 4 nasopharyngeal, 17 frontal, 34 parietal, and 196 occipital. Van Nouhuys and Bruyn (1964) estimated the incidence of anterior encephaloceles to be 1 in every 35,000 live births, but Suwanwela and Hongsaprabhas (1966) assessed the incidence in Thailand to be 1 in every 5000 births.

The anterior encephalomeningoceles can be divided into two groups on the basis of their locations: the sincipital encephalomeningoceles occur near the root of the nose, and the basal encephalomeningoceles occur within the nose, the pharynx, or the orbit. Von

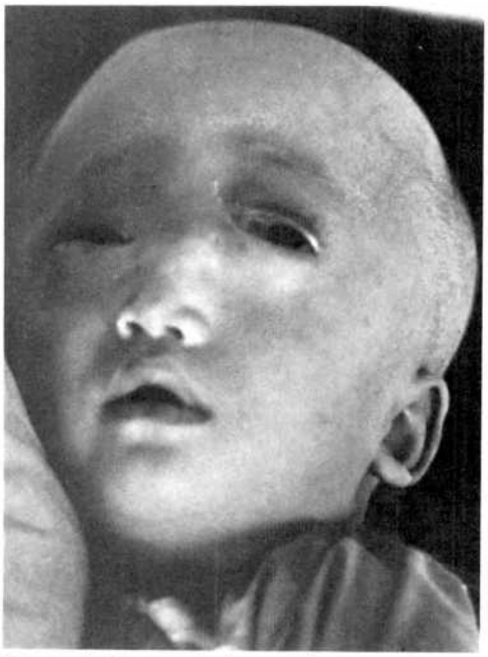


FIG. 3.—A left naso-orbital encephalomeningocele, passing between the ethmoid, frontal, and lacrimal bones into the anteromedial part of the cavity of the orbit.

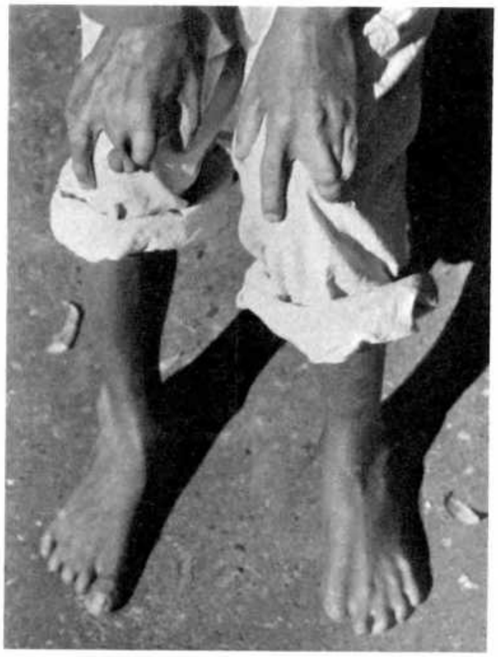


FIG. 4.—Congenital abnormalities of the fingers and toes in a patient who also had a nasofrontal encephalomeningocele which is seen in *Figs.* 10 and 11.

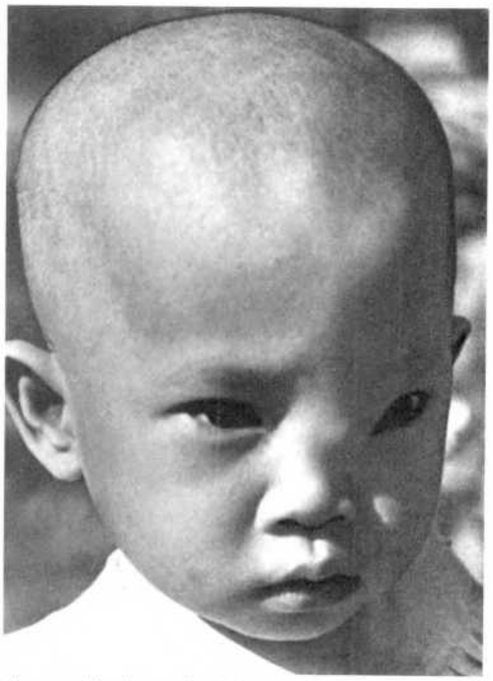


FIG. 5.—Simple, small, solid type of sincipital encephalomeningocele.

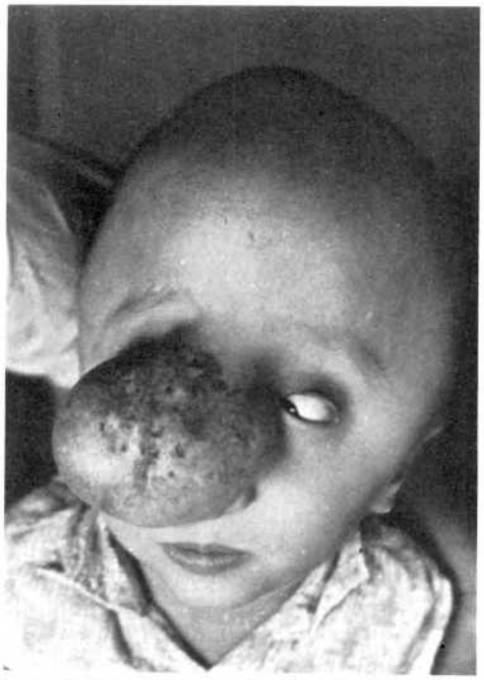


FIG. 6.—A large right naso-ethmoidal encephalomeningocele which contains a mixture of solid and cystic elements.

Meyer (1890) further classified the sincipital encephalomeningoceles into the following groups:—

1. Nasofrontal: Passing between the nasal and frontal bones and producing a rounded skin-covered mass in the midline at the root of the nose (*Fig.* 1).

2. Naso-ethmoidal: Passing between the ethmoid, frontal, and nasal bones to appear on the side of the nose at the cartilaginous and bony junction (*Fig.* 2).

3. Naso-orbital: Passing between the ethmoid, frontal, and lacrimal bones into the anteromedial part of the cavity of the orbit (*Fig.* 3).

CLINICAL MATERIAL

For a 9-month period from September, 1969, to May, 1970, the author was appointed as Colombo Plan Adviser in Neurosurgery to the Ministry of Health, Government of the Union of Burma. During this period over 50 cases of anterior encephalomeningocele were seen either in the Neurosurgical Unit in Rangoon General Hospital or in other parts of the country during lecture or inspection tours. Thirty of these cases were admitted for treatment to the Neurosurgical Unit in Rangoon and were studied in detail. Fourteen of these patients were operated upon.

Of the 30 patients studied, 19 were male and 11 were female. Ages ranged from babies of a few days old to a female of 39 years. There was an obvious regional distribution in Burma as 24 of the cases came from lower Burma, 4 from middle Burma, and only 2 from upper Burma. However, it is possible that overall population studies of Burma would show a proportional geographical representation. The age of the parents at the patient's birth was probably significant as 36 parents were over 30 years of age and 13 were over 40 years. The Burmese tend to marry while still young. Four of the mothers had febrile illnesses during the first 3 months of pregnancy but only 2 admitted to taking indigenous native medicines at that time. In 3 patients there was a family history of congenital abnormalities, none of which was an encephalomeningocele. All the patients were born at full term and were delivered by normal delivery. In 29 of the 30 cases a swelling was present at birth;

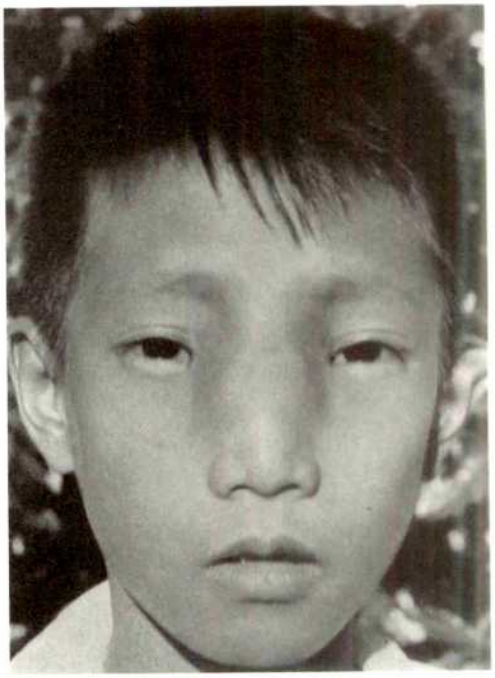
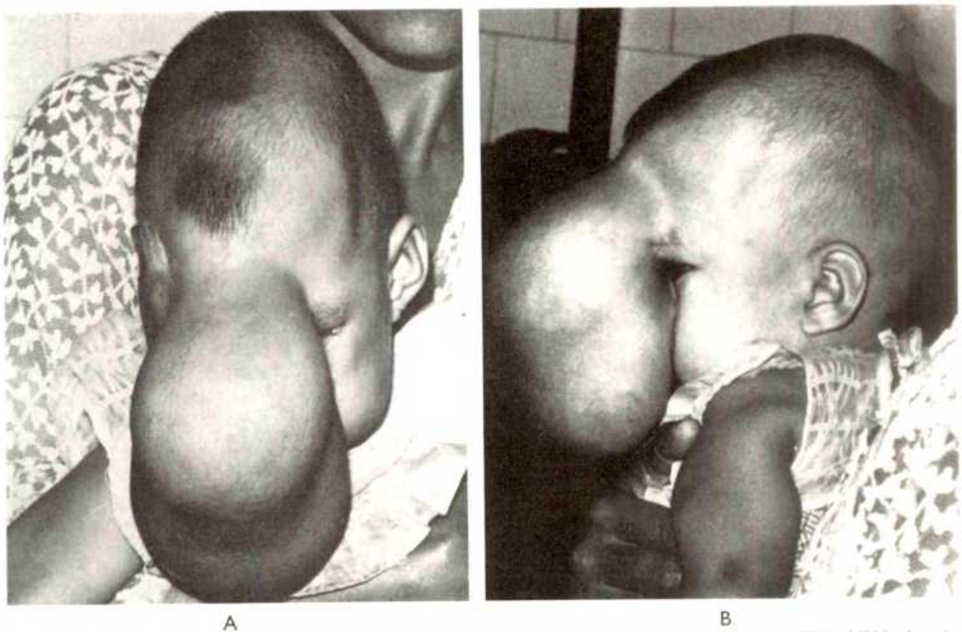


FIG. 7.—A diffuse type of nasofrontal encephalomeningocele.



A

B

FIG. 8.—A rapidly enlarging cystic variety of encephalomeningocele encroaching on the eyes, nose, and mouth. This child had a microcranium and a hydrocephalus.

the remaining case developed hydrocephalus shortly after birth and a naso-orbital encephalomeningocele 3 months later. In 25 of the patients the lesion was still enlarging: in 7 cases the lesion was rapidly enlarging and in 18 cases slowly enlarging. Four patients had clinical evidence of hydrocephalus at the time of their admission and 3 infants had microcrania; 2 with a solid lesion and 1 with a cystic lesion. Three patients had other neurological deficits. A boy of 16 had a sixth-nerve paresis, a 3-year-old boy suffered from grand-mal epilepsy, and a 39-year-old woman was totally blind in her right eye and had a psychotic illness. One patient had associated congenital abnormalities with syndactyly of the fingers and toes (*Fig.* 4). Two patients had an encephalomeningocele which had recurred after previous external surgical repair.

Clinical Presentation.—Of the 30 patients studied, 21 patients had a nasofrontal encephalomeningocele, 8 had a naso-ethmoidal encephalomeningocele, and 1 patient presented with a naso-orbital lesion. As well as seeing all three varieties of sincipital encephalomeningocele there were many different presentations within these varieties. The commonest was the simple, small, hard, nasofrontal or naso-ethmoidal swelling which grew only slowly and, at this stage, presented only a cosmetic problem (*Fig.* 5). Large lesions tended to contain a mixture of solid and cystic elements and very advanced lesions of this type encroached on the eyes and nose and became urgent problems (*Fig.* 6). A diffuse nasofrontal variety was seen, extending in a flattened form down over the nose (*Fig.* 7). The most urgent type was the purely cystic type, rapidly growing and often associated with either hydrocephalus or microcrania and causing great problems with vision, breathing, and feeding (*Fig.* 8). Advanced examples of nasofrontal encephaloceles containing a mixture of solid and cystic elements assumed an 'elephant-trunk' form, hanging down over the nose and mouth (*Fig.* 9). Two cases which were seen had recurred after previous attempts at external excision of the lesion (*Fig.* 10).

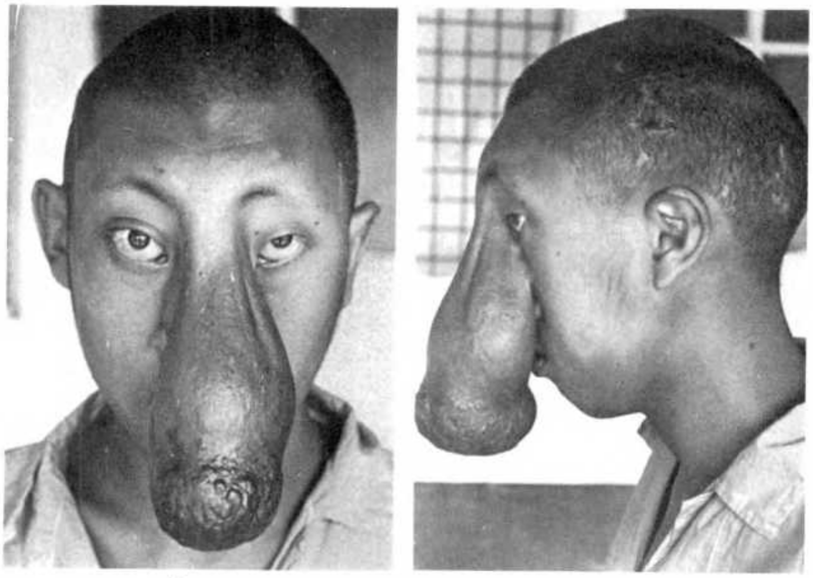

A B

FIG. 9.—A huge 'elephant-trunk' type of solid and cystic nasofrontal encephalomeningocele.

The encephalomeningoceles varied in size from 1 to 19 cm. in the greatest diameter. All the cases had skin coverings to their lesions but in some the skin was extremely fragile and in 1 case the skin had perforated, resulting in a cerebrospinal fluid leak on the surface of the encephalomeningocele. Some lesions were hard and solid, while others were cystic, fluctuant, and translucent. The swellings were never tender on palpation but would often fill or become tense when the patient coughed, strained, or cried. In some cases a defect could be palpated at the neck of the lesion through the anterior facial bones. In many cases separation of the orbits was seen. None of the cases could be reduced by compression.

Diagnosis.—As other types of nasofrontal swelling such as dermoid cysts and teratomas were extremely rare in Burma, the diagnosis of sincipital encephalomeningocele was usually made with confidence on clinical grounds alone. Although such differentiation is academic the subvarieties of sincipital encephalomeningocele were easily recognized. There are only two radiological investigations of any value:—

1. Plain skull radiographs or tomograms to establish the presence, size, shape, and location of the bony defect. This opening in the skull was usually difficult to visualize, particularly in infants and children, but postero-anterior projections at various angles proved useful, as recommended by Suwanwela and Hongsaprabhas (1966).

2. A lumbar air encephalogram to reveal an established hydrocephalus. Air does not enter the encephalomeningocele sac probably because of the tight approximation of the meninges and brain to the bony-defect orifice. It was felt that there was no

lace for the direct injection of air or contrast naterial into the encephalomeningocele sac because f the risk of establishing a cerebrospinal fluid leak r promoting infection.

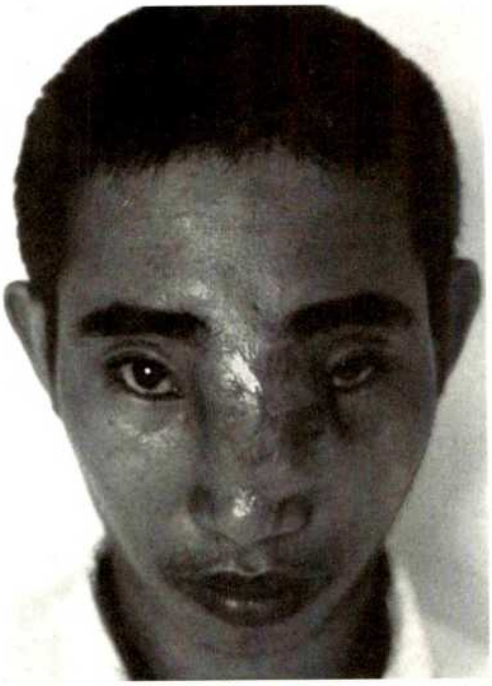


FIG. 10.—A recurrent left naso-ethmoidal encephalomeningocele. An external excision had been performed 12 years previously, but the lesion had started to recur after 3 years.

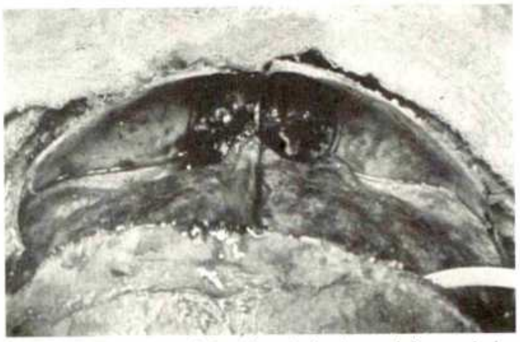


FIG. 12.—Exposure of the rim of the bony defect and the hernial contents after partial division of the meningeal sheath.

Management.—The only effective permanent treatment for suitable lesions is surgical repair. Contra-indications in Burma to surgical repair were small cosmetic lesions which were not rapidly enlarging and patients whose lesions were incompatible with survival or a useful independent life. Therefore the indications for surgical intervention were as follows:—

1. Rapidly enlarging encephalomeningoceles.
2. Encephalomeningoceles encroaching on the eyes, nose, or mouth.
3. Encephalomeningoceles in danger of rupturing.
4. Encephalomeningoceles associated with hydrocephalus.

Surgical treatment should be performed as early as possible in life to avoid further enlargement of the lesion, increasing brain damage, and a risk of development of hydrocephalus. In Burma, however, because of local conditions non-urgent cases were postponed until the child was older or until progression of the lesion necessitated intervention.

Surgical Procedures.—Direct therapeutic tapping of a cystic encephalomeningocele was felt to be contra-indicated because of the risk of establishing cerebrospinal fluid leak or causing infection. Direct external removal was not performed because of the risk of recurrence, infection, or cerebrospinal fluid leak.

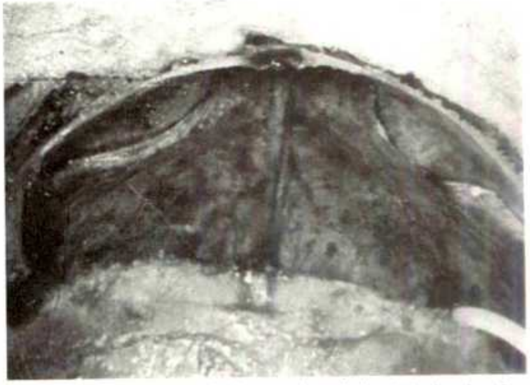


FIG. 11.—Exposure of the meningeal hernial sheath after bifrontal craniotomy and reduction of the intracranial pressure by ventricular drainage. The tube is slack and lying in the midline.

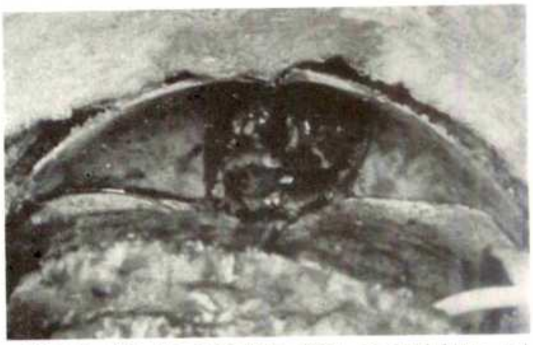


FIG. 13.—The rim of the bony defect, the dural fringe, and the encephalomeningocele contents after completion of division of the meningeal sheath.

If the patient was found to have an associated hydrocephalus a ventriculo-atrial shunt was first performed. In some patients who had a small, purely cystic encephalomeningocele this seemed the only procedure necessary as the external swelling deflated and shrank. However, to prevent the recurrence of the lesion if the shunting procedure should become blocked an internal repair was performed if the patient's condition would allow it.

An elective, direct, intracranial operation was thought to be the only real means of offering the patient a permanent non-recurrent repair. If the patient had an associated hydrocephalus this repair was performed 2 weeks after the shunting procedure. In all cases an extradural approach through a bifrontal craniotomy was used, as recommended by Suwanwela and Hongsaprabhas (1966). Intracranial tension was reduced by allowing the free flow of cerebrospinal fluid from an indwelling catheter placed in the frontal horn of the right lateral ventricle. Once this had been achieved the inner layer of dura was easily stripped from the anterior cranial fossa by blunt dissection and the hernial meningeal tube and its contents were identified as they passed forwards from the medial parts of the frontal lobes to the bony opening (*Fig.* 11). Although most of the circumference of the dural sheath could be mobilized and identified, there was usually difficulty in freeing the most inferior part from the dura of the anterior fossa and from remnants of the crista galli and the cribriform plate. This part of the dural sheath could only usually be identified when division of the rest of the sheath was near completion.

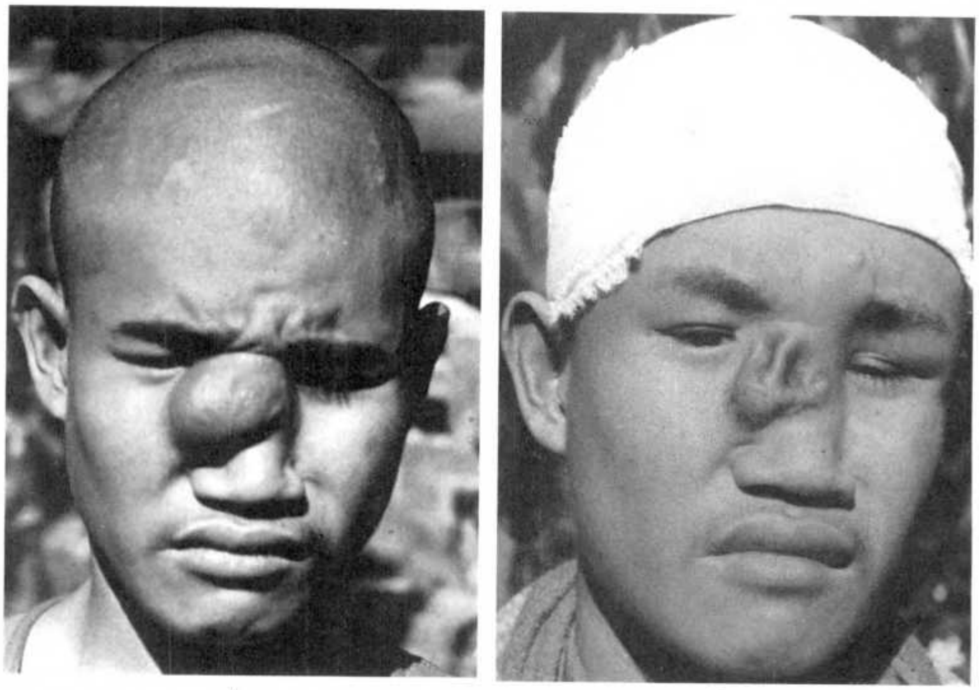


FIG. 14.—A small, cystic, right naso-ethmoidal encephalomeningocele before and 1 week after the intracranial repair.

The dural sheath was usually divided with a sharp knife, after diathermy coagulation, 1 cm. proximal to the bony opening, commencing on the superior surface and working laterally on either side. The contents of the sheath were divided by a mixture of sharp and blunt dissection (*Fig.* 12). The contents were never unduly vascular but contained strands of hard connective tissue passing into the depths of the bony opening. The inferior parts of the dural sheath were divided, after coagulation, as they became apparent. No attempt was made to remove the contents of the encephalomeningocele sac from within, but brain tissue was removed from the orifice of the bony opening to facilitate the subsequen closure (*Fig.* 13). The dural defect over the brain wa approximated by interrupted sutures, if this wa possible, without tension. In other cases the defec was repaired with a Teflon patch or simply covered with a sheet of Sterispon.

The permanent watertight closure of the skull defect is the most important single step of the operation. Workers in the past have recommended many different methods and have utilized various materials. The recommended materials include dura mater autografts, preserved human dura, temporalis fascia, fascia lata, pericranium, muscle patches, autogenous bone from the skull, ribs, ilium, or tibia, autogenous sliding bone-grafts, methyl methacrylate, Teflon, Dacron, Sterispon, bone wax, and oxidized cellulose. In 2 patients in this series the bony defect was covered with a Teflon patch, but great difficulty was encountered in suturing this into position as the dura mater of the surrounding anterior fossa in these cases is too thin and friable. For the same reason it was found impossible to cover the defect with a reflected or sliding autogenous dural flap. In 1 patient methyl methacrylate was used to plug the bony opening, but it proved unsatisfactory from three points of view: it was impossible to ensure a watertight approximation to the bony margin; it was difficult to fix securely in position; and it tended to assume a collar-stud shape distal to the bony opening which would hamper its removal should this prove necessary.

The method finally adopted for this closure was to utilize the dura of the hernial sheath. The sheath was divided as previously described, 1 cm. proximal to the bony opening. The contents were cleaned out level with the rim of the bony defect and then the dural sheath was itself closed in the midline vertically using nterrupted 000 silk sutures. A muscle patch or Sterispon patch was placed over the suture line. In all the cases in which this method was used the repair appeared to be watertight as judged by the postoperative shrinking of the encephalomeningocele. The craniotomy was closed in a standard fashion after removal of the ventricular drain. With large or solid encephalomeningoceles an external plastic repair was usually performed 1–2 months after the intracranial procedure.

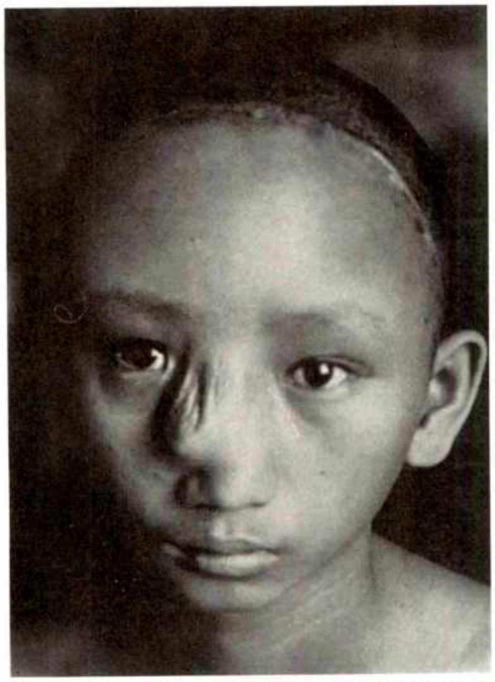


FIG. 15.—A right naso-ethmoidal encephalomeningocele 2 weeks after operation. A right frontal porencephalic cyst was pushing the interal bony defect over to the left. Note the domed right forehead and the postoperative shrinking of the lesion.

Surgical Statistics and Results.—Of the 30 patients reported, 14 patients were operated on, 20 operations being performed in all. Eleven patients received an intracranial repair, 3 of these being preceded or followed by a ventriculo-atrial shunt; 3 patients later had an external plastic repair. Three patients had shunt procedures alone.

In all the cases after intracranial repair or ventriculo-atrial shunt alone there was an immediate reduction in the bulk and tension of the encephalomeningocele except for the small solid types which were not appreciably affected at first. Within 2 weeks the small cystic varieties shrank until they were only apparent as skin folds (*Fig.* 14).

There were 2 deaths in this series, both in infants. One died from a postoperative aspiration pneumonia and autopsy showed no adverse intracranial complications. The other child died from respiratory arrest after operation when he developed status epilepticus and vomiting. Permission for autopsy was refused in this second case.

Observation at Operation.—

1. *Site of the Internal Bony Defect.*—Of the 11 patients who had a direct intracranial repair, 8 patients had a midline bony defect and in 7 of these it was at the site of the foramen caecum while 1 defect was slightly inferior to this with a small remnant of crista galli present superiorly. Seven of these 8 patients had a nasofrontal encephalomeningocele. In 3 cases the bony deficit was deviated from the midline and was situated over either the left or right anterior cribriform plate. A boy of 16 with a naso-ethmoidal encephalomeningocele was noted before operation to have a domed right forehead. At operation a large porencephalic cyst of 300-ml. capacity was found to be occupying the territory of the right frontal lobe (*Fig.* 15). The bony opening lay over the left anterior cribriform plate and the crista galli was split into two vertical portions, the superior one lying to the right of the defect and the inferior one bisecting the lower part of the bony deficit. The two parts of the crista galli had to be nibbled away before closure could be effected. In a boy of 12 years with a left naso-ethmoidal encephalomeningocele the bony opening was found at the bottom of a conical bony tunnel in the region of the left anterior cribriform plate. A small portion of the crista galli jutted out above and to the right of the opening. In a boy of 12 years with a left naso-ethmoidal encephalomeningocele the bony deficit was lying over the right anterior cribriform plate with the deformed oblique crista galli lying on its left side.

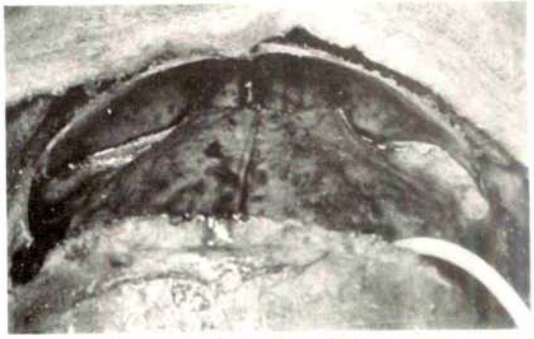


FIG. 16.—On opening the dural sheath, discrete prolongations of both frontal lobes were seen passing into the encephalomeningocele sac separated by a prolongation of the falx.

2. *Size of the Bony Opening.*—The bony deficit varied in size from 1½ to 2½ cm. in diameter; 9 of the 11 cases had an opening of 1½ cm.

3. *Shape of the Bony Opening.*—In all the cases the internal rim of the bony opening was circular or elliptical. In 1 midline case the crista galli only remained as a small superior jutting fragment. In 3 cases the crista galli was seen inferiorly. In 3 cases with a lateral bony deficit the crista galli was either split or lay to the left or right of the midline. In 4 cases the crista galli was not seen at all.

4. *The Meningeal Tube and its Contents.*—The meningeal tube usually consists of normal or thickened dura and was firmly attached to the rim and walls of the bony canal. It was usually not tense once the intracranial tension had been reduced with ventricular

drainage. It was not unduly vascular. There were often dense adhesions between the dura and the underlying arachnoid covering the brain tissue. Cerebrospinal fluid was observed to be lying in this space. The contents of the meningeal sheath were shown by pathological examination to be composed of brain, glial, fibrous, and connective tissues. In even the cystic cases there is very little escape of cerebrospinal fluid during the division of the tube. In no case was a connexion found between the lateral or third ventricle and the encephalomeningocele.

Usually the contents of the hernia were connected proximally to the medial sides of both frontal lobes and thus the proximal ends of the meningeal tube were central. In 1 case, however, on opening the dural sheath discrete prolongations of both frontal lobes were seen separated by a continuation of the falx—all three structures disappearing through the bony canal into the encephalomeningocele (*Fig.* 16).

5. *Postoperative Hydrocephalus.*—The patient with the largest lesion, a man of 20 years with a nasofrontal encephalomeningocele, developed hydrocephalus after the intracranial repair. Preoperative screening did not reveal hydrocephalus and at operation the ventricles were not enlarged. One week after surgery the patient's bone-flap started to elevate and investigation revealed a communicative hydrocephalus. It is interesting to note that there was no associated rise in tension of the encephalomeningocele, which, in fact, continued to shrink after operation. The patient's hydrocephalus was treated with a ventriculo-atrial shunt and the bone-flap settled back into position.

DISCUSSION

The pathogenesis of sincipital encephalomeningoceles is still in doubt. Mood in his paper on congenital anterior herniations of the brain in 1938 summarized the many and varied theories up to that date.

In 1827 Geoffrey St. Hillaire published his adhesive theory, attributing the lesions to adhesions between the dura, brain, and skin of the cranium resulting in maldevelopment of the bony vault and subsequent outgrowth of the brain. Himly (1829) and Serres (1832) suggested that during ossification and fusion of the skull-bones clefts were normally present and that the hernias formed through these clefts. Spring in 1854 concluded that many of the lesions were connected with the ventricles, and presumed that the encephalomeningoceles arose secondary to hydrocephalus. He assumed that frontal lesions arose from dilatation of the anterior horn of the lateral ventricles, trans-sphenoidal lesions from the third ventricle, and occipital lesions from the fourth ventricle. He explained the solid growths on the grounds of arrested hydrocephalus, reducing the cystic part of the lesion during intra-uterine life, leaving only protrusion of the solid part.

Klementowsky in 1868 thought that malformations of the skull occurred as a result of tabes, rickets, or syphilis and that the lesion protruded through a malformation. Ankermann (1882) believed that the cystic encephalomeningoceles were secondary to hydrocephalus but that the solid ones were due to microcranial maldevelopment with resultant extrusion of the brain. Berger in 1890 thought that the solid lesions were true new growths and called them 'encephalomata'.

Sternberg (1929) reviewed the available embryological knowledge on the closure of the neural groove and pointed out that the anterior and posterior ends close a week later than the rest of the tube. The anterior neuropore which closes at the beginning of the 4th week is situated at the site of the foramen caecum which in mature embryos lies at the level of the root of the nose between the eyes. This neuropore is separated from the skin by the ingrowth on each side of mesoderm which will later form the skull. If, however, this connexion with the skin persists mesodermal invasion is prevented, skull development is impossible, and a skull defect will form at this point, thus allowing herniation of the brain through the remaining thin epithelial membrane. When the mesodermal invasion is prevented entirely the brain and encephalomeningocele are connected with a pedicle. The corpus callosum originates from the region of the anterior neuropore, and Sternberg in 1929 reported a case of absence of the corpus callosum in a patient with an anterior encephalocele. Gardner in 1968 discussed states of hydrocephalus and hydromyelia which are physiological in embryonic life. He cited the studies on living pig embryos of Weed (1917), who showed that after closure the neural tube becomes distended with a protein-rich fluid before the appearance of the choroid plexus. With the advent of the choroid plexuses and secretion of cerebrospinal fluid the rate of neural tube distension increases and the diluted fluid begins to percolate through permeable areas in the rhombic roof to open up the subarachnoid spaces. Gardner (1968) stated: 'at this stage (6th–8th weeks) the head of the human embryo resembles a translucent bubble about to burst'. If the rhombic roof does not become adequately permeable at this stage fluid will not open up the subarachnoid spaces and a communicating type of hydrocephalus may persist. Gardner (1968) suggested that overdistension of the neural tube may distort the overlying cutaneous ectoderm and the surrounding mesoderm. Coalescence of general layers and adherence between the roof plate of the neural tube and the overlying cutaneous ectoderm may occur.

Holtzer (1952), in an experimental analysis of the development of the spinal column, showed that the diameter of the neural tube determined the diameter of the enclosing spinal canal. He stated: 'migrating pre-cartilaginous cells respond in a discriminatory and stereotyped fashion to the presence of any neural tissue by maintaining a characteristic distance from the neural tissue. The pre-cartilaginous cells are deployed in such a fashion that a lumen will eventually be formed in the cartilage whose size is a function of the enclosed nerve bundle.' This concept of maldevelopment could be applied to the bony skull defects that occur anteriorly in the causation of sincipital encephaloceles.

In order to understand the pathological defects that occur in the skull in these lesions the embryogenesis of the cranium will now be discussed. The bone of the vault of the skull and face are developed by ossification in membrane, and the base of the skull by ossification in cartilage. Most of the separate skull and face bones are ossified by the time of birth but they are mobile on each other and are fairly eadily disarticulated in the macerated skull. Their mobility on each other is most marked in the vault, and the power of overlap provides that moulding of he cranium which so generally occurs during parturition. The bones of the vault including the frontal bone do not interdigitate in sutures as in the adult but are separated by linear attachments of ibrous tissue (Last, 1956).

At the beginning of the 2nd month of intra-uterine ife the mesoderm surrounding the developing cerebral vesicles increases in thickness and forms ocalized masses. These localized mesodermal masses represent the earliest stage of formation of the skull. Early in the 2nd month mesodermal condensation surrounds the hypophysis and then extends forwards to form the basis of the pre-sphenoid and ethmoid bone and the nasal septum. These structures include the crista galli, cribriform plates, and ethmoid abyrinths. Chondrification of the base of the skull begins in the 2nd month of intra-uterine life and commences in the occipital plates. The sphenoid, the auditory capsule, the ethmoid, the roots of the greater and lesser wings of the sphenoid, and finally the nasal septum become chondrified in turn. The latter structure is well developed by the end of the 3rd month. The ethmoid bone is ossified from three centres, one for the perpendicular plate and crista galli, which appears during the first year after birth, and one for each labyrinth appearing during the 4th and 5th months of intra-uterine life. The cribriform plate ossifies from all three centres.

The vault of the skull first appears about the 13th day of intra-uterine life as mesodermal plates arising lateral to the developing brain and then extending superiorly to blend with each other and inferiorly to blend with the base. The ossification of the membranous part of the skull begins about the 8th week of foetal life with the appearance of four ossification centres on each side. The centres for the frontal bones are at the site of the frontal eminence. The two frontal ossifications fuse at the end of the first year, the metopic suture which separates them disappearing then.

At the end of the 3rd month of intra-uterine life the frontal and ethmoid bones are still apart although they are adjoining at birth. The nasal, lacrimal, and frontal processes of the maxillary bones are formed from membrane and are ossified in the membrane that overlies the cartilages of the nose. The centres of ossification of these bones appear about the 3rd month of foetal life.

To elucidate further the pathogenesis of encephalomeningoceles some of the pertinent findings at operation are re-emphasized. In 7 patients the site of the internal bony opening was at the foramen caecum in the midline and in 1 case it was slightly posterior to this. In 3 cases the defect was at the anterior ends of the left or right cribriform plate, in 1 of these cases the bony defect being pushed over by a porencephalic cyst. The internal rim of the bony defect was almost constant in size at 1½ cm. diameter; the 2 patients having defects larger than this (2 and 2·5 cm.) were the 2 patients with the largest external encephalomeningoceles. The defects were always smooth and rounded and clearly punched out. They were never cleft or split-like. This appearance would suggest that the meningeal and brain protrusions exist first and that the bony defect is later formed around them. The proximal end of the meningeal tubes were always in the midline. When a defect through the anterior end of the cribriform plates was present the crista galli was always present although deformed. In 4 cases of midline bony deficit the crista galli was not present at all and in 1 other case it was present but rudimentary. This would tend to suggest that the meningeal and brain protrusions occurred before the formation of the ethmoid and nasal septum at or about the 6th week of intra-uterine life. Chondrification of the crista galli and cribriform plates does not occur until the 3rd month. Four patients in the original series of 30 cases had clinical evidence of hydrocephalus at the time of their admission and 1 patient developed hydrocephalus after an intracranial operation.

Summarizing the theories of previous workers, noting the embryological facts of development of the skull and brain, and utilizing the observations made in this series of cases, the following explanation of the pathogenesis of encephalomeningoceles is offered.

With the closure of the neural groove the anterior neuropore, which closes last at the beginning of the 4th week of foetal life, is situated at the site of the future foramen caecum. Overdistension of the neural tube which occurs physiologically at this time plus unknown aetiological factors cause adhesions of the anterior neuropore to the overlying ectoderm. This prevents the primitive mesoderm from intruding and thickening between the developing brain in the region of the anterior neuropore and the overlying ectoderm and skin. Thus, a defect in the mesoderm is formed and it is further prevented from resolving by an actual protrusion of the primitive brain and its coverings which occurs when the neural tube becomes severely distended with cerebrospinal fluid as the choroid plexus is formed and secretes cerebrospinal fluid between the 6th and 8th weeks of foetal life. The mesodermal defect at the junction of the future frontal and ethmoid bones therefore persists and the surrounding mesoderm undergoes chondrification and ossification. If the cerebrospinal fluid in the developing ventricles does not penetrate the rhombic roof and open the subarachnoid space a state of communicating hydrocephalus will coexist with the encephalomeningocele. When the bony defect is laterally placed at the anterior cribriform plate one may postulate the existence of an abnormal pathological state of the developing brain or bone that pushes the early encephalomeningocele laterally. This pathological state may later disappear and therefore not be seen at operation or it may persist, as in the case of the porencephalic cyst in this series. The site of the externally emerging encephalomeningocele depends on the pathway taken through the developing bones overlying the internal defect. A nasofrontal lesion would emerge through a developmental defect at the junction of the frontal and nasal bones. A naso-ethmoidal lesion would pass through a defect at the junction of the ethmoid, nasal, and frontal processes of the maxillary bones and a naso-orbital lesion through a defect between the frontal and lacrimal bones.

At first the developing protrusion is formed from the enlarging lateral cerebral ventricles and their overlying neuro-epithelium, but as the development of the cerebral mantle of the forebrain proceeds the encephalocele loses its connexion with the ventricle. In time the subarachnoid space surrounding the herniating brain is developed and opened, providing a cerebrospinal fluid communication between the encephalomeningocele and the intracranial subarachnoid space.

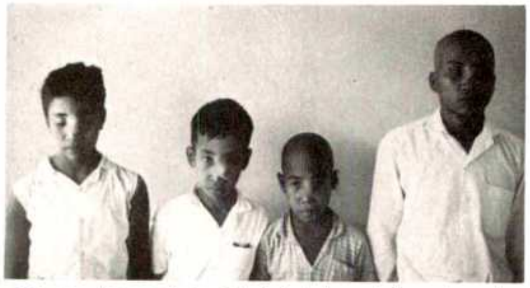


FIG. 17.—Four patients with sincipital encephalomeningoceles who were admitted to the neurosurgical unit in 1 week.

In 25 patients in this series it was stated on admission that the encephalomeningocele was enlarging. In 7 patients the cause of this enlargement was obviously increased intracranial pressure, as 4 of the patients had hydrocephalus and 3 had pathologically small skulls and were thus extruding excess brain or cerebrospinal fluid into the lesion. In the remaining 18 patients a persistent state of increased intracranial pressure was not apparent, but one can perhaps postulate two causes of increasing protrusion of the encephalomeningocele. First, a valve-like defect may exist in the subarachnoid space in the region of the meningeal tube to the internal bony rim. At times of intermittent increased intracranial pressure, as in straining or crying, cerebrospinal fluid may be forced into the lesion but prevented from returning to the intracranial compartment. Secondly, the plug of brain tissue and meninges is often adherent to the encephalomeningocele sac and therefore cannot retract. Intermittent increased intracranial pressure may further protrude the brain tissue. The five lesions that were not enlarging on admission may either have become firmly adherent at the internal bony rim or may have lost, through adhesions, the subarachnoid connexion.

The aetiology of this condition remains unknown. Many authors have stated that they are developmental, non-familial, and not necessarily associated with other congenital defects. Several cases have been reported which indicate that encephaloceles are not confined to man but are found in lower animals. Rawlings (1904) cited Norsa Gurrieri who described a case of encephalocele in an embryo of *Mus decumanus vel albinus* and stated that the developmental error involves bones of either cartilaginous or membranous origin. In the Burmese national press of January, 1970, there appeared a report and a photograph of twin piglets each weighing 4 kg. and bearing strange features: 'Both piglets had small tubes in the head suggestive of elephant trunks.'

There is no doubt that anterior encephaloceles are more common in the south-east Asia peninsula than elsewhere in the world (*Fig.* 17). Suwanwela and Hongsaprabhas (1966) commented on the frequency in Thailand and stated: 'It is interesting to speculate whether the mongolian type of head with its flat nose on a wide base contributes to the development of the lesion.' The majority of the patients in the present series were of pure Burmese stock, only one or two being thought to have mixed racial parentage. Racially the Burmese are thought to have derived from the same ancient Mongolian stock as the Thais. The author has also ascertained that anterior encephaloceles are found in increased frequency in certain parts of southern India, in East Pakistan, in Laos, and in Malaysia.

The aetiology of the cases in this series could be due to:—

1. Defective germ plasm inherent in certain races in the south-east Asia peninsula.
2. Infections in the mother during the first few months of pregnancy.
3. The effect of indigenous and perhaps pharmacologically unknown medicines during the first few months of pregnancy. Other congenital abnormalities are plentiful in Burma including thalidomide-like limb deformities although that drug has not been used in Burma.
4. The effect of some unknown inherent dietary factor.

Acknowledgements.—The author expresses his gratitude to his colleagues in Burma: Dr. U. Saw Nyunt, Dr. U. Aung Kyan, Dr. U. Wan Maung, and Dr. U. Maung Ohm for their advice and help.

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HEREDITARY SACRAL AGENESIS ASSOCIATED WITH PRESACRAL TUMOURS

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SUMMARY

This paper reports a family in which 6 females and 3 males have sacral agenesis. Four of the female members of the family have associated presacral tumours: 1 meningocele, 1 dermoid, and 2 of an undetermined nature at present. Similar sacral lesions associated with presacral meningoceles in 4 female members of a family of 29 have been reported by Cohn and Bay-Nielsen (1969).

SACRAL ossification is an extremely complex process as all students of anatomy are well aware. Each sacral segment is ossified from three primary centres and multiple secondary centres. Considering the complexity of this process congenital sacral abnormalities are relatively rare. Sacral agenesis was first described by Hohl in 1852, and Werthein described a further case in 1857. Shands and Bundens (1956) reviewed the spinal radiographs of 700 children admitted to the Alfred du Pont Institute between 1940 and 1955 and found 136 cases with spinal abnormalities—an incidence of 19·4 per cent. There were 3 cases of partial or complete absence of the sacrum—an incidence of 0·43 per cent. By 1966 there were 111 cases of sacral agenesis on record, and of these, 69 had anterior sacral meningoceles. Sixty of these patients were females. Nash (1959) divided sacral defects into two types: sacral agenesis, which may be partial or complete, and sacral dysgenesis, which includes such defects as spina bifida.

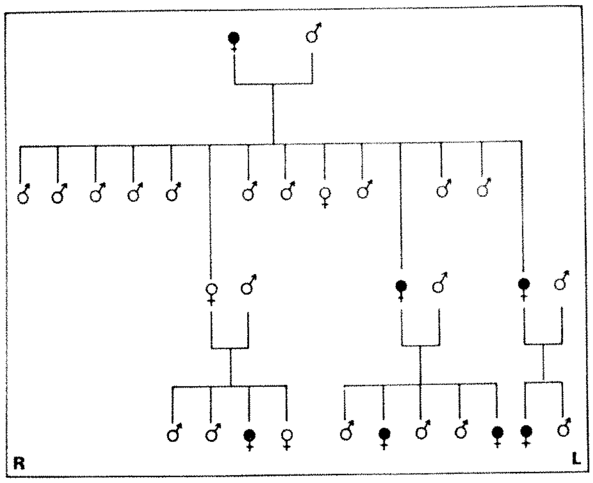

FIG. 1.—Family pedigree of the series reported by Cohn and Bay-Nielsen (1969).

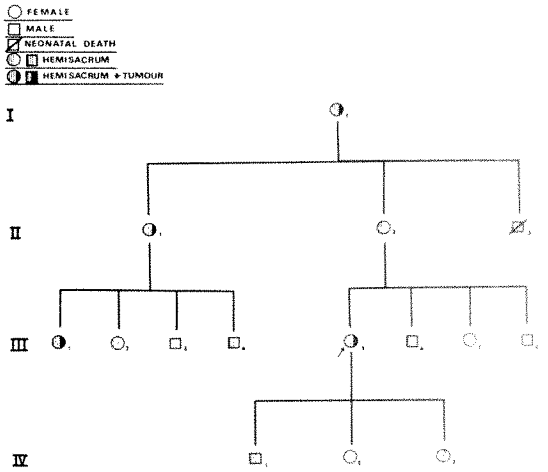

FIG. 2.—Family pedigree of the present series.

The aetiology of sacral agenesis is unknown. Cramer (1961) and Garner (1966) suggested that spinal abnormalities were due to increased pressure in the neural tube in embryonic life as a result of reduced permeability of the roof of the fourth ventricle. Meucke (1964) has shown that minute trauma in the embryo can produce cloacal exstrophy. Conditions analogous to sacral agenesis have been described in two animal species, the chicken and the mouse. The incidence of congenital abnormalities in children of diabetic mothers is considerably higher than normal (6·4 per cent compared with 0·9–2·1 per cent; Pedersen, Tygstrup, and Pedersen, 1964). Pouzet (1938) described an identical sacral defect in a father and son. The only other evidence of sacral defects occurring in one family is the very interesting report by Cohn and Bay-Nielsen (1969), who reported 2 females, aged 3 and 8 years, who were cousins with anterior sacral meningoceles and absence of the right half of the lower three sacral segments and of the coccyx. On investigating the remaining members of the family (*Fig.* 1), 4 others were discovered with identical sacral defects, 2 of whom had anterior sacral meningoceles. The cases extended over three generations and all the members with sacral agenesis were females. They suggested that the abnormality was transmitted as a sex-linked dominant trait.

The following case report is of a similar family, extending over four generations, in which 6 females and 3 males have congenital defects of the sacrum and coccyx. One of the females had a presacral dermoid tumour, another had a presacral meningocele, and 2 others have presacral tumours of an undetermined nature. There was no evidence of any tumour in the 3 males.

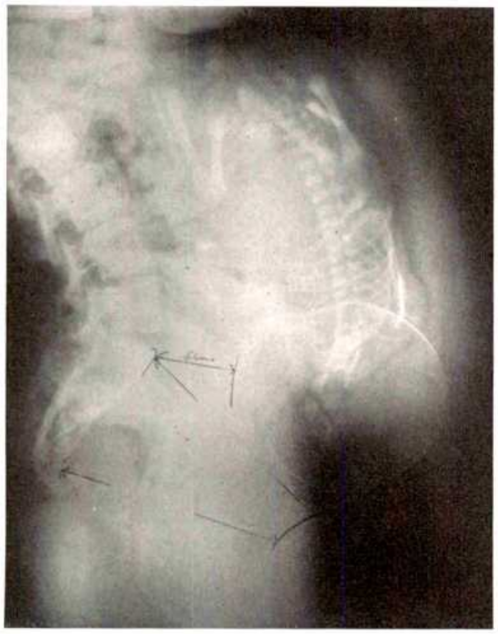

FIG. 3.—*Case* 1. Radiograph showing a foetal head arrested at the pelvic brim.

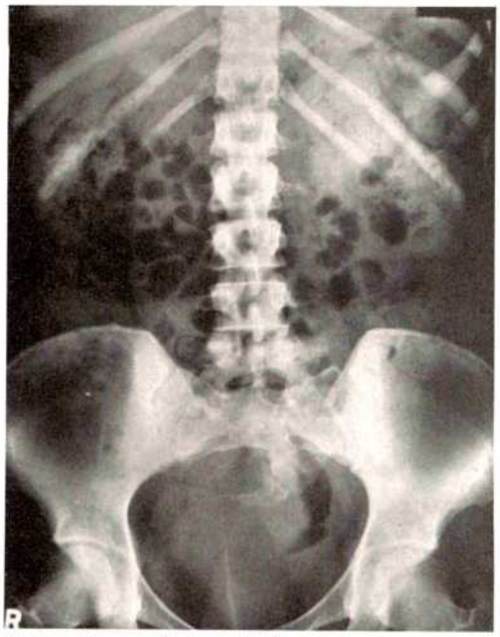

FIG. 4.—*Case* 1. Radiograph showing the absence of the lower three sacral segments on the right side. The tumour is also visible.

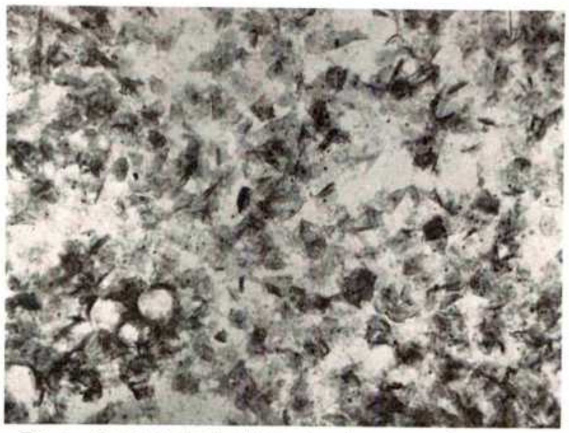

FIG. 5.—*Case* 1. Aspiration biopsy showing masses of squamous cells. (× 40.)

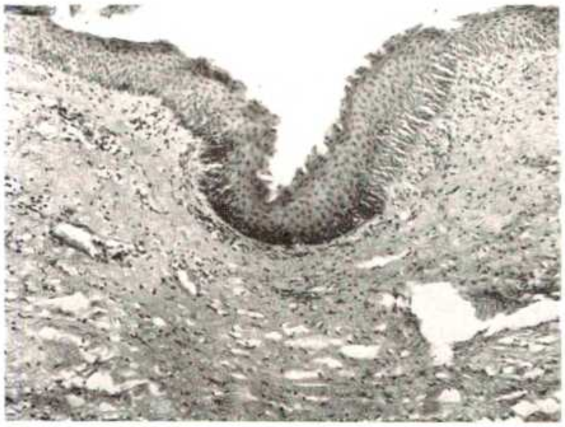

FIG. 6.—*Case* 1. Histological section showing the squamous epithelium lining the presacral dermoid. (× 40.)

CASE REPORTS

Case 1.—The propositus, Mrs. J. G., aged 20 years (III, 5, *Fig*. 2), was admitted to the Royal Free Hospital in September, 1970, for investigation of vaginal bleeding. She had had three Caesarean sections performed for disproportion, and on each occasion the foetal head had failed to enter the true pelvis (*Fig*. 3). On rectal examination she was found to have a presacral tumour displacing the rectum and uterus forwards. She had no other symptoms or signs. A radiograph of the sacrum (*Fig*. 4) showed absence of the lower three sacral segments on the right side, and the lower left half of the sacrum and coccyx were curved forwards and medially. The tumour was also visible. Aspiration biopsy of the tumour through the perineum revealed a creamy-brown fluid which on microscopy consisted of masses of squamous cells (*Fig*. 5)

At operation through a left paramedian incision there was a multilocular presacral cystic tumour, measuring 15 × 10 × 10 cm. The tumour was attached to the upper margin of the sacral defect near the midline. The rectum was separated from the tumour and the lesion was excised completely. It was felt that the tumour was more likely to be a presacral meningocele, but the subsequent histological examination (*Fig*. 6) showed that the tumour was lined with squamous epithelium and was certainly a presacral dermoid cyst. The patient's postoperative course was uneventful.

Case 2.—Mrs. E. W., now aged 65 years (I, 1, *Fig.* 2), was admitted to the London Hospital in August, 1948, with acute retention of urine. On examination she had a full bladder, both buttocks were poorly developed, especially on the right side, and she had a perianal saddle-shaped area of anaesthesia. She had a presacral cystic mass, and a radiograph of the sacrum (*Fig.* 7) showed agenesis of the ower sacral segments. On 23 Aug., 1948, 325 ml. of cerebrospinal fluid were aspirated from the cyst. Total excision of the meningocele was performed through a posterior approach by Mr. D. W. C. Northfield, and her postoperative course was uneventful. Histological examination (*Fig.* 8) confirmed the diagnosis of a presacral meningocele.

Case 3.—Mrs. I. C., aged 38 years (II, 1, *Fig.* 2), attended for examination on request. She was asymptomatic and had had four normal vaginal deliveries. On rectal examination she had a presacral tumour approximately 5 cm. in diameter, and a radiograph of her sacrum (*Fig.* 9) showed sacral agenesis and a presacral tumour. At present we do not feel justified in pursuing further investigations.

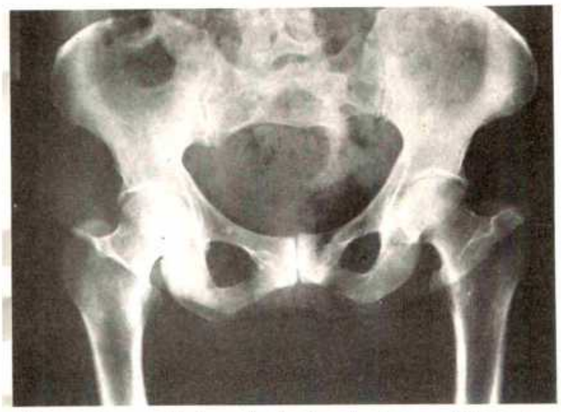

FIG. 7.—*Case* 2. Radiograph showing the absence of the lower sacral segments.

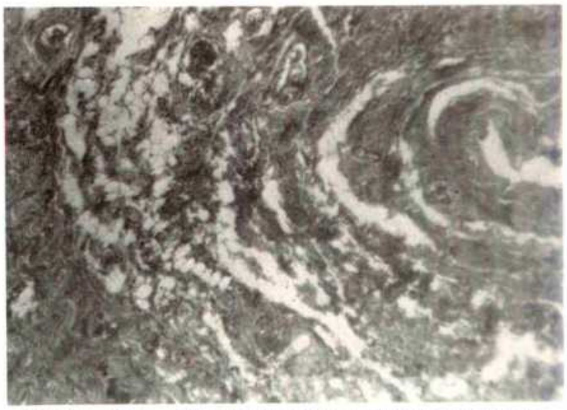

FIG. 8.—*Case* 2. Histological section showing the wall of the presacral meningocele. (× 40.)

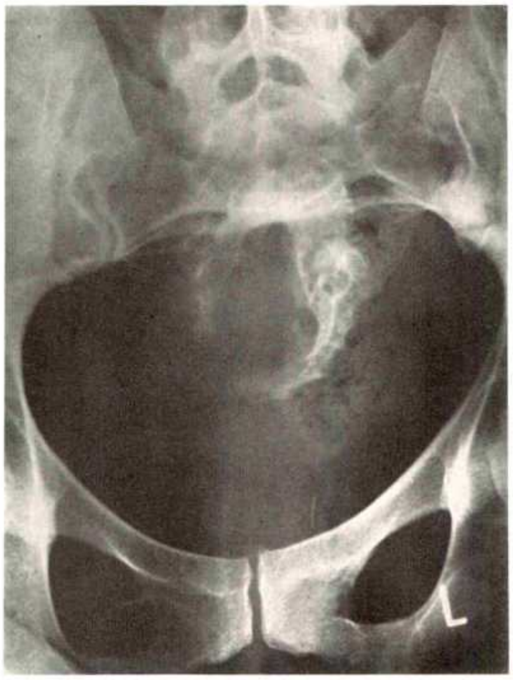

FIG. 9.—*Case* 3. Radiograph showing sacral agenesis and a presacral tumour.

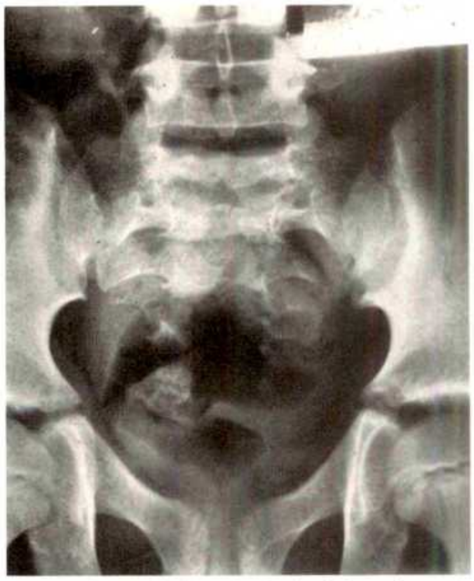

FIG. 10.—*Case* 7. Radiograph showing left sacral agenesis.

Case 4.—Miss J. C., aged 16 years (III, 1, *Fig.* 2), was found to have a presacral tumour, measuring about 5 cm., and sacral agenesis. She is asymptomatic and is being kept under observation as an out-patient.

Cases 5, 6, *and* 7.—The 3 male members of the family (III, 4 and 6; IV, 1, *Fig.* 2) all have a similar sacral defect with the absent segments on the left side (*Fig.* 10). Members III, 4 and 6 both have spina bifida of the first and second sacral segments. However, at present there is no evidence of any presacral tumour in the male members of this family.

DISCUSSION

Congenital deformities of the sacrum are frequently associated with other congenital abnormalities of the musculoskeletal system, genito-urinary tract, and lower gastro-intestinal tract. Of the 44 cases reported by Freedman (1949), 50 per cent had club-foot deformities and 18 per cent had congenital dislocation of the hip-joint. Spina bifida, hemivertebra, and fused ribs may also occur.

Visceral abnormalities were present in 35 per cent of Freedman's (1949) cases. The main genito-urinary disorders were neurogenic bladder, ureteric reflux, hydronephrosis, and duplication of the ureters. Williams and Nixon (1957) reported 8 cases of sacral agenesis with associated rectal disorders (mainly incontinence), and Koontz and Prout (1968) reported 8 further cases, 3 of which had an imperforate anus. Neurological disorders of the lower limbs vary from mild muscular paresis to total paraplegia. The more severe lesions tend to be associated with extensive sacral defects.

Presacral tumours have been classified by Lovelady and Dockerty (1949) into congenital abnormalities, bone tumours, neurogenic tumours, and miscellaneous tumours. The symptoms produced by these lesions are due to pressure on the pelvic viscera or associated neurological disorders. Pressure symptoms result in constipation, retention of urine, and dysmenorrhoea. Large tumours interfere with parturition and may necessitate Caesarean section. Neurological disorders are mainly due to loss of sphincteric control, sensory and motor deficiencies of the lower limbs, or intermittent increase in the cerebrospinal fluid pressure due to meningoceles. Infection in presacral dermoid tumours may result in unusual postanal discharges and sinuses.

In the cases reported in this paper one very consistent feature was constipation, and evacuation of the rectum was necessary in all the cases in order to obtain proper radiographs. The propositus (III, 5) had had three Caesarean sections performed. Members II, 1, and III, 1 have presacral tumours. Their nature has not been elucidated as yet but they are under out-patient supervision.

Member I had the presacral meningocele excised via a posterior approach while member II, 5 had her tumour removed via an abdominal approach. The surgical treatment of presacral tumours has been well documented and the main hazards are nerve injury and meningitis.

In the family reported in this paper 6 females and 3 males have a very similar sacral defect, suggesting that this condition is transmitted in this family as a dominant trait. The 4 patients with presacral tumours are all female, indicating that this lesion is transmitted as a sex-linked dominant trait. The only other report of a similar familial congenital sacral defect is the family reported by Cohn and Bay-Nielsen (1969) in which 6 female members of a family of 29 had congenital sacral agenesis, 4 of which were associated with presacral meningoceles. A search of the literature failed to reveal any record of sacral agenesis associated with a presacral dermoid tumour

Acknowledgements.—I wish to thank Mr. Emlyn Williams, F.R.C.S., the Royal Free Hospital, London under whose care the propositus was admitted. I would also like to thank Drs. E. H. Henderson G. Finlay, and M. Henry for assistance in tracing the other members of the family. My thanks are also due to Professor Doniac and the Records Department, the London Hospital, to Mr. C. Gilson, the Photographic Department, the Royal Free Hospital, and to Dr. J Cohn for permission to reproduce *Fig.* 1.

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THE MANAGEMENT OF UPPER GASTRO-INTESTINAL TRACT HAEMORRHAGE

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SUMMARY

Two hundred successive patients with upper gastro-intestinal tract haemorrhage were admitted to a surgical unit for management. One hundred and thirty-five patients (67·5 per cent) had a chronic peptic ulcer, 33 patients (16·5 per cent) had acute lesions (either an erosive gastritis or an acute gastric ulcer), and 32 patients (16 per cent) were a mixture of other diagnoses, of which 13 (6·5 per cent) were simple conditions but 19 (9·5 per cent) were conditions with a bad prognosis, e.g., carcinoma of the stomach, oesophageal varices, aortic aneurysm. Surgery was undertaken for massive, continuing, or recurrent bleeding and was as 'conservative' as thought possible. In duodenal ulcer this consisted of suture of the ulcer with vagotomy and pyloroplasty, and suture of the ulcer with vagotomy where possible in cases of anastomotic ulcer. In gastric ulcer only those less than 2 cm. in diameter were treated by suture with vagotomy and pyloroplasty. Ulcers greater than 2 cm. in size requiring surgery were treated by gastrectomy.

In the 181 patients whose underlying condition had a good prognosis there were 7 deaths (4 per cent). In this group 81 operations were carried out; 61 were 'conservative' operations for peptic ulcer, 2 were for repair of a hiatus hernia, and there were 18 gastrectomies, usually for a large gastric ulcer. There were 2 deaths among the operated patients; 1 after gastrectomy and 1 after a 'conservative' operation. There were 5 deaths among the 100 patients in the group which was treated non-operatively. There were 8 deaths among the 19 patients with underlying conditions of grave prognosis.

The case for the admission of patients with upper gastro-intestinal tract bleeding to a surgical unit is fully discussed and it is advocated together with a selective policy for operation. Where operation is necessary this should be as conservative as possible for bleeding duodenal ulcer, chronic gastric ulcer less than 2 cm. in size (ulcers of larger size may well respond but the method was not assessed for such ulcers), solitary acute gastric ulcer, and anastomotic ulcer. Gastric resection should be retained for the few patients with diffuse erosive gastritis requiring surgery and possibly for patients with a very large chronic peptic ulcer.

UPPER gastro-intestinal tract haemorrhage can be a life-threatening emergency, which it has been customary to manage in medical units, seeking the advice of the surgeon only in cases of massive or continuing bleeding. Even in a well-integrated hospital where surgeons work closely with doctors in the medical units and see all such patients on admission the surgeons' subsequent advice may be sought at a rather late stage, and it is possible that the patient could be better dealt with by primary admission into a surgical unit.

It is well established that the most frequent cause of upper gastro-intestinal haemorrhage is acute or chronic peptic ulceration and that many patients with these complaints will cease to bleed spontaneously, although surgery is indicated for massive, continuing, or recurrent bleeding. The type of surgery to be performed in the emergency situation is still not completely resolved, but the experience gained from a study of 40 consecutive gastrectomies carried out by one of us (R. T. G.) coupled with the reported high mortality of gastrectomy for upper gastro-intestinal tract bleeding from many other sources made us feel that we ought to adopt a policy of conservative surgery rather than radical resection in the emergency situation wherever possible. The results of these policies are reported in this paper.

CLINICAL MATERIAL

From January, 1967, all the patients presenting with upper gastro-intestinal tract haemorrhage were admitted to a surgical unit, and this report deals with the first 200 consecutive patients so managed. The patients were all treated initially by non-operative means with regular observations of the pulse and blood-pressure, and blood transfusion was given as indicated by these vital functions. Full blood-count, liver-function tests, and chest radiographs as well as early contrast radiology of the upper gastro-intestinal tract were carried out routinely. Operation was undertaken if the bleeding was massive, continuing, or recurrent. The operation carried out was as conservative as possible. This, in most instances, consisted of suture of the ulcer with unabsorbable material in addition to vagotomy and pyloroplasty. The only exception to this was in patients with chronic gastric ulcers greater than 2 cm. in diameter in whom it was felt that suture would be technically difficult, thus making control of bleeding dubious and presumably carrying a higher risk of re-bleeding. Gastric resection was carried out in this subgroup. All the operative treatment was undertaken by three consultant surgeons in accordance with this policy.

RESULTS

One hundred and thirty-five out of 200 patients (67·5 per cent) with upper gastro-intestinal tract bleeding had a chronic peptic ulcer. Thirty-three

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patients (16·5 per cent) had an acute gastric ulcer or erosive gastritis, making a total of 168 patients (84 per cent) who had bleeding from an acute or chronic peptic ulcer. There were 9 patients (4·5 per cent) with hiatus hernia, 9 patients (4·5 per cent) with carcinoma of the stomach, and 4 patients (2 per cent) with oesophageal varices. There were 10 patients (5 per cent) with other causes of gastro-intestinal tract bleeding (*Table I*).

It is clear that referring doctors find it far from easy to say whether a patient has bled from the upper gastro-intestinal tract. On many occasions a patient was admitted urgently with a diagnosis of bleeding but was found not to have bled from the upper gastro-intestinal tract. During the period under review 63 such patients were admitted, some of whom had vomited, but the vomit did not contain blood, some of whom had bled from the nose or lungs, and some who had neither vomited nor bled.

Table I.—DIAGNOSIS AND TYPE OF TREATMENT IN 200 PATIENTS WITH UPPER GASTRO-INTESTINAL TRACT BLEEDING

DIAGNOSIS	TOTAL NO. OF PATIENTS	NO. OF PATIENTS UNDERGOING OPERATION		NO. OF PATIENTS HAVING MEDICAL TREATMENT
		'Conservative'	Resection	
Duodenal ulcer	96	45	1	50
Gastric ulcer	28	7	13	8
Anastomotic ulcer	11	5	2	4
Gastritis	33	4	1	28
Hiatus hernia	9	2	—	7
Oseophageal varices	4	2	—	2
Carcinoma of the stomach	9	—	5	4
Mallory–Weiss syndrome	3	—	—	3
Pseudoxanthoma elasticum	1	—	1	—
Leiomyoma of the jejunum	1	—	1	—
Aortic aneurysm	1	—	1	—
Lymphosarcoma	1	—	—	1
Renal failure	2	—	—	2
Haemophilia	1	—	—	1

Operations were carried out on 90 of the 200 patients. Of these, 26 per cent are described as urgent (carried out within 24 hours of admission), 40 per cent are described as emergency (carried out between 24 hours and 7 days after admission), and 34 per cent were early elective procedures (carried out between 1 week and 1 month after admission). The overall mortality was 15 out of 200 patients (7·5 per cent). Nineteen patients had either tumours or non-ulcerative lesions with a bad prognosis, e.g., varices, aortic aneurysm, or a bleeding tendency such as uraemia or haemophilia. There were 8 deaths in this group of 19 patients. Of the other 181 patients with 'innocent' lesions, there were 7 deaths (4 per cent). In this group there were 2 deaths among the 81 patients having operations (3 per cent) and 5 deaths among the 100 patients (5 per cent) who were treated non-operatively.

Conservative surgery was possible in 45 out of 46 patients whose duodenal ulcer required operation, the only exception being one massive duodenal ulcer which it was felt better to treat by gastrectomy. Only 7 out of 20 operations for gastric ulcer were conservative because the ulcer was considered too large to be sutured in 13 cases. There were 7 operations for an anastomotic ulcer of which 5 were conservative (vagotomy and suture of the ulcer), 5 operations for acute erosive gastritis or acute gastric ulcer of which 4 were conservative, and 2 operations for repair of a sliding hiatus hernia.

Age and Sex (*Table II*).—There was a considerable predominance of male patients with a duodenal or anastomotic ulcer but there was a wide age range There seemed to be little difference between the average age and sex distribution in the operative and non-operative groups. However, the average age of the patients with anastomotic ulcer was rather younger than that of the other groups.

Table II.—AGE AND SEX OF PATIENTS WITH BLEEDING PEPTIC ULCER

DIAGNOSIS		NO. OF PATIENTS		AGE (yr.)	
		Male	Female	Mean	Range
Duodenal ulcer	All patients	83	13	54	20–91
	Operative	43	3	53	22–79
	Non-operative	40	10	55	20–91
Gastric ulcer	All patients	17	11	57	28–87
	Operative	14	6	52	28–68
Gastritis	All patients	19	14	47	14–81
Anastomotic ulcer	All patients	10	1	40	25–68

Table III.—MORTALITY AND INCIDENCE OF RECURRENT HAEMORRHAGE IN 181 PATIENTS WITH BENIGN CONDITIONS CAUSING UPPER GASTRO-INTESTINAL HAEMORRHAGE

TYPE OF OPERATION	NO. OF PATIENTS	NO. OF DEATHS	RECURRENT HAEMORRHAGE	TIME OF RECURRENCE
Vagotomy, pyloroplasty, and suture for chronic ulcers	57	0	2	8 and 12 d.
Vagotomy, pyloroplasty, and suture for erosions	4	1	1	Immediately
Gastrectomy	18	1	1	2 mth.
Repair of a hiatus hernia	2	0	1	8 d.
None	100	5	—	—

Further Bleeding (*Table III*).—Sixty-one cases had vagotomy and suture of a peptic ulcer. Of these, 3 had significant further bleeding. One was a patient with multiple gastric erosions and undoubtedly the bleeding continued from this erosive gastritis. Two patients re-bled after suture of a chronic duodenal ulcer at 8 and 12 days. They were treated by further surgery; 1 had simply a resuture of the ulcer but the other patient had a Polya gastrectomy. In both these patients the second procedure produced a satisfactory result. In 18 patients who had a gastrectomy as the primary operative procedure there was one recurrence of the bleeding. This occurred in a young patient who had a massive posterior gastric ulcer which had probably been induced by radiotherapy carried out 18 months previously for a left renal tumour. Two months after his gastrectomy he bled again massively and fatally and was found at post-mortem examination to have a recurrent massive gastric ulcer. One of the 2 patients who had a repair of a hiatus hernia re-bled 8 days after operation, and laparotomy showed that this elderly woman had a chronic duodenal ulcer which had been overlooked at the first operation. She made a satisfactory recovery after the ulcer had been dealt with by vagotomy, pyloroplasty, and suture.

Mortality.—The 8 deaths in the group of patients with malignant or vascular disease were probably inevitable owing to the nature of the disease process (*Table IV*). There were 2 deaths after the 81 operations for peptic ulcer; 1 of these was caused by massive, continuing bleeding from an erosive gastritis which was not controlled by suture. It might have been better to do a gastrectomy in this case. The other death was in the patient who had had previous radiotherapy and had a recurrent massive gastric ulcer with fatal bleeding 2 months after operation (*Table III*).

Table IV.—HOSPITAL MORTALITY IN 19 PATIENTS HAVING CONDITIONS WITH A BAD PROGNOSIS

DIAGNOSIS	NO. OF PATIENTS	OPERATION	NO OPERATION	NO. OF DEATHS
Carcinoma of the stomach	9	5	4	5*
Lymphosarcoma	1	0	1	0
Leiomyoma of the jejunum	1	1	0	0
Renal failure	2	0	2	1
Oesophageal varices	4	2	2	2†
Aortic aneurysm	1	1	0	0
Haemophilia	1	0	1	0

* Two postoperative. † One postoperative.

There were 5 deaths among the 100 patients who were not treated by operation. Two patients (1 with a chronic duodenal ulcer and 1 with a chronic gastric ulcer) were moribund on admission and despite massive blood transfusion died before they could be brought to operation. Three deaths occurred in patients with a chronic duodenal ulcer in all of whom other severe coexistent medical conditions were present. None of these patients died from exsanguination; in fact, there was considerable evidence that the bleeding had stopped. One patient died of a coronary thrombosis and 2 of congestive heart failure. It is unlikely that these patients would have done any better had they been subjected to surgery but, of course, their inclusion in the non-operative group biases the figures slightly. The overall mortality is 7 out of 181 'benign' cases (4 per cent) and the total mortality in all the patients is 15 out of 200 cases (7·5 per cent).

Influence of Drugs.—All the patients were closely questioned about the ingestion of aspirin or steroid-containing compounds. There was a highly significant difference between the general group of patients in whom 12 per cent gave a history of aspirin ingestion and the patients who had an erosive gastritis or an acute gastric ulcer in whom 50 per cent gave such a history. Certain patients appeared to have developed a chronic duodenal or gastric ulcer whilst on steroids, but the significance of steroid ingestion was impossible to evaluate.

Blood Transfusion.—There was a significantly greater amount of blood given to the patients requiring operation, as one would expect from the policy of selection. In the patients with a duodenal ulcer, those who came to operation required a mean of 6·7 pints of blood, whilst those who were treated non-operatively required a mean of 4·6 pints. This difference was even more marked in the patients with gastric ulcer, of whom those who were treated operatively required a mean of 9·2 pints of blood whilst those who were treated without operation required a mean of 2·5 pints of blood.

DISCUSSION

Haemorrhage from the upper gastro-intestinal tract is a common cause of hospital admission and is responsible for 45 per cent of deaths in patients with a peptic ulcer (Weinberg, 1961; Read, Huebl, and Thal, 1965). There are many causes of bleeding from the upper gastro-intestinal tract but the commonest cause—a peptic ulcer—should be readily treated and have a good prognosis. In the present series of 200 consecutive patients with bleeding from the upper gastro-intestinal tract, 67·5 per cent had a chronic peptic ulcer (either gastric or duodenal or anastomotic) and a further 16·5 per cent had erosive gastritis or an acute ulcer. These figures compare with those of Zollinger and Nick (1970) in which 61 per cent had a peptic ulcer and 8 per cent had gastritis and of Halmagyi (1970) in which 59 per cent had a chronic ulcer and 7·5 per cent had erosions.

The common method of hospital care for patients with an upper gastro-intestinal tract haemorrhage is for them to be admitted under the care of a physician and for the surgeon to be involved subsequently. This policy presumably evolved to allow the physician to select the correct patients for surgery. Read and others (1965) stated that only 31 per cent of a randomly selected group of patients with upper gastro-intestinal haemorrhage responded satisfactorily to medical measures alone and that this group had a significantly higher mortality-rate of 15·4 per cent compared with 9·8 per cent in a group which was treated by immediate surgery. Enquist, Karlson, Dennis, Fierst, and Shaftan (1965), who treated three groups, one by immediate operation, one by selection for operation, and one by no operation, found the lowest mortality (14·1 per cent) in the selected operation group. This supports a policy of selection, and we believe that our criteria for selection have been justified by the results in the present series.

Having accepted the desirability of a selective policy, the question arises of whether more may be lost by delaying surgery in the common group of haematemeses, viz., peptic ulcer, than is gained from the increased diagnostic sophistication of the physician in the rare group. It should be recalled that Jones in 1969 found that only 5 per cent of cases of upper gastro-intestinal tract haemorrhage were due to rare causes. A diagnosis can usually be made with confidence when a detailed history has been taken, a physical examination has been made, and the necessary investigations, including contrast radiology, have been carried out. We have found this latter investigation most useful, in contrast to Herrington (1964) and Read and others (1965), who concluded that a barium meal interfered with the comfort and treatment of dangerously ill patients and was a poor diagnostic aid.

Schiller, Truelove, and Williams (1970) point out that despite improved diagnosis, treatment, and operative technique over the past 15 years there has been little improvement in the mortality for upper gastro-intestinal haemorrhage. This is probably due to failure to bring all the patients who will require surgical treatment to operation at a sufficiently early stage. A more ready recourse to operation can be achieved by admitting the patients to a surgical ward, for if the bleeding has to be stopped by operation it is advisable for the surgeon to have the patient under his direct supervision so that operation can be carried out at the optimal time with due urgency. In our series, 45 per cent of the patients required surgical treatment and no less than 26 per cent of these had their operation within 24 hours of admission. We agree with Schiller and others (1970), who advocated a more aggressive approach to upper gastro-intestinal tract bleeding, and believe that this has been achieved by admitting the patients to a surgical ward directly.

A wide age range was present in both the patients undergoing operation and those treated by medical measures alone, and there is no significant difference between the two groups. This would tend to support Northfield (1971) in his view that continuing or repeated bleeding is not necessarily more common in the elderly. Patients presenting with erosive gastritis or acute gastric ulcer were slightly younger than the other patients, but of greater significance was the increased incidence of aspirin ingestion in the former patients. This observation agrees well with previous reports (Goulston and Coome, 1968; Valman, Parry, and Goghill, 1968; Blane and Fryers, 1970; Langman, 1970a, b).

Gastrectomy for the patient with a peptic ulcer without haemorrhage has an acceptable mortality, but when the gastrectomy is for a bleeding ulcer this figure rises to an unacceptable level, such as the 15 per cent reported by Ward-McQuaid, Pease, Smith, and Twort (1960) and the 12 per cent observed by one of us (R. T. G.) in an unpublished series of 40 gastrectomies for bleeding peptic ulcer. Vagotomy and pyloroplasty with undersewing of the bleeding point as an alternative to gastrectomy in the emergency treatment of bleeding duodenal ulcer was suggested by Smith and Farris (1958) and has received support from other observers (Dorton, 1961; Carruthers, Giles, Clark, and Goligher, 1967; Schiller and others, 1970; Boulos, Harris, Wyllie, and Clark, 1971; Bradley and Pollock, 1972). These workers have all reported a reduced mortality without a significant increase in re-bleeding, and our findings would tend to support this.

Treatment of gastric ulcers by a conservative operation is still controversial although it has its advocates (Burge, 1964; Hendry and Bahram, 1965), but little has been written about the treatment of a bleeding gastric ulcer by these means although Read and others (1965) expressed their approval. We have treated gastric ulcers with a diameter of 2 cm. or less by this method with uniformly good results and we consider that even larger gastric ulcers may also be suitable. Acute gastric erosions or gastritis in general respond well to medical treatment, and only 5 out of 33 of our cases required surgery. This agrees with the findings of Schiller and others (1970). Our experience of surgery in this group is too small for any firm conclusion to be drawn, although of the 4 cases treated by conservative operation, 1 continued to bleed and eventually died of blood-loss. One other patient had satisfactory control of the bleeding by the undersewing of four separate acute ulcers. This indicates the principal difficulty in this group, namely the potential multiplicity of ulcers, and clearly it is possible to overlook a significant bleeding ulcer. It has proved possible to carry out a 'conservative operation' in 5 out of 7 anastomotic ulcers with control of the bleeding in all 5 patients.

A conservative operation was performed in 61 patients while resection was carried in only 18 patients (13 of these were for gastric ulcers greater than 2 cm.). Of the 61 conservative operations with suture of the ulcer, there were only 3 patients in whom there was failure to control bleeding. One of these was a patient with erosive gastritis and must be considered to have been a bad selection, 1 was a patient with a large duodenal ulcer which re-bled 8 days after operation, and the other was a patient with a smaller duodenal ulcer. The 2 patients with duodenal ulcers required reoperation at which the bleeding was successfully controlled. There was no re-bleeding after suture of a gastric ulcer with vagotomy and pyloroplasty and we feel that perhaps ulcers greater than 2 cm. could be treated by this means. The only death after a conservative operation was the patient with erosive gastritis who continued to bleed.

It seems that in the case of duodenal ulcers, anastomotic ulcers, and gastric ulcers with a diameter of less than 2 cm. vagotomy, pyloroplasty, and suture of the ulcer comprise a safe and efficacious operation with a low mortality and little danger of re-bleeding. Treatment of solitary acute gastric ulcers by this method appears to be equally satisfactory, but diffuse erosive gastritis not responding to medical measures still requires gastric resection.

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GASTRODUODENAL ULCERATION AND HAEMORRHAGE OF NEUROGENIC ORIGIN

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SUMMARY

The incidence, clinical experience, and management of gastroduodenal ulceration following intracranial disease over a 5-year period at the Royal Children's Hospital, Melbourne, are reported.

Usually the children present with a decline in the conscious state and falling blood-pressure. The maximum danger period is the first 7–10 days after an acute episode of brain-stem compression. The gastro-intestinal bleeding may not be overt, but the haemoglobin falls steadily. Small premonitory haemorrhages may herald torrential blood-loss. Early vagotomy and pyloroplasty with oversewing of the ulcer provide the best operation for these children, and there have been no major postoperative gastrointestinal symptoms in a short-term follow-up.

IT has been known for many years that there is an association between ulceration of the stomach and duodenum and brain disease. This is not a common clinical problem, but it has been noted to be increasing over the past 10 years, possibly due to the increased survival of neurosurgical patients.

The terminology is confusing, as the pathological mechanisms are unknown in spite of much experimental work. 'Stress ulcer' and 'Cushing's ulcer' are common terms, and examination of the literature shows that there is confusion between multiple small ulcers, gastric softening, and the punched-out single large ulcer in the duodenum, which is referred to here as a 'neurogenic' ulcer.

Clinical recognition of gastroduodenal bleeding or ulceration can be difficult, particularly in the unconscious patient. The risk of the use of steroids (knowing their possible role in ulceration) is ever present.

Treatment is controversial; many workers advocate a non-operative approach, whereas others insist on radical excision.

This paper attempts to reappraise the clinical situation by giving a short historical review, presenting some new cases, and examining clinical experience.

HISTORICAL REVIEW

At a time when gastroduodenal ulceration was almost unknown as a clinical entity to physicians and pathologists, Schiff (1867) wrote: 'In the study of human pathology it has long been recognized that certain diseases of the brain and especially disturbances of the base are associated with particular disorganization of the mucosa of the stomach characterized by haemorrhagic spots and partial softening, and most of these observations have been made on infants.' Schiff quotes other writers on this subject, but he seems to have been unaware of the significant contribution of John Hunter some 100 years before. Hunter, in 1772, had already noted a connexion between head injury and 'gastromalacia'. Rokitansky in 1841 (cited by Cushing, 1932) described this association and mentioned hyperacidity as a probable cause of the gastric lesions.

Cushing made a further contribution to this subject in his Balfour lecture of 1932 when he described a series of patients some of whom were found at autopsy to have gastromalacia similar to that described by Hunter. Other cases in this series had gastric or oesophageal erosions or ulceration.

Meanwhile Curling in 1842 had described acute lesions of the duodenum occurring as a complication of severe burns in young people. He described 4 personal cases and collected a further 8 from the literature in whom death occurred as a result of massive haemorrhage from an ulcer situated on the posterior wall of the first or second part of the duodenum. These ulcers measured up to 2 cm. in diameter. According to the clinical records of the Royal Children's Hospital, Melbourne, the gastroduodenal lesions that have occurred in acute intracranial disorders corresponded more closely to Curling's description than that of Cushing and previous writers, and therefore they are currently referred to as 'neurogenic' ulcers.

In the subsequent literature dealing with the relationship between lesions of the nervous system and gastroduodenal ulceration or haemorrhage (Schiff, 1867; Cushing, 1932; Heslop, 1938; Watts and Clark, 1969) three facts emerge:—

1. This is an association which occurs especially in infancy and childhood.
2. It is a complication of acute rather than of chronic lesions of the brain, often occurring after operation.

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3. It is not related to any single brain pathology, having been described as a complication of tumour, trauma, infection, haemorrhage, or ischaemia, or of the immediate postoperative period following craniotomy for any of these lesions. No particular region of the brain can be shown to be responsible.

Table I.—INCIDENCE OF GASTRO-INTESTINAL LESIONS RELATED TO THE SITE OF THE BRAIN TUMOUR AT AUTOPSY (1958–68)

SITE OF TUMOUR	NO. OF GASTRO-INTESTINAL LESIONS	TOTAL NO. OF CASES	PERCENTAGE INCIDENCE
Brain-stem, thalamus	3	8	37·5
Supratentorial	3	15	20
Infratentorial	3	29	10
Total	9	52	

Physiologists from the late nineteenth century onwards have demonstrated that erosions and ulcers of the stomach can be produced by lesions of the hypothalamus and brain-stem. More recent work (Beattie and Sheehan, 1934; Heslop, 1938; French, Porter, Van Amerongen, and Raney, 1952; Porter, Movius, and French, 1953; Feldman, Burnbaum, and Behar, 1961; Leonard, Long, Thomas, Nicoloff, and Wangensteen, 1963) suggests that the two most important systems are the anterior and posterior hypothalamus and their connexions with vagal nuclei in the medulla. Gastroduodenal lesions occur as a result of stimulation of the anterior hypothalamus or of ablation of the posterior hypothalamus. This experimental work, however, has added little to the knowledge of the cause of gastroduodenal ulceration, as no relationship to the clinical situation has been found.

CLINICAL EXPERIENCE

During a 5-year period from 1965 to 1970 at the Royal Children's Hospital, Melbourne, approximately 100 tumours and 1600 head injuries were admitted.

Table I shows the incidence of gastro-intestinal lesions related to the tumour site at autopsy in a series of children with tumours. Note the high incidence (37·5 per cent) of lesions in the brain-stem and thalamus.

Table II.—DETAILS OF CHILDREN WITH CEREBRAL LESIONS AND CLINICAL HAEMORRHAGE FROM THE GASTRO-INTESTINAL TRACT IN THE PRESENT SERIES, 1965–1970

CASE NO.	AGE	SITE OF CEREBRAL LESION	SITE OF HAEMORRHAGE	STEROIDS	TREATMENT	RESULT	FOLLOW-UP
1	10 yr.	Posterior fossa tumour	Stomach	–	Vagotomy and drainage	Satisfactory	18 mth
2	14 yr.	Posterior fossa tumour	Duodenum	–	Oversewing of ulcer Partial gastrectomy and gastroenterostomy Vagotomy	Death due to further bleeding	
3	3 yr.	Posterior fossa tumour	Unknown	–	Non-operative	Satisfactory	Death from recurrence at 2 yr
4	3½ yr.	Posterior fossa tumour	Unknown	+	Non-operative	Satisfactory	Death from recurrence at 18 mth.
5	3½ yr.	Posterior fossa tumour	Duodenum	–	Vagotomy and drainage	Satisfactory	Death from septicaemia at 10 mth.
6	5 yr.	Posterior fossa tumour	Duodenum	–	Vagotomy and drainage	Satisfactory	2½ yr
7	9 yr.	Subdural haematoma	Duodenum	Unknown	Vagotomy and drainage	Satisfactory	2 yr.
8	13 yr.	Subdural haematoma	Duodenum	Unknown	Vagotomy and drainage	Satisfactory	2 yr
9	3½ yr	Posterior fossa tumour	Oesophagus Stomach	–	Non-operative	Death; bleeding in terminal stages	
10	5 yr. 10 mth.	Multiple injuries, right temporal injury, cerebral oedema	Duodenum	+	Vagotomy and drainage	Satisfactory	2½ yr.
11	12 yr	Posterior fossa tumour	Unknown	+	Non-operative	Satisfactory	1½ yr.
12	4 yr.	Posterior fossa tumour	Unknown	+	Non-operative	Satisfactory	Death from pulmonary embolus at 6 mth.
13	3½ yr.	Major head injury with cerebral oedema	Duodenum	+	Vagotomy and drainage Partial gastrectomy	Satisfactory	1 yr.
14	9 yr	Subdural haematoma	Unknown	Unknown	Non-operative	Satisfactory	2 yr.
15	12 yr.	Multiple injuries, right frontal injury	Unknown	+	Non-operative	Satisfactory	2 yr
16	7 yr.	Astrocytoma of lateral wall of third ventricle	Duodenum	+	Non-operative	Satisfactory	Death 3 weeks after diagnosis from effect of tumour

Clinical experience with this form of gastro-intestinal haemorrhage comprises 16 patients, including 10 with cerebral tumours, 4 with acute haematomas, and 2 patients with massive cerebral oedema (*Table II*). In every child there was acute and severe embarrassment of brain-stem function at some stage, and this was sufficient in several cases to cause respiratory arrest for periods of up to 30 minutes.

Every child who needed operation had major blood-loss, which in some cases amounted to almost complete exsanguination. The time interval between injury and haemorrhage varied from 48 hours to 10 days. There was no constant relationship between the state of the patient and the time of the haemorrhage.

CASE REPORTS

Case 1.—A 10-year-old boy presented with a 2-month history of back pain, ataxia, and headache. On examination he showed bilateral papilloedema, nystagmus on looking to the left, and poor co-ordination on both sides. The gait was broad-based and Romberg's sign was positive. Investigation confirmed the presence of a posterior fossa tumour, and at operation a large cystic and solid astrocytoma was removed from the right cerebellar hemisphere. It had spread to the left side and was continuous with the ependyma of the fourth ventricle.

Postoperatively the patient was slow to regain normal consciousness, and he required daily lumbar puncture to reduce his intracranial pressure. He was improving when on the sixth postoperative day he suddenly had a haematemesis, followed by melaena stools. The haemoglobin fell from 13·3 to 9 g. per cent over 12 hours.

Laparotomy was performed within 24 hours of the start of bleeding, but no localized ulcer was found. The haemorrhage was coming from multiple gastric surface ulcers. Vagotomy and pyloroplasty was performed, and the bleeding stopped. His subsequent course was of continued slow improvement, further lumbar punctures being necessary for the relief of high intracranial pressure. He was finally discharged 8 weeks after admission and 6 weeks after his haemorrhage.

Case 5.—A boy of 3½ years presented with a history of vomiting for 3 months, clumsiness for 2 months, and increasing ataxia. On examination he was a well-nourished boy with a head tilt to the right, nystagmus on gaze to left, wide-based gait, and bilateral intention tremor. Bilateral papilloedema developed in hospital.

Investigation confirmed the presence of a posterior fossa tumour and a ventriculo-atrial shunt was performed. A preoperative dose of vincristine per 2 mg. m.^{2} was given. Two days later a medulloblastoma was removed from the fourth ventricle. During the removal of the last portions of the tumour from the floor of the fourth ventricle, bradycardia and then respiratory arrest occurred. Both these continued for a period of 30 minutes.

Postoperative recovery was uneventful, although the patient had a right hemiparesis and right abducens palsy at this stage. He commenced nasogastric feeding the morning after operation. On the third postoperative day he developed a tachycardia of 130–160 per minute, which was followed over several hours by pallor and a fall of blood-pressure to 70 mm. Hg and of haemoglobin to 5 g. per cent. There was no external evidence of blood-loss, no blood in the gastric aspirate, no melaena, and no abdominal distension or tenderness.

Anaemia due to infection was suspected, but a normal white-blood count appeared to exclude this. A blood transfusion was given and the patient responded satisfactorily. Twelve hours later his pulse again rose, the blood-pressure fell, and the haemoglobin was 6 g. per cent; more blood was given. Twenty-four hours later he had his first melaena and some blood was seen in the gastric aspirate. Further large melaenas occurred and two transfusions of fresh blood were given. Bleeding continued, with further melaena stools and fresh blood aspirated from the nasogastric tube. Rapid transfusion just maintained a peripheral pulse in a pale unconscious child, and a moribund patient was presented to the surgeon.

Laparotomy revealed the whole gut to be distended with blood. On opening the duodenum the gastroduodenal artery pulsated in the base of a large posterior duodenal ulcer. The vessel was underrun with a silk suture, and routine vagotomy and pyloroplasty were performed. Two and a half litres of blood were transfused in the operative and immediate postoperative periods. The haemoglobin was 13·2 g. per cent on the day after operation. No further fresh bleeding occurred and the boy made an uneventful recovery from this operation. Total blood replacement over the whole period was 4 litres.

The patient was discharged well after radiotherapy and cytotoxic therapy 2 months after admission. He was readmitted 10 months later with an abdominal wound infection, which was drained, but he developed septicaemia and died. At his death there was a recurrence of the tumour, but no clinical evidence of further ulceration. Autopsy showed a scar in the posterior wall of the first part of the duodenum.

Case 9.—This child first presented to the Royal Children's Hospital, Melbourne, when aged 3½ years, with vomiting, headache, and neck stiffness. Lumbar puncture revealed blood-stained cerebrospinal fluid, but investigations failed to find a cause for this. After recurrent subarachnoid haemorrhages he had a posterior fossa exploration, which showed the presence of blood-clot only, followed by a second operation 1 month later which revealed a medulloblastoma on the floor of the fourth ventricle. His course during this time was stormy, but after the second operation he began to improve and was finally discharged from hospital with residual right facial weakness and mild spasticity of the legs. One year later he presented with sudden onset of drowsiness, slurred speech, ataxia, and left-sided fits. Investigations revealed a right subdural collection which was aspirated and he made a good recovery. A ventriculo-atrial shunt was performed for developing hydrocephalus 3 years after his presentation. A shunt infection occurred and the shunt had to be removed. Two months later he was readmitted following haematemesis, from which he died 3 years and 2 months after his initial presentation. At autopsy there were multiple superficial ulcers of the oesophagus and stomach with residual tumour around the operation site and down the spinal cord. There was recent cerebral and spinal cord haemorrhage.

These 3 cases illustrate the full range of clinical manifestations in the series. The first boy (*Case* 1) presented with bleeding while he was clinically improving, having had complete removal of his tumour, 1 week after operation. The second boy (*Case* 5) presented early in the postoperative period. In this child the severity of the bleeding was not recognized early, and a severely shocked child was presented for surgery. The third boy (*Case* 9) bled as a terminal episode with recurrent tumour 3 years after surgery.

Eight patients came to operation (*Table II*). Of these, 7 had a large penetrating ulcer on the posterior aspect of the first or second part of the duodenum, eroding the gastroduodenal artery. The only patient in the series who died following operation for gastroduodenal bleeding had three operations (*Table II*, *Case* 2). On the first occasion a simple suturing of the ulcer was performed. Because of recurrent bleeding this was followed successively by partial gastrectomy, and finally vagotomy 1 month after the initial haemorrhage.

One child who had vagotomy and pyloroplasty (*Table II*, *Case* 13) had further ulceration for two reasons: (1) severe head trauma with cerebral oedema; (2) large doses of steroids. Although vagotomy and pyloroplasty controlled the gastro-intestinal haemorrhage he continued to be unwell, and after 9 days there was marked abdominal distension with evidence of small-bowel obstruction on radiography. On re-exploration there were subphrenic abscesses on both sides, and the suture line of the pyloroplasty had broken down. A Polya-type gastrectomy was performed but sepsis continued and the suture line parted, discharging fluid through the abdominal wound. At the third operation this suture line was reconstituted with a few wide sutures and the area was drained. As the child improved, the wound slowly healed. The failure of vagotomy and drainage was probably due to a combination of sepsis and large doses of steroids.

Overall the methods of treatment may be considered in three groups:—

Group I (8 patients): Non-operative treatment.

Group II (5 patients): Conservative régime followed by operation.

Group III (3 patients): Early operation.

Of the 8 patients in group I, 2 patients were considered to be of hopeless prognosis owing to the nature of the cerebral lesion (*Table II*, *Cases* 9 and 16), while the remainder had small haemorrhages which at no time produced major changes in their haemodynamic state.

The children in the remaining two groups had major blood-loss, and in all the cases in group II conservative treatment with alkalis, cholinergic drugs, and carbenoxolone for several days failed to prevent massive recurrent haemorrhage. This is hardly surprising in view of the operative findings of large penetrating ulcer craters with the erosion of a major vessel. This finding is the main reason for the bias towards early surgery in these children. An ulcer which erodes a major vessel will not heal, and early operation avoids the complications caused by severe blood-loss and multiple blood transfusions.

Most gastro-enterological surgeons now favour vagotomy and some form of gastric drainage (usually pyloroplasty) as the treatment for duodenal ulcer; therefore this method was selected for the children who required surgery. As only 1 of these patients had either recurrent bleeding or gastro-intestinal symptoms (*Table II*, *Case* 13) during ensuing periods of up to 2½ years, the selection of this method appears justified. In addition, its simplicity when compared with the alternative procedure of gastrectomy seems desirable in the very sick patient. It may also avoid the long-term complications of gastric resection in childhood.

DISCUSSION

In previous papers much emphasis has been placed on experimental work, stimulating or destroying areas of the hypothalamus, or measuring the acidity of gastric juice, but too little on the relationship between the two.

There are two postulated physiological pathways by which the brain can influence gastric function to produce ulceration: (1) via the pituitary–adrenal axis, by corticosteroid release; (2) via the vagus, stimulating (*a*) parietal-cell activity or (*b*) gastrin release.

Some earlier workers implicate the pituitary–adrenal axis. Porter, Movius, and French (1953) showed that stimulation of the posterior hypothalamus produced a later increase in gastric secretion which was not abolished by vagotomy or cervical chordotomy but was abolished by adrenalectomy which he attributed to a humoral pathway via adrenocorticotrophic hormone and the adrenal cortex. However, the importance and even the presence of this pathway have since been in doubt (Davenport, 1966), and cannot be used at this stage to explain gastroduodenal ulceration.

It is simple to postulate that vagal overactivity occurs for two reasons:—

1. Although there is a diversity of cerebral lesions which can produce gastric or duodenal ulceration, the common factor is usually cerebral oedema, and its impact is predominantly on the hypothalamus and brain-stem, producing distortion or displacement. This indirect effect can lead to thrombosis of vessels, oedema, and petechial haemorrhage in the area. The vagal nuclei in the brain-stem are affected, and vagal stimulation, or lack of inhibition, occurs.
2. The success of vagotomy and drainage as a treatment in these patients points to vagal overactivity being a factor.

The crux of the matter seems to be whether there is hyperacidity associated with ulceration or ulceration due to some other mechanism. The literature is divided on this point (Feldman and others, 1961, Watts and Clark, 1969). Rokitansky, as early as 1841, suggested that uninhibited action of the vagus was the most likely cause of the ulceration owing to 'extreme acidification of the gastric juice'.

If gastric hyperacidity is not implicated there must be either a vascular effect or a local change in the mucus secretion to account for ulceration. These latter two changes would explain the common finding of multiple petechial spots or superficial ulcers in the gastro-intestinal tract after acute cerebral disorders, but it is hard to see how they may cause a single 'punched-out' ulcer in the duodenum.

Steroids have long been implicated as a major factor in the formation of gastric or duodenal ulcers in neurosurgical patients. They are known to change the constitution of the gastric mucus and to delay the normal regeneration of gastro-intestinal mucosal cells, which are continuously being lost, but exogenous steroids cannot be the only factor. Six patients in the present series did not receive steroids.

It is important to note that the patients reported in this series were all seriously ill, and yet with early operation the prognosis was good. Many of the patients were unconscious or semiconscious, and the first indication of the haemorrhage was a noticeable decline in the state of consciousness which, of itself, seemed to point to some intracranial complication. In every case, however, the decline in consciousness was accompanied by a significant fall in the blood-pressure, which is unusual in acute cerebral disturbance. A falling haemoglobin level established the fact that bleeding was occurring. The initial warning haemorrhage was followed by further episodes, and in 7 patients catastrophic bleeding occurred with a severe fall in blood-pressure, sometimes within a few hours of the onset of symptoms. In earlier patients in the series surgery was often postponed until this stage, and the operation was performed on a severely shocked patient, with all its added hazards. The reason for such delay is obvious, as the patients were in the early postoperative phase after intracranial surgery. However, early operation was followed in all cases by a good result. In the 2 patients who required more than one operation, one case was diagnosed late and had four ulcers (*Case* 13, *Table II*), and the other was so ill that the shortest procedure possible was chosen (*Case* 2, *Table II*) but further bleeding occurred and the patient died.

Early treatment depends on an awareness of gastro-intestinal haemorrhage as a complication of brain disease, and very close observation from the time that warning blood-loss occurs. Blood must be available at this time to avoid adding hypovolaemic shock in an already seriously ill patient. A continuing fall in the haemoglobin level and continued need for blood replacement are indications for operation. In children the operation of choice is vagotomy and gastric pyloroplasty drainage with direct control of bleeding points where possible.

Acknowledgements.—Part of this work was supported by a grant from the Research Foundation of the Royal Children's Hospital, Melbourne, to whom I am grateful. My thanks are due to the neurosurgeons who allowed me to report these cases and to the surgeons of the hospital who performed the surgery.

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CARCINOMA OF THE PROSTATE

A RETROSPECTIVE ANALYSIS OF CONVENTIONAL MANAGEMENT IN 110 CASES

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Summary

This paper reports a retrospective analysis of the results of conventional management of prostatic carcinoma in 110 patients. The 5-year probability survival was 23 per cent. A correct initial diagnosis was made in only 53 per cent of the patients. Indices of prostatic carcinoma as opposed to benign prostatic hypertrophy would appear to be a higher age-group, the occurrence of retention without preceding prostatism, and obstructive uropathy disproportionately severe in relation to symptoms. A normal serum prostatic acid phosphatase does not preclude the diagnosis of carcinoma of the prostate.

Treatment with oestrogenic hormones produced regression of the primary neoplasm in 60 per cent of the patients but rarely affected metastatic lesions. The principal cause of death was not metastatic disease but lower urinary-tract obstruction or operations for its relief.

In England and Wales in 1968, 3390 men died from prostatic cancer and 4228 from accidents (Registrar General's statistics). The accident figures regularly provoke considerable public concern, whereas the comparable and more miserable mortality from prostatic carcinoma is fatalistically accepted, largely because the disease affects older men whose life span is already limited. The established views on the anatomy of the prostate, on the pathogenesis of prostatic carcinoma, and on the efficacy of hormonal treatment of this disease have been seriously questioned (Herbst, 1941, 1942; Huggins and Hodges, 1941; Huggins, Stevens, and Hodges, 1941; Nesbit and Baum, 1951; Franks, 1956; McNeal, 1965, 1968, 1969), with the result that the average clinician treating cancer of the prostate finds the situation confusing. In an attempt to gain an overall view of this disease and to assess the results of its conventional management we have reviewed the clinical data of 110 patients with cancer of the prostate attending a large regional hospital. While retrospective studies must always be interpreted with care, in the absence of information and guidance from controlled prospective clinical surveys we feel that a comprehensive clinical review may give perspective to the problem of prostatic cancer.

MATERIAL AND METHODS

The case records of 110 patients who had attended St. Woolos and the Royal Gwent Hospitals, Newport, between 1960 and 1969 inclusive were analysed. Only adequately documented patients were included. Complete follow-up was obtained in 86 per cent of patients.

RESULTS

Age.—Most of the patients (91 per cent) were aged between 60 and 80 years, with the peak incidence in the eighth decade (*Fig.* 1). Only 1 patient was less than 50 years old and 10 were aged under 60 years.

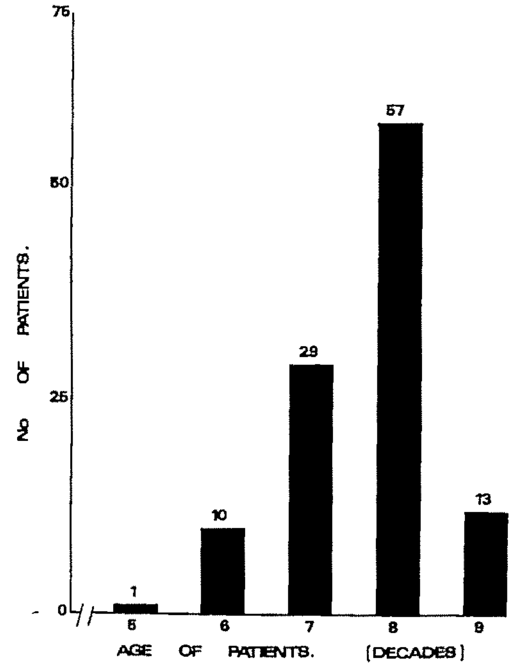

FIG. 1.—The age distribution in 110 patients with prostatic carcinoma.

Clinical Features.—The reasons for clinical presentation are shown in *Table I*. The commonest cause of presentation was retention of urine (acute or chronic) and it was interesting that in many instances retention was not preceded by significant symptoms of prostatism. At presentation, 34 patients (31 per cent) had metastatic disease (*Table II*) and of these, 17 (15 per cent) had symptoms due solely to metastases. Symptomless bone secondaries were present in only 2 patients. The bones of the rib-cage, upper limbs, and skull were affected by metastases only in the presence of advanced carcinomatosis. In 98 patients (90 per cent) symptoms had been present for under 1 year and 38 of those presenting with lower urinary-tract obstruction had been previously symptom-free.

Table I—REASONS FOR CLINICAL PRESENTATION

Reason for Presentation		*No. of Patients*
Urinary retention		63
Acute retention with prostatism	12	
Acute retention without prostatism	38	
Chronic retention with overflow incontinence	13	
Prostatism (without frank haematuria)		26
Metastases (local or general)		17
Haematuria		3
Rectal pain		1
Total		110

Investigations.—Severe anaemia was present in only 2 patients and both were moribund at presentation (*Table III*). The blood-urea was elevated in 44 per cent of patients and 8 patients were sub-uraemic at presentation. The serum prostatic acid phosphatase (S.A.P.) was elevated in 31 patients (30 per cent). Microscopic haematuria was common. Although intravenous pyelograms were performed in only 52 patients (47 per cent), in a third of these there was evidence of upper urinary-tract abnormality —hydro-ureter, hydronephrosis, or a non-functioning kidney.

Table II.—SITES OF METASTATIC SPREAD IN 34 PATIENTS AT PRESENTATION

Metastatic Involvement		*No of Patients*
General skeletal carcinomatosis		16
Solitary osseous metastases		13
Lumbosacral spine	8	
Pelvis	4	
Femoral head	1	
Lateral pelvic walls, with oedema of the legs		4
Rectovesical fistula		1
Total		34

Table III.—SUMMARY OF THE CLINICAL INVESTIGATIONS AT PRESENTATION

INVESTIGATION	FINDINGS	NO. OF PATIENTS
Haemoglobin	<50 per cent 50–70 per cent Normal No record	2 10 90 8
Blood-urea	>100 mg. per cent 40–100 mg. per cent Normal No record	8 33 53 16
Erythrocyte-sedimentation rate (Westergren)	>50 mm. per hr. 21–50 mm. per hr Normal No record	15 20 32 43
Serum prostatic acid phosphatase*	>10 units per ml 4–10 units per ml Normal No record	16 15 71 8
Midstream specimen of urine	Pyuria alone Microscopic haematuria alone Pyuria and microscopic haematuria Normal No record	13 11 44 25 17
Intravenous pyelography	Prostatic filling defect Upper urinary-tract abnormality Normal No record	8 21 33 48

* Assayed before the commencement of oestrogenic hormone therapy (normal <4 units per ml.).

Diagnosis and Management.—Even with the help of laboratory and radiological investigations, a correct initial diagnosis was made in only 58 patients (53 per cent; *Table IV*). Forty-four patients were diagnosed as having benign prostatic hypertrophy and in these cases the correct diagnosis became apparent only when difficulty was experienced at prostatectomy or when material became available for histological examination.

All the patients except the 2 who were moribund at presentation received oestrogenic hormone therapy, and in 40 (36 per cent) this was the sole method of treatment. Operative procedures were carried out in 71 patients (64 per cent; *Table V*), mostly to relieve urinary obstruction. No patient underwent pituitary or adrenal ablation.

Table IV.—METHODS OF FINAL DIAGNOSIS OF PROSTATIC CARCINOMA

INITIAL DIAGNOSIS	NO. OF PATIENTS	METHOD OF ESTABLISHMENT OF FINAL DIAGNOSIS	NO OF PATIENTS
Benign prostatic hypertrophy	44	Histology following 'Prostatectomy'	31
		Transurethral resection	13
Fibrous prostate	3	Histology following transurethral resection	3
Prostatic calculi	3	Histology following transurethral resection	3
Urethral stricture	1	Histology following transurethral resection	1
Vesical neoplasm	1	Histology following transurethral resection	1
Prostatic carcinoma	58	Clinically (per rectum; S.A.P.; osseous metastases on radiograph)	37
		Elevated S.A.P.	8
		Osseous metastases on radiograph	2
		Histology following transurethral resection	9
		Autopsy	2

Table V.—OPERATIVE PROCEDURES PERFORMED IN 71 PATIENTS

Operation	*No. of Patients*
Prostatectomy	28
Attempted prostatectomy	3
Transurethral resection	30
Suprapubic cystostomy	7
Orchidectomy	3
Total	71

Histological Diagnosis.—Material for histological study was obtained in 66 patients (60 per cent); the neoplasm was poorly differentiated in 23 cases and well differentiated in 33. Carcinoma of the prostate coexisted with benign prostatic hypertrophy in 10 patients (9 per cent); in 7 cases the neoplasm represented a focal lesion in an adenomatous area, whereas in the remaining 3 cases it was situated peripherally and was incompletely removed at 'prostatectomy'.

Response to Oestrogenic Therapy.—The response of the primary tumour to oestrogens could be assessed in 53 patients who received no treatment other than these hormones. In 30 patients (60 per cent) there was objective evidence of regression of the primary lesion, in that spontaneous micturition was established and the prostate became softer. Conversely, in 23 patients there was clear evidence of progression of the disease while on oestrogen therapy; in 13 patients within 1 year, and in a further 8 within 2 years. These patients developed lower urinary-tract obstruction with evidence of local extension of the primary lesion.

The response of the primary tumour to oestrogens did not appear to be related to the level of the S.A.P. at presentation. Thus, regression of the primary lesion occurred in 16 of 29 patients with a normal S.A.P. and in 11 of 18 patients with an elevated S.A.P. During the first 2 years after presentation there was no difference in the survival of patients with normal or elevated levels of S.A.P. at presentation.

The response of metastatic lesions to oestrogens could be assessed in 28 patients. There was objective evidence of regression in 2 patients, and in a further 2 cases the disease appeared to have been arrested. In contrast, 24 patients appeared to derive no, or at best minimal, benefit from oestrogenic hormone therapy, for new metastatic lesions appeared within 3–12 months.

Table VI.—CAUSES OF DEATH IN 81 PATIENTS

Cause of Death	*No. of Patients*	
Prostatic carcinoma		47
Carcinomatosis	19	
Uraemia due to obstructive uropathy	15	
Hospital deaths directly attributed to post-operative complications (e.g., shock, secondary haemorrhage, sepsis, anaesthesia)	13	
Causes unrelated to prostatic carcinoma		26
Cardiovascular disease (myocardial infarction, pulmonary embolus, cerebrovascular accident)	15	
Unknown		8
Total		81

Table VII.—CAUSES OF HOSPITAL DEATHS IN 26 OF 71 PATIENTS WHO WERE SUBJECTED TO SURGERY

Cause of Death	*No. of Patients*	
Postoperative complications (excluding cardiovascular disease)		13
Following prostatectomy	7	
Following transurethral resection	6	
Cardiovascular complications		8
Following prostatectomy	4	
Following transurethral resection	3	
Following suprapubic cystostomy	1	
Uraemia following suprapubic cystostomy		3
Carcinomatosis following suprapubic cystostomy		2
Total		26

Fate of the Patients.—Complete follow-up data were available for 95 patients (86 per cent), of whom 14 were alive and 81 dead (*Table VI*). Most of the deaths occurred within 1 year of presentation and no patient with metastases at presentation was alive 3 years later. The overall 5-year probability survival was 23 per cent. Relatively few patients died from carcinomatosis. Thus, although 34 patients had evidence of metastatic disease at presentation and a further 11 developed osseous metastases during the course of treatment with oestrogens, only 19 (16 per cent) actually died from the effects of distant disease. In contrast, 28 patients died from local disease, i.e., lower urinary-tract obstruction or operations for its relief. Of the 26 patients who died from causes unrelated to their carcinoma, 15 died from cardiovascular disease.

There was a crude correlation between the level of the S.A.P. at presentation and survival. Thus, no patient with an elevated S.A.P. at presentation was alive 5 years later, whereas all 5-year survivors had a normal S.A.P. at presentation. This is in keeping with our findings that elevated levels of S.A.P. were found in 30 per cent of patients with poorly differentiated primary lesions but in only 10 per cent of patients in whom the primary was well differentiated.

Of the 71 patients who were subjected to surgery, 26 (36 per cent) died in the postoperative period (*Table VII*).

DISCUSSION

The meagre 5-year probability survival emphasizes that prostatic carcinoma is indeed a lethal disease. Moreover, the fact that some 30 per cent of patients had metastatic disease at presentation indicates that initially the condition may produce trivial or no symptoms. Even when symptoms do arise the diagnosis is often missed. From an analysis of our clinical material the following features would seem to be useful indices in differentiating prostatic cancer from benign prostatic hypertrophy:—

1. The condition has a higher peak age incidence.
2. It often presents as retention without previous prostatism or with only a short history of urinary-tract symptoms.
3. The degree of upper urinary-tract obstruction is often disproportionately severe in relation to the short duration of symptoms.

The fact that the S.A.P. was elevated in less than 30 per cent of the patients needs emphasis. Thus, although an elevated S.A.P. provides useful corroborative evidence of carcinoma, a normal assay in no way refutes this diagnosis. In our series the diagnosis of carcinoma was made on the basis of an elevated S.A.P. alone in only 8 patients (7 per cent; *Table IV*).

Although surgery for the relief of urinary obstruction may become mandatory in patients with carcinoma of the prostate, patients with this condition are clearly poor operative risks, for of 71 patients who underwent operation, 26 died in the post-operative period and 9 more within 1 year. Indeed, it seems worth re-emphasizing that more patients died from lower urinary-tract obstruction or from operations for its relief than from carcinomatosis. Clearly, therefore, operation should be avoided wherever possible in patients with prostatic carcinoma, and more effective drug treatment of the primary lesion without recourse to surgery might be expected significantly to improve survival. In our series many patients were subjected to surgery in the mistaken belief that they were suffering from benign prostatic hypertrophy. If the correct diagnosis had been established initially then fewer patients would have undergone surgical procedures. Hence, more accurate diagnosis, with perhaps resort to prostatic cytology and biopsy, might favourably influence survival.

Treatment with oestrogenic hormones produced regression of the primary neoplasm in approximately 60 per cent of patients. In contrast, metastat lesions appeared to be more often hormone resistan The latter finding is disturbing, since recent wo has suggested that treatment with oestrogens m precipitate or aggravate cardiovascular disea (Arduino, Moines, Bailar, and others, 1967), and the present series 15 patients died from such cause Since our results showed that metastases were rare responsive to oestrogenic hormones, our finding contrary to those in the report of Arduino and othe (1967), would suggest that these hormones be us only in the treatment of the primary lesion. Whi we appreciate that the present study is a retrospecti one we feel that our figures indicate the necessity f a prospective controlled trial designed to define t usefulness or otherwise of oestrogenic hormones i the treatment of metastatic prostatic carcinoma.

It is interesting to speculate as to whether prostat carcinoma passes through two phases: an initi phase, when the primary lesion is hormone sensitiv and a later phase, when the metastatic lesions an possibly the primary are hormone resistant. Altern tively there may be two distinct types of prostat carcinoma: one which is hormone sensitive and t other hormone resistant *ab initio*.

Acknowledgements.—We are grateful to M H. G. Roberts, Mr. L. P. Thomas, and Mr. D. I Sturdy for allowing us to include patients under the care and for their help in the preparation of t paper, to Mr. Nigel Pierce for preparing the illu tration, and to Mrs. O. Palmer and Mrs. A. Blake f secretarial assistance.

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INTRAPELVIC DERMOID CYSTS IN ADOLESCENT GIRLS PRESENTING WITH URINARY RETENTION

A REPORT OF 2 CASES

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RETROVERTED gravid uterus, uterine fibroids, pelvic abscess, or ovarian carcinoma are well-recognized causes of acute retention of urine in females. However, although urinary symptoms of frequency, dysuria, and suprapubic pain are mentioned in large reviews of ovarian dermoid cysts (Peterson, Prevost, Edmunds, Hundley, and Morris, 1955; Forshall, 1960; Boles, Hardacre, and Newton, 1961; Thatcher, 1963) only 1 case of acute retention of urine can be found (Glinski, 1969). Retroperitoneal dermoid cysts arising from the sacrum are much less common. One previous case of a presacral dermoid cyst in a 40-year-old male producing an acute retention of urine has been reported (Talbot, 1959). Two cases are reported here, one a presacral dermoid cyst and the other an ovarian dermoid cyst, in patients who presented with acute retention of urine.

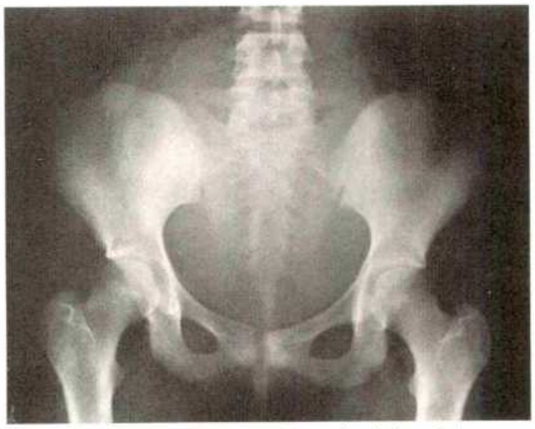

FIG. 1.—*Case* 1. Plain radiograph of the pelvis.

CASE REPORTS

Case 1.—A 13-year-old girl, who was on holiday in Scotland, was admitted to the Western Infirmary, Glasgow, on 17 April, 1969, with acute retention of urine. She had not voided urine for 14 hours and on examination her abdomen was dull to percussion up to her umbilicus. A catheter was passed and produced only 450 ml. of urine. The lower abdominal swelling persisted and a rectal examination revealed a fluctuant retroperitoneal mass just above the anal canal.

A straight radiograph of the abdomen at this stage showed a round radio-opaque mass 15 cm. in diameter centred over the anterior of the sacrum (*Fig.* 1). Diagnostic ultrasound reported 'a large transonic cystic mass, containing a few scattered solid areas, arising out of her pelvis; consistent with a dermoid cyst' (*Fig.* 2).

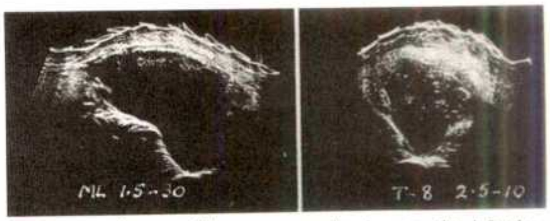

FIG. 2.—*Case* 1. Ultrasonogram showing on the left the inferior edge of the cyst outlining the anterior aspect of the sacrum.

As the patient was in Glasgow for only a few days, she returned home to Bournemouth where she was operated on 2 weeks later. The cyst was aspirated and over 4 litres of sebaceous-looking fluid were obtained. Her postoperative recovery was slow owing to a pelvic abscess. Since discharge from hospital she has had no urinary symptoms.

Case 2.—A 13-year-old girl was first seen at the Western Infirmary, Glasgow, on 10 Nov., 1967, with acute retention of urine. She was catheterized and 800 ml. of urine were

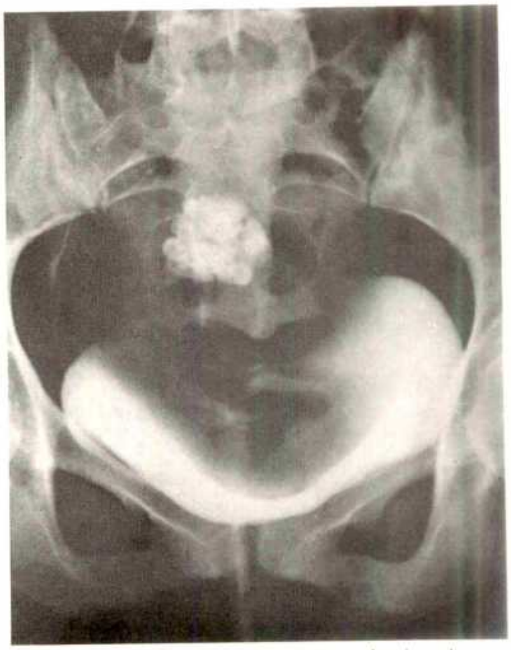

FIG. 3.—*Case* 2. Intravenous cystogram showing the cyst, containing teeth, indenting the bladder.

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obtained. She remained trouble free for 2 years till 15 Nov., 1969, when she was readmitted with further retention of urine, on this occasion passing 930 ml. of urine after being given 0·25 mg. of intramuscular carbachol. She was again symptom free for 2 years until 2 Oct., 1971, when a 900-ml. retention of urine was similarly relieved. Urine cultures were negative on each occasion and it was felt that each episode of retention had been related to a stressful situation.

The patient was then referred to the Urological Department where intravenous pyelography showed her bladder to be considerably indented by a soft-tissue mass with opacities in its centre, suggesting the presence of teeth within a dermoid cyst (*Fig.* 3). Diagnostic ultrasound showed the presence of a large complex cystic mass rising out of the pelvis low down posteriorly with the bladder enlarging over and above it (*Fig.* 4). The appearance was consistent with the radiological diagnosis of an ovarian dermoid cyst.

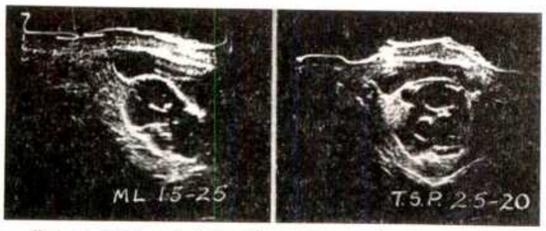

FIG. 4.—*Case* 2. Lateral ultrasonogram showing on the left the bladder flattened at its base by the impacted cyst. (*Reproduced by kind permission of the 'British Journal of Radiology', Vol.* 43, *p.* 611.)

Cystoscopy and an examination under anaesthetic were performed. The bladder mucosa and bladder neck were normal, but there was a midline bulge into the bladder base which was slow to fill out. On bimanual examination a ballotable cyst was felt in the posterior fornix.

At operation on 2 Nov. a large cyst arising from the left ovary filled the pelvis (*Fig.* 5). The left Fallopian tube was seen stretched out over its circumference and the bladder extruded above and in front of it. The uterus was squashed flat against the bladder neck by the tense, impacted, non-adherent cyst. The cyst was easily removed and macroscopic examination showed the 13-cm. thin-walled cyst to contain mucoid sebaceous material with several well-formed teeth and daughter cysts arising from a cartilaginous pedicle. Histology showed various tissues and epithelia but no evidence of malignancy.

Postoperatively the patient had a transient retention of urine until 12 hours after anaesthesia when this resolved spontaneously. Her subsequent progress was unremarkable.

DISCUSSION

The acute retention of urine in both the cases presented here appears to be the culmination of a chronic process.

Overflow incontinence from chronic retention in which an ovarian dermoid cyst perforated into the bladder has been reported (Wood, 1953). The retention in this case was thought to be due to severe cystitis and differs from that in the cases in the present report. Both cases had considerable extrinsic obstruction at the bladder neck. The mechanism must be similar to the retention produced by lower uterine fibroids, retroverted gravid uterus, pelvic abscess, or ovarian carcinoma. Talbot (1959) felt that progressive distortion stretches the bladder neck, disturbing the neuromuscular mechanism and leading to hypertrophy of the wall. This hypothesis is supported by the quick relief obtained by carbachol, the ease of catheterization, and the ultrasonic picture obtained in *Case* 2 (*Fig.* 4).

The single case reported from Poland was of an infected dermoid cyst incarcerated in the pelvis (Glinski, 1969). Catheterization produced 900 ml. of urine. That this was an acute or chronic episode is supported by the upper urinary-tract hydronephrosis and hydro-ureter seen preoperatively which had disappeared 40 days later.

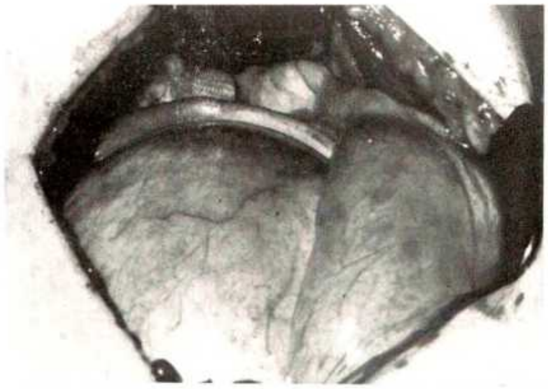

FIG. 5.—*Case* 2. Operative photograph, showing the bladder on the right with the more spherical cyst behind it, crossed by the left Fallopian tube.

The knowledge that girls may develop slowly growing ovarian or presacral dermoid cysts should remind the surgeon to exclude this possibility when examining a girl with an acute retention of urine.

Both the cases presented here illustrate the extremely valuable role of diagnostic ultrasound in the diagnosis of pelvic masses (Morley and Barnett, 1970). While still complementary to good radiographs, ultrasound has added a new dimension to the preoperative assessment of size, position, and content of dermoid cysts.

Acknowledgements.—My thanks are due to Dr. P. Morley and Mr. K. F. Kyle for their help in preparing this paper.

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RUPTURED SPLEEN: A RADIOLOGICAL PITFALL AND A SUGGESTED MODIFICATION

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SUMMARY

The diagnosis of splenic injury may be obvious from the outset, or it may either be masked by other injuries or present much later in the phase of convalescence. Delayed rupture may occur as late as 1 month after injury, at which time it may be embarrassing for the doctor and dangerous for the patient. Any additional diagnostic measure is therefore considered appropriate in cases of abdominal trauma. Schorr and Danon (1967) described the value of a film taken in the left lateral decubitus position with barium in the stomach, and noted the significance of a distance of more than 3 cm. from the greater curvature of stomach to the lateral abdominal wall. A case is described in the present paper in which a false-positive result was obtained with the method of Schorr and Danon (1967) owing to interposition of a heavy mobile omentum. A right ateral decubitus film had been taken while the patient had a gas-filled stomach, and had revealed a distance of only 2·2 cm. between the greater curve and lateral abdominal wall. In this projection the mobile omentum had obviously fallen away, allowing the stomach to rise towards the left abdominal wall and thus demonstrating the absence of a fixed mass in this region.

Although it would appear that this technique is more useful in cases of delayed rupture than in acute cases, it is suggested that routine use be made of the right lateral decubitus film with a gas-filled stomach, prior to films being taken according to Schorr and Danon's (1967) method. This modification might also be useful in the diagnosis of diseases of the spleen, and in following the progress of patients after treatment.

TRAUMA to the spleen has assumed more significance recently owing to the increasing number of motor-car accidents and other forms of blunt abdominal injury. The typical case of acute splenic rupture usually does not present major difficulty in management, for even f the classic story of trauma followed by the development of signs of 'acute abdomen' and evidence of continuing internal bleeding does not pinpoint the exact pathology, it at least indicates the need for aparotomy, at which time the diagnosis will become apparent and correct treatment will be carried out. On the other hand, the clinical course of delayed or occult splenic rupture may entail some considerable embarrassment for the clinician and danger for the patient.

The following case reports are presented to show how a modification of a previously described radiological method for the diagnosis of splenic rupture may assist the surgeon, and to indicate one form of false-positive result that may be obtained with the unmodified method.

CASE REPORTS

Case 1.—A heavily built 47-year-old policeman was admitted to hospital following a motor-car accident. He had sustained a moderate concussion, a large right supra-orbital haematoma with laceration, and a simple posterior dislocation of the right hip. There was no chest or abdominal pain or tenderness, and the neurovascular supply of the right lower limb was intact. His laceration was sutured and the hip was relocated without difficulty under general anaesthesia.

His early postoperative course was uneventful and he remained apyrexial until the tenth post-injury day. At this stage a low-grade fever became evident but no obvious cause could be found. Three days later some deep-seated bruising appeared over his lower left costal margin and he complained of some pain in the left loin. The possibility of delayed splenic rupture was considered. Radiological examination of the chest was normal apart from a doubtful fracture line in the left ninth rib. Antero-posterior films of the abdomen revealed a gas-distended stomach in the normal situation (*Fig.* 1). A right lateral decubitus film (*Fig.* 2) showed the greater curve of the stomach to be lying approximately 2·2 cm. from the inner aspect of the left ninth rib. A left lateral decubitus film taken with barium in the stomach (*Fig.* 3) revealed the corresponding distance to be 11·3 cm. and in view of this gross increase it was decided to carry out laparotomy with the presumptive diagnosis of delayed splenic rupture and perisplenic haematoma.

At operation the greater omentum, which was heavily laden with fat, was interposed between the stomach and the inner aspect of the left lower costal margin in front of the spleen. Traction was required to dislodge the omentum from this position, after which it was noted that the spleen, although slightly enlarged and firmer than usual, was intact. There was no haemorrhage in the left subphrenic region. The liver was enlarged and firm with an appearance of active cirrhosis. A biopsy of the liver was taken and the operation was completed without incident. The post-operative course was uneventful.

Histological examination of the liver showed an active cirrhosis of the alcoholic type.

Case 2.—A 62-year-old female was admitted as an emergency after having fallen from a chair and sustained a blow to the lower left chest. Examination revealed localized tenderness over the costal margin anteriorly, but respiration was fairly adequate and the lung fields were clear. The abdomen was soft and non-tender to palpation. Radiographs did not reveal any fractures.

The patient was sent home, but she returned to hospital 2 weeks later complaining of exacerbation of pain in the left hypochondrium and persistent pain on breathing. Examination showed well-marked bruising in the left hypochondrium and a tender palpable mass projecting below the rib margin. A presumptive diagnosis of delayed splenic rupture and perisplenic haematoma was made and she was submitted to a radiographic study. The stomach was distended with gas by the ingestion of a teaspoonful of sodium bicarbonate with a quarter of a teaspoonful of tartaric acid. A right lateral decubitus film was taken and showed that the proximal end of the greater curve of the stomach closely approximated to the inner margin of the lower left ribs (parietal peritoneum), but that the distal border was indented and 'displaced' away from the lateral peritoneal line. It was thought that the gaseous distension might be inadequate, and therefore an additional amount of the gas-forming substance was administered. The subsequent film (*Fig.* 4) showed quite unequivocally that there was no space-occupying lesion in the splenic area. In fact, the excellent contrast provided by the air in the stomach enabled a very clear outline of the spleen to be seen. In view of this finding operation was withheld and subsequent examinations suggested that the mass was probably a haematoma attached to the anterior wall of the left hypochondrium. The patient has remained in good health.

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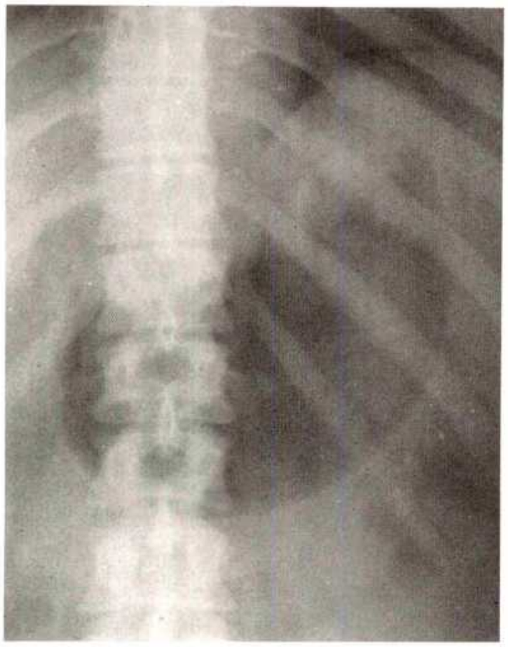

FIG. 1.—*Case* 1. Erect film of the abdomen, showing a gas-filled stomach in the normal undisplaced position.

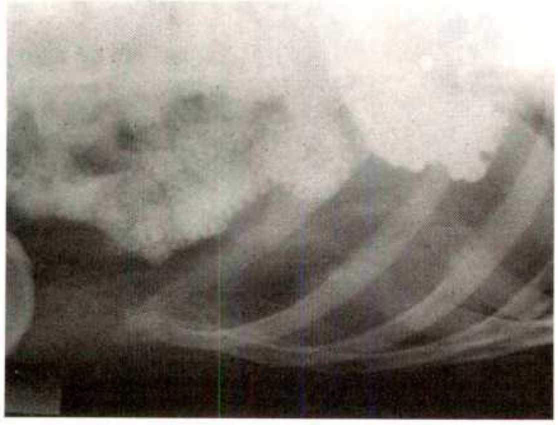

FIG. 3.—*Case* 1. Left lateral decubitus film of the barium-filled stomach, showing the greater curvature of the stomach displaced upwards away from the lateral peritoneal border (a positive result according to the criteria of Schorr and Danon, 1967).

Several young patients who had been involved in accidents and who were suspected of having a splenic or other visceral injury have also been subjected to this radiological procedure in the acute phase. In 1 male patient an exploratory laparotomy was postponed because of the normal 'ascent' of the greater curve with gas distension and his condition soon began to improve. He recovered without operation and with the retrospective diagnosis of retroperitoneal haematoma. Three other patients who were subjected to laparotomy and in whom the gas-filled stomach ascended to the peritoneal border were all found to have lesions away from the splenic area to account for their abdominal symptoms.

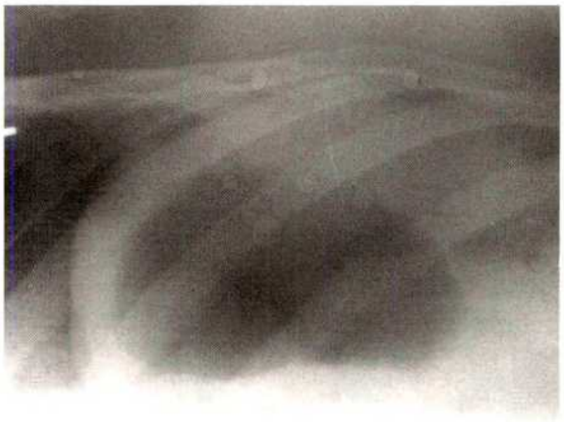

FIG. 2.—*Case* 1. Right lateral decubitus film, showing the greater curvature of the gas-filled stomach lying close to the lateral peritoneal border.

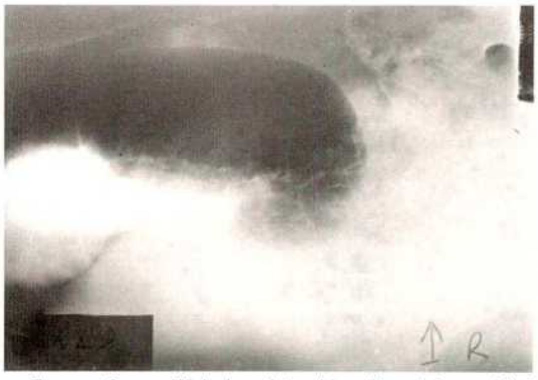

FIG. 4.—*Case* 2. Right lateral decubitus film of the gas-filled stomach with the greater curvature lying in the normal situation close to the lateral border of the peritoneum. Note that a clear outline of the normal-sized spleen can be seen.

DISCUSSION

It is not infrequent that a patient, having recently sustained multiple injuries, leaves hospital only to return within a short time with signs of 'acute abdomen'. The diagnosis of delayed splenic rupture is made and is usually verified by operation, but it can be wrong in a small number of cases. Sizer, Wayne, and Frederick (1966), in a review of the literature, reported that delayed rupture occurred more than 1 month after the initial injury in 10 per cent of cases, while Wilkinson (1968), in a review of 90 cases of splenic rupture seen at the Johannesburg Hospital, noted that 27·2 per cent of the cases of delayed rupture occurred later than 1 month after injury.

In view of the dangers inherent in delayed rupture of the spleen, any additional diagnostic measures which might lead to the earlier diagnosis of splenic injury should be considered. In 1967 Schorr and Danon described the method of radiographing the patient in the left lateral decubitus position after the oral administration of barium, and noting the position of this medium along the greater curvature of the stomach in relation to the lateral abdominal wall, as indicated by the inner margin of the lower ribs. They stated that the distance between these two points should not exceed 3 cm. and pointed out that values in excess of this figure indicate the presence of a space-occupying peri- or parasplenic mass. The reliability of this sign was noted to be positive in 71 per cent of the cases of Schorr and Danon (1967), while Wilkinson (1968) noted that it was positive in 87·5 per cent of cases in which it was used. Schorr and Danon (1967) stated that this method obviated the false-positive results which are obtained when the small intestine and colon interposed between the stomach and parietes. While this may be true for an empty bowel, it might well not apply to a fully loaded colon or fluid-distended loop of small intestine which may be as heavy as a barium-filled stomach. The present *Case* 1 demonstrated that Schorr and Danon's (1967) premiss does not apply when a heavy, bulky, and mobile omentum interposes itself between stomach and left lateral parietes.

Scant reference has been made to Schorr and Danon's (1967) technique in the recent literature. State, Getzen, and Laning (1969), in an analysis of 100 cases of splenic rupture, mentioned that they found 'no particular diagnostic examination to be of specific unequivocal benefit' in these cases, while Sargison, Cole, and Kyle (1968), in their series of 45 cases, used radiographs merely to confirm the presence of fractured ribs or other intrathoracic injuries.

The present *Case* 1 illustrates how the left lateral decubitus/barium method may give a positive result according to Shorr and Danon's criteria, but that the cause may not be related to splenic trauma. A mobile structure may certainly interpose itself between the barium-filled stomach and the parietes, but taking a radiograph of the gas-filled stomach in the right lateral decubitus position will allow the greater curvature to 'ascend' towards the left parietes as the mobile mass moves away by gravity. A fixed mass such as a perisplenic haematoma would not be expected to drop away. By this additional manœuvre, evidence may be forthcoming either in favour of or against the diagnosis of splenic injury.

The author suggests that this modification might also be used without the barium study in cases in whom it is deemed inadvisable to give barium by mouth.

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GASTRODUODENOSCOPY USING AN IRRIGATING CYSTOSCOPE*

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PERORAL fibre-optic gastroscopy is well established but duodenoscopy is less reliable (Morrissey, Tanaka, and Thorsen, 1967; Shearman, Warwick, Macleod, and Dean, 1971). It may be difficult to be sure that all the bulb has been examined, and in some patients the instrument may not pass through the pylorus. Kirk (1970) found at operation in 123 patients with duodenal ulcers or scars that the pyloroduodenal canal was less than 10 mm. in diameter in more than 40 per cent of the patients, yet the duodenoscope exceeds this diameter.

The surgeon may be faced with a difficult decision at operation, particularly in two circumstances. First, from time to time he is asked to explore the abdomen of a patient suffering from incapacitating dyspeptic pain in whom all the investigations have proved negative or only suggestive of peptic ulcer; he finds no abnormality in the abdomen and the duodenal bulb is unscarred. Secondly, he operates for the cure of a well-established duodenal ulcer, with typical features demonstrated on the barium-meal films; to his surprise he finds no evidence of duodenal ulcer or scarring.

It is not possible to exclude peptic ulcer or scar by examining the outside of the bowel. In 900 laparotomies 9 active ulcers (4 duodenal, 2 post-bulbar, and 3 gastric) were found when the bowel was opened that were completely undetectable from outside the bowel.

It is usual to perform gastroduodenotomy when seeking a peptic ulcer and to close this in the form of a Heineke-Mikulicz pyloroplasty. If the surgeon finds a duodenal ulcer he completes the procedure by performing a vagotomy. If he does not find an ulcer he has irrevocably damaged the antral pump and pylorus, possibly adding to the patient's disability. Even when an ulcer is found, many surgeons would prefer to leave the pylorus untouched and to carry out highly selective vagotomy as the elective procedure.

Various instruments have been tried in order to inspect the inside of the stomach and duodenum through a gastrotomy, including sigmoidoscopes, protoscopes, various specula, and retractors. These have all proved unreliable, especially for examining the duodenal bulb. The only dependable instrument that has been tried is the irrigating cystoscope.

TECHNIQUE

A gastrotomy, 0·5 cm. long, is made in the anterior gastric antral wall and encircled with a purse-string seromuscular suture. The gastric contents are aspirated. The cystoscope is inserted, the purse-string suture is tightened around it, clamped, and given to the care of an assistant. Non-crushing clamps are placed across the cardia of the stomach or lower oesophagus and the first loop of jejunum. The stomach and duodenum are filled with sterile water from a reservoir placed not more than 10 cm. higher than the stomach.

The whole stomach, duodenal bulb, and ampulla of Vater may be examined. If the duodenal loop is mobilized it is possible to see almost to the duodenojejunal junction.

When the examination is completed the cystoscope is withdrawn, and the stomach contents are aspirated. The purse-string suture is tightened, tied, and reinforced with further sutures. The clamps are removed from the upper stomach and jejunum.

ADVANTAGES

The cystoscope will pass through all but the narrowest pyloroduodenal canals. Because it is rigid it can be manœuvred easily and its position in the bowel can be checked by feel and by observing the light through the bowel wall. The optical system allows excellent views of the mucosa. All general surgeons have been well trained in handling the cystoscope.

Although peroral fibre-optic gastroscopy will normally have been carried out before operation for gastric ulcer, re-examination with a cystoscope can be done at operation. If the small biopsy specimen removed through the peroral instrument leaves doubt about the nature of the ulcer, Lowsley's forceps may be inserted to take a larger specimen. Diathermization of bleeding points could be performed; Youmans, Patterson, McDonald, and Derrick (1970) reported the diathermization of bleeding lesions in the stomach using a resectoscope inserted through a gastrostomy.

It is as a duodenoscope that the cystoscope is most valuable. A duodenal ulcer or scar has been confidently confirmed or excluded on 16 occasions. Biopsy specimens could be removed, avoiding the need for duodenotomy. The ampulla of Vater can be seen and biopsy specimens can be removed, avoiding the need for duodenotomy. The ampulla could potentially be cannulated using a cystoscope fitted with an Albarran lever. The duodenum may be inspected without the need to damage the pyloroduodenal canal.

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* Based on a paper read to the British Society of Digestive Endoscopy on 11 March, 1972.

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REGENERATION OF PARIETAL AND VISCERAL PERITONEUM

A LIGHT MICROSCOPICAL STUDY

By A. T. RAFTERY

DEPARTMENT OF ANATOMY, SCHOOL OF MEDICINE, UNIVERSITY OF LEEDS

SUMMARY

1. The healing of visceral and parietal peritoneum has been investigated using conventional light microscopy, Häutchen preparations, and by using 1 μ sections of epoxy-resin-embedded material to follow the activity of peritoneal macrophages labelled with polystyrene spheres (0·79 μ in diameter).

2. Healing has been found to occur rapidly and for the most part without adhesion formation. Parietal peritoneum and caecum are covered by a new mesothelial membrane in 8 days, while the liver is covered in 7 days.

3. It has not been possible to support the theory that peritoneal macrophages are transformed into mesothelial cells via fibroblasts. The results obtained in the present investigation suggest that the new mesothelial layer is derived directly from the subperitoneal fibroblast.

CONFLICTING opinions still exist with regard to the precise nature of peritoneal regeneration. Hertzler (1919) showed that when a defect was made in the parietal peritoneum of an animal 'the entire surface becomes endothelialized simultaneously and not gradually from the borders as in epidermitization of skin wounds'. This finding has been confirmed by others (Robbins, Brunschwig, and Foote, 1949; Johnson and Whitting, 1962; Ellis, Harrison, and Hugh, 1965; Eskeland, 1966a; Hubbard, Khan, Carag, Albites, and Hricko, 1967). However, disagreement exists among these workers with regard to the origin of the cells which form the new mesothelial lining. Some workers (Robbins and others, 1949; Williams, 1955; Ellis and others, 1965; Hubbard and others, 1967) consider that regeneration of the mesothelial lining takes place by metaplasia of the subperitoneal fibroblasts, while others (Cameron, Hassan, and De, 1957; Johnson and Whitting, 1962; Bridges and Whitting, 1964) consider that mesothelial cells are detached from the adjacent intact peritoneum and become implanted on the wound surface where they proliferate and eventually give rise to a continuous sheet of mesothelial cells. Johnson and Whitting (1962) also suggest that monocytes and macrophages present in the wound exudate can become transformed into mesothelial cells—a suggestion which has received support from Eskeland (1966a, b) and Eskeland and Kjaerheim (1966a, b). Much of the difficulty in the study of peritoneal regeneration arises in the problem of identifying mesothelial cells in histological sections cut perpendicular to the wound surface, but this can be overcome by using Häutchen preparations which permit inspection of the surface cells *en face*. The present study was undertaken in an attempt to clarify the problem of which type of cell is responsible for the new mesothelium, and also, in view of the fact that little attention has been given to the healing of visceral peritoneum, to compare the healing of defects of visceral peritoneum with that of defects of parietal peritoneum using Häutchen preparations.

MATERIALS AND METHODS

A total of 100 adult male Sprague-Dawley rats, weighing 220–250 g., were used in this investigation. The rats were anaesthetized with ether. The abdominal cavity was opened by a 5-cm. midline incision. Wounds approximately 1 mm. deep and either ½ cm. or 1 cm. square were made in the liver capsule by a tangential cut with a scalpel blade. A wound was also made on each side of the midline in the parietal peritoneum, that on the left side being 2 cm. square and that on the right side 1 cm. square. The peritoneum together with the underlying layer of muscle was removed within this area. In other animals the caecum was delivered through the wound and the peritoneum was stripped from the antimesenteric border over areas of about 1 × 1 cm. or 1 × 2 cm. Haemostasis was obtained by applying pressure from a gauze swab. The abdominal incision was closed in two layers, catgut sutures being placed through the musculoperitoneal layer and silk sutures through the skin. Animals were killed by exsanguination under ether anaesthesia at intervals of 12 hours up to 3 days, then at daily intervals up to 8 days, and at 10 and 14 days after operation.

The liver was removed, rinsed briefly in 5 per cent glucose, immersed in 0·25 per cent silver nitrate for 30 seconds, rinsed again in 5 per cent glucose, and then fixed in 10 per cent formol–saline for 8–12 hours. The wounds in the parietal peritoneum were removed together with a wide margin of normal peritoneum, pinned flat on cork, and treated in the same manner as the liver. A ligature was placed around the ileocaecal junction and the ascending colon, and the distended caecum was removed *in toto*. It was then treated as described above. Häutchen preparations of the wounds were subsequently made, as described by Eskeland (1966a), and stained with haematoxylin. In other animals the wounds were excised, fixed in formol–sublimate or Bouin's fluid, dehydrated, and embedded in paraffin wax. Serial sections were cut perpendicular to the wound surface at 6 μ. These sections were stained with haematoxylin and eosin, and either by the picro-Gomori method or Ledrum's stain (Humason, 1962) for fibrin and collagen. Smears of peritoneal fluid were obtained at each stage, and were either air-dried and stained with Wright's blood-stain or fixed in equal parts of ether and absolute alcohol and stained by the method of Papanicolaou.

Specimens of parietal peritoneum, liver, and caecum were also fixed in 2·5 per cent glutaraldehyde in 0·1 *M* cacodylate buffer, post-fixed in 1 per cent osmium tetroxide in 0·1 *M* phosphate buffer, dehydrated in graded solutions of ethanol, and embedded in Araldite. Sections 1 μ thick were cut on an ultramicrotome and stained with methylene blue–Azure II (Richardson, Jarett, and Finke, 1960).

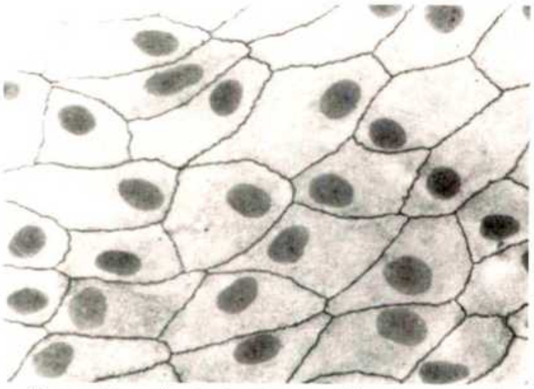

FIG. 1.—Normal parietal peritoneum. Häutchen. (× 222.)

In order to label the peritoneal macrophages some animals were given an intraperitoneal injection of 2·5 ml. of a 0·2 per cent suspension of polystyrene spheres (0·79 μ diameter Dow–Latex; Serva, Feinbiochemica, Heidelberg) in 0·9 per cent saline at the time of operation. Specimens from these animals were processed for Häutchen preparations in order to check if the inflammatory reaction caused by the polystyrene spheres had had any effect on the nature of healing. Some specimens were fixed in 2·5 per cent glutaraldehyde, processed as described above, sectioned at 1 μ, and stained with methylene blue–Azure II. Smears of peritoneal fluid from these animals were fixed in equal parts of ether and absolute alcohol and stained by the method of Papanicolaou. Some non-operated animals were given an intraperitoneal injection of 2·5 ml. of a 0·2 per cent suspension of polystyrene spheres. Specimens of both visceral and parietal peritoneum were fixed in 2·5 per cent glutaraldehyde and processed as described above. Smears of peritoneal fluid from these animals were stained by the method of Papanicolaou.

RESULTS

1. Macroscopic.—Adhesions to the wounds were found in only 6 animals and in each case the liver wound was adherent to the midline wound. During the first 2 days the wounds were uneven and haemorrhagic; thereafter the wounds became paler and by 5 days were usually smooth and glistening. In particular the wounds in the liver capsule were easily seen up to 10 days when they appeared as shiny, greyish-white, puckered areas. In the case of parietal peritoneum it was difficult to distinguish the wound from the surrounding peritoneum after 7 days After 5 days it was difficult to see the wound in th caecum.

2. Microscopic.—

a. Peritoneal Fluid.—Normal peritoneal fluid wa found to contain macrophages, monocytes, lympho cytes, eosinophils, mast cells, and a small number o large cells with a pale, occasionally fragmented nucleus and indistinct cell boundary. The peritonea fluid of operated animals contained the same types of cell except that the macrophages were larger and contained phagocytosed material; in addition, polymorphonuclear leucocytes were present but decreased in number after the third day. In specimens from animals injected with polystyrene spheres the large cells with fragmented nuclei and indistinct cel boundaries were found to contain polystyrene spheres. These cells are most likely either dead macrophages or macrophages which had been damaged when the smears were made. No cells which resembled mesothelial cells were seen in the smears of either normal or operated animals.

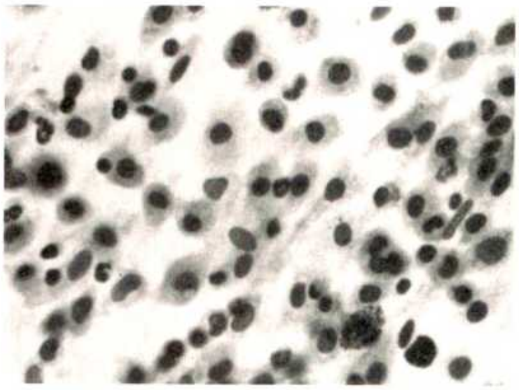

FIG. 2.—Parietal peritoneum at 1 day. Macrophages, monocytes, polymorphs, eosinophils, lymphocytes, and the occasional mast cell are seen on the wound surface. The majority of cells are of the monocyte/macrophage type. Häutchen. (× 222.)

b. Parietal Peritoneum.—Normal parietal peritoneum as seen in a Häutchen preparation is shown in *Fig.* 1. At 12 and 24 hours after injury the surface of the wound was covered by a fibrinous exudate containing red blood-corpuscles and nucleated cells Most of the latter cells resembled peritoneal macrophages and monocytes although polymorphs, eosinophils, lymphocytes, and mast cells were also present (*Fig.* 2).

At 2 days the appearance of the wound surface resembled that at 1 day. During the first 48 hours changes were seen in the mesothelial cells adjacent to the wound. These changes were characterized by widening and loss of definition of the silver lines in Häutchen preparations, pronounced cytoplasmic basophilia in the perinuclear region, and the appearance of two or more prominent nucleoli within the nucleus (*Fig.* 3). By the second day occasiona mitotic figures were seen in the adjacent peritoneum

At 3 days there were marked changes on the wound surface (*Fig.* 4). Polymorphs, lymphocytes, eosinophils, and mast cells were no longer seen and the only cells of the initial inflammatory reaction which remained were round cells with a dark-staining, eccentric kidney-shaped nucleus which were identified as monocytes or macrophages.

A further type of cell was seen at this stage which had a poorly defined cell boundary, was larger than the monocyte, possessed a large, round, or oval nucleus containing one or more prominent nucleoli, and was occasionally multinucleate. In addition, some had pronounced basophilic cytoplasm and resembled the cells seen on the surface of the adjacent peritoneum during the first 48 hours. In some areas of the wound surface these cells were numerous while in others cells of the monocyte/macrophage type were predominant. At this stage silver lines were present around cells in some areas but were wide and often ill defined. Mitotic figures were seen on the wound surface at this stage and were numerous in the mesothelial cells adjacent to the wound.

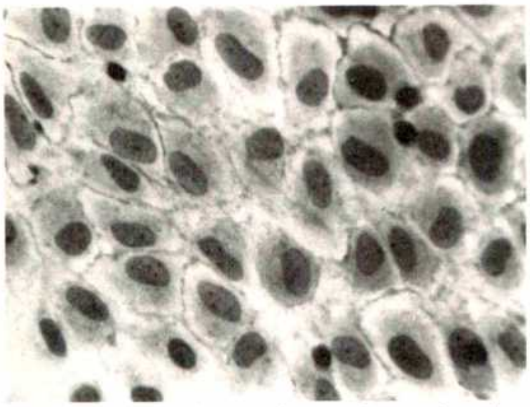

FIG. 3.—Parietal peritoneum adjacent to the wound at 2 days. Note the indistinct silver lines, pronounced cytoplasmic basophilia, and the prominent nucleoli. Häutchen. (× 222.)

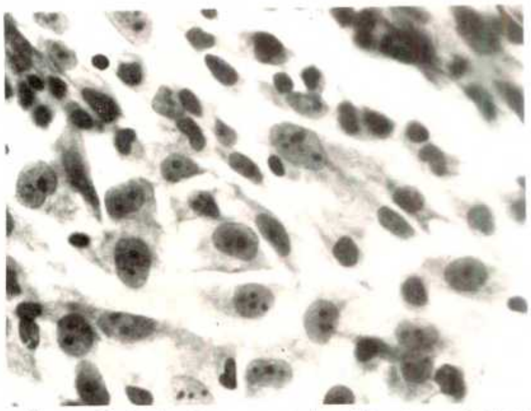

FIG. 4.—Parietal peritoneum at 3 days. Two types of cell are seen on the wound surface, one resembling a monocyte, the other a large cell with indistinct boundary and many prominent nucleoli. Häutchen. (× 222.)

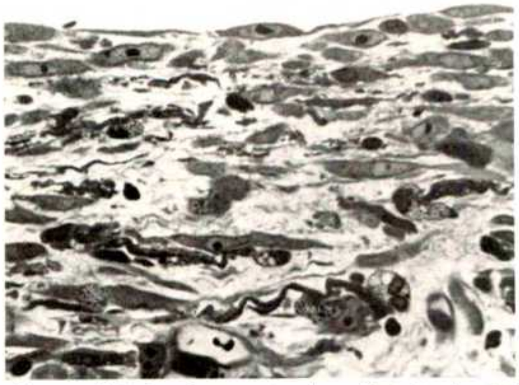

FIG. 5.—Parietal peritoneum at 4 days. Note the elongated flattened cells on the wound surface. They resemble the fibroblasts in the deeper part of the wound except that the cells on the wound surface possess a brush border. Methylene blue–Azure II. (× 222.)

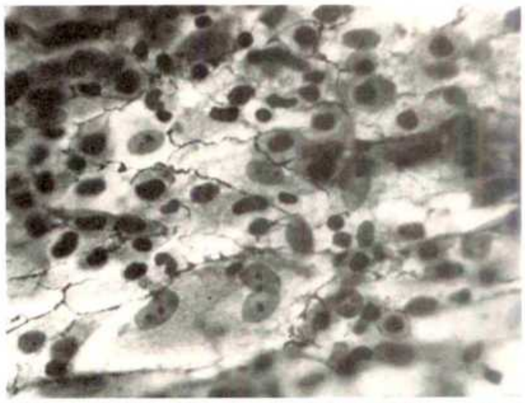

FIG. 6.—Parietal peritoneum at 5 days. Two types of cell are still present on the wound surface but silver lines are seen around the larger cells in some areas. A multinucleate cell is seen on the lower left-hand side. Häutchen. (× 222.)

The appearances on the wound surface were similar at 4 days. In sections cut perpendicular to the surface marked fibroblast proliferation was seen in the base of the wound and occasional strands of fibrin were present in the more superficial parts of the wound. On some areas of the wound surface cells which resembled fibroblasts were seen; they were elongated and flattened and had an oval nucleus with a thin, regular rim of chromatin and a prominent nucleolus (*Fig.* 5). They were considered to be identical with the large cells with prominent nucleoli and pronounced cytoplasmic basophilia seen in the Häutchen preparations. Other cells seen on the surface at 3 and 4 days were round, with a kidney-shaped nucleus with denser chromatin and were identified as cells of the monocyte/macrophage type.

At 5 days the appearance of the wound surface varied from one specimen to another and also in different areas of the same Häutchen preparation. In some areas the surface resembled that of normal peritoneum in that the silver lines were narrow and more regular, although they were less distinct than in normal peritoneum (*Fig.* 6). The cytoplasm still showed marked basophilia and multinucleate cells were seen. In other areas (*Fig.* 7) cells with indistinct boundaries and large nuclei with several prominent nucleoli were present. Scattered between these cells were small cells resembling monocytes. Mitoses were seen on both the wound surface and in the adjacent mesothelium. Sections cut perpendicular to the surface showed flattening of the surface cells in some areas giving the appearance of a continuous layer of mesothelium (*Fig.* 8), while in other areas breaks were seen in the surface layer and cells resembling monocytes were present (*Fig.* 9). Fibroblasts in the base of the wound were now alined parallel to the surface and bundles of collagen were present.

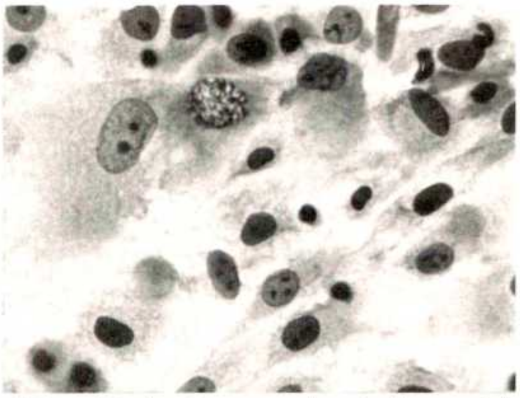
FIG. 7.—Parietal peritoneum at 5 days. Another area of the same preparation as *Fig.* 6. Two types of cell are present but the large cells with prominent nucleoli do not have distinct boundaries. Häutchen. (× 222.)

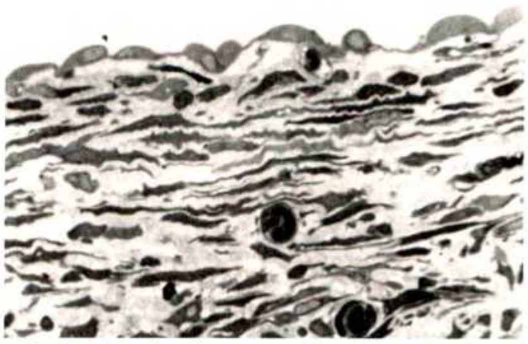
FIG. 8.—Parietal peritoneum at 5 days. The surface layer of cells is beginning to flatten, giving the appearance of a continuous layer of mesothelium. Methylene blue–Azure II. (× 222.)

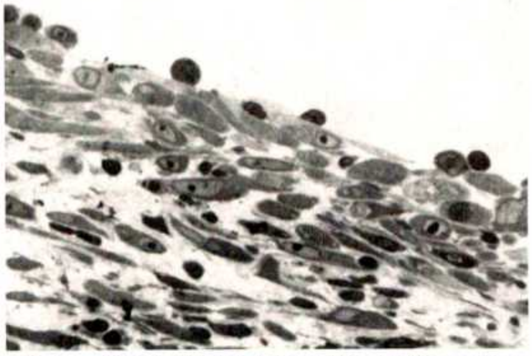
FIG. 9.—Parietal peritoneum at 5 days. Healing is not as advanced as that shown in *Fig.* 8. Small monocyte-like cells are present on the wound surface. Methylene blue–Azure II. (× 222.)

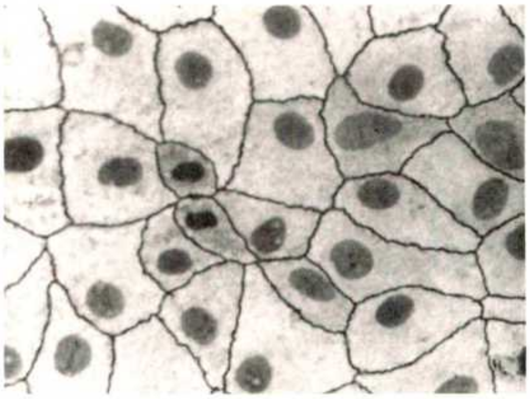
FIG. 10.—Parietal peritoneum at 8 days. There is complete healing of the mesothelial layer. A mitotic figure is seen at the centre of the field. Häutchen. (× 222.)

At 6 days the silver lines between most cells were regular and complete although sometimes they were broader than in normal mesothelium. Cells with prominent nucleoli were often seen. In some areas cells resembling monocytes were still present and occasional multinucleate cells remained on the wound surface.

At 8 days no cells resembling monocytes were seen on the wound surface. The surface was lined with a continuous layer of flattened cells which resembled normal mesothelium except that a few mitotic figures were seen. The prominent cytoplasmic basophilia had disappeared, nucleoli were not as prominent within the nucleus, and the silver lines between cells were sharp and regular (*Fig.* 10). The surrounding mesothelium had also reverted to its normal appearance. Thick bundles of collagen now occupied the base of the wound. At 2 weeks no distinction could be made in Häutchen preparations between the wound surface and normal peritoneum. A thin layer of fibrous tissue covered by a continuous layer of mesothelium occupied the site of the original defect.

There was no difference in the time or nature of healing between wounds 1 cm. and 2 cm. square.

c. Visceral Peritoneum.—

i. *Liver*: Healing of the wounds in the liver capsule resembled the healing of parietal peritoneum for the most part. At 24 and 48 hours appearances were identical with those of the parietal peritoneum both in the wound area and in the adjacent peritoneum.

Two types of cell were seen at 3 days: the small cell of the monocyte/macrophage type and the larger cell with indistinct boundaries and a large nucleus with prominent nucleoli. Again, as in parietal peritoneum, many of the latter types of cell were very large and multinucleate. Some areas showed quite advanced healing at this time when compared with parietal peritoneum. Silver lines occupied many areas although they were broad and incomplete. The exudate around and between monocyte-like cells was impregnated with silver. Mitotic figures were seen in the adjacent mesothelium at this stage.

At 5 days the majority of the cells on the wound surface were large and contained a large nucleus with prominent nucleoli. There was marked cytoplasmic basophilia.

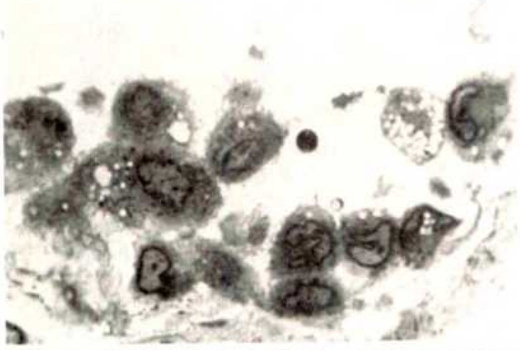

FIG. 11.—Parietal peritoneum at 2 days. Polystyrene spheres, which appear as white dots in the dark cytoplasm, are seen within the macrophages on the wound surface. In some cells the polystyrene spheres are aggregated and appear as white patches within the cytoplasm. Methylene blue–Azure II. (×900.)

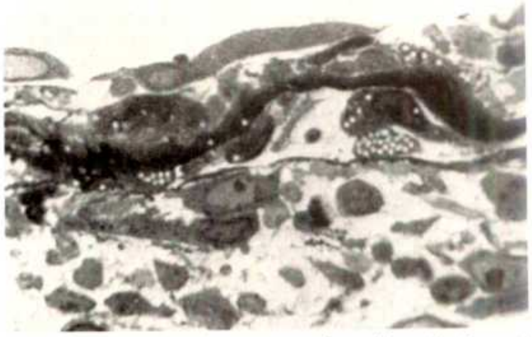

FIG. 12.—Parietal peritoneum at 4 days. Note the flattened surface cell with a brush border. No polystyrene spheres are seen in this type of cell although they may still be seen in the macrophages. Methylene blue–Azure II. (×900.)

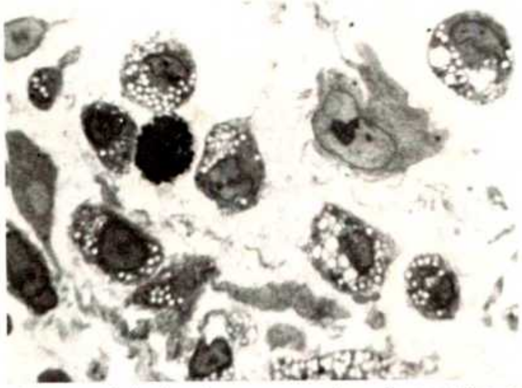

FIG. 13.—Parietal peritoneum at 4 days. Same section as shown in *Fig.* 12, but a deeper part of the wound. Note the large number of polystyrene spheres in the macrophages, while none is seen in the fibroblasts. Methylene blue–Azure II. (×900.)

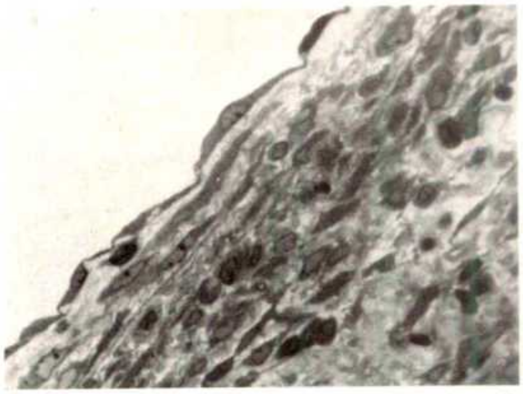

FIG. 14.—Parietal peritoneum at 6 days. The surface cells resemble the underlying fibroblasts. No polystyrene spheres are seen in these cells. Methylene blue–Azure II. (×222.)

At 6 days the silver lines were complete although in some areas wider than normal, the cytoplasm remained basophilic, but monocyte-like cells were not seen. Mitoses were seen on the wound surface. Healing appeared more advanced when compared with parietal peritoneum in that no multinucleate cells or monocyte-like cells were seen on the wound surface.

At 7 days the surface layer could not be distinguished from normal mesothelium. The larger wounds were found to heal as rapidly as the smaller ones.

ii. *Caecum*: This closely resembled the healing of parietal peritoneum. After an initial inflammatory response, the surface at 3 days showed the same two types of cell seen on the surface of the liver and parietal peritoneum. At 5 days silver lines were seen but these were wide and irregular. The majority of cells at this time were large with marked cytoplasmic basophilia and large nuclei with prominent nucleoli. Some multinucleate cells and also monocyte-like cells were seen at this stage. At 8 days healing was complete. Large wounds healed as rapidly as smaller ones.

d. Healing following Intraperitoneal Injection of Polystyrene Spheres.—Following intraperitoneal injection of a suspension of polystyrene spheres an inflammatory reaction was produced within the peritoneal cavity. Polystyrene spheres were seen within peritoneal macrophages, polymorphs, and monocytes. No polystyrene spheres were seen in mesothelial cells or subperitoneal fibroblasts.

Intraperitoneal injection of polystyrene spheres at the time of operation had no effect on the time or nature of healing in the case of either parietal or visceral mesothelium.

At 1 and 2 days polystyrene spheres were seen in cells on the surface of the wound (*Fig.* 11). These cells, which were round with an irregular or kidney-shaped nucleus with a thick irregular rim of chromatin and a 'ruffled' cell membrane, were macrophages. At 3 and 4 days two types of cell were seen on the wound surface. One contained polystyrene spheres and was identical with the macrophage described above; the other was flattened and elongated, and had an oval nucleus with a thin, regular rim of chromatin and a prominent nucleolus. Some of these cells had a brush border (*Fig.* 12). Apart from the brush border they resembled fibroblasts. Polystyrene spheres were never seen in these cells nor in subperitoneal fibroblasts even when macrophages in the base of the wound were filled with polystyrene spheres (*Fig.* 13). Once the cells of the monocyte/macrophage type had left the wound surface no polystyrene spheres were seen in the cells of the surface layer. As healing progressed the cells in the surface layer appeared to come into close contact with one another and eventually formed a continuous sheet of cells. The cells which ultimately formed the new mesothelial layer resembled the subperitoneal fibroblasts (*Fig.* 14). No polystyrene spheres were seen in the new mesothelial cells although they often remained in peritoneal macrophages for up to 2 weeks.

DISCUSSION

When conventional histological sections, cut perpendicular to the wound surface, are examined it is easy to see how investigators using this method alone have formed the opinion that mesothelial regeneration has occurred when the surface cells become flattened. However, when Häutchen preparations (viewed *en face*) are examined the absence or incompleteness of silver lines shows that these flattened cells are not in contact with one another as in normal mesothelium. Only when the silver lines are regular and complete, as in normal mesothelium, can regeneration be considered to have finished and this does not occur until some time after the surface cells become flattened. Therefore the appearance of a layer of flattened cells on the wound surface as seen in sections cut perpendicular to the wound surface is not an adequate criterion for assessing the completeness of mesothelial regeneration. Eskeland (1966a) pointed out that Häutchen preparations have certain drawbacks. Certainly it is difficult to obtain optimal photomicrographs since cells embedded in the celloidin do not always lie in the same plane; also more than one layer of cells may adhere to the celloidin in the early stages of wound healing. It is, however, difficult to agree with Eskeland that the method is time consuming. It is quicker than serially sectioning the wound perpendicular to the surface and much more can be learned in a shorter time from a single Häutchen preparation than from numerous serial sections.

The findings in the present investigation differ from those of Eskeland (1966a) on certain points. At 3 days Eskeland's preparations showed only one type of cell, which had a pale-staining oval or reniform nucleus with conspicuous chromatin, pale cytoplasm, and an indistinct cell border. In the present investigation two well-defined types of cell were present at this stage: a small round cell with a dark-staining, eccentric, kidney-shaped nucleus, which was identified as a cell of the monocyte/macrophage type, and a large cell with an ill-defined boundary, having a large, round, or oval nucleus containing one or more prominent nucleoli and with pronounced cytoplasmic basophilia. These cells resembled fibroblasts. Many of the latter type of cell were multinucleate in the early stages of healing. The number of monocyte-like cells on the wound surface gradually decreased and eventually only the larger type of cell remained. These cells came into contact with one another, as shown by complete silver lines in Häutchen preparations, and reconstituted the new mesothelium.

This study has thrown some light on the type of cell responsible for the new mesothelium. At the end of 48 hours the majority of cells on the wound surface were of the monocyte/macrophage type and some of these cells persisted until the sixth day. Eskeland and Kjaerheim (1966a) claimed that these macrophages became transformed into fibroblasts and that the cells in the most superficial layer gradually attained the characteristics of mesothelial cells. It has not been possible to substantiate this theory in the present investigation. Using polystyrene spheres to label peritoneal macrophages, it has been shown that no polystyrene spheres were seen in fibroblasts, nor were they seen in the flattened cells on the surface of the wound at 3 days which resembled fibroblasts and which ultimately formed the new mesothelium. If macrophages gradually became transformed into fibroblasts it is likely that at some stage polystyrene spheres would be seen in fibroblasts and also in the flattened cells of the superficial layer. At a time when macrophages were filled with polystyrene spheres none was seen in the flattened cells of the superficial layer and none in the reconstituted mesothelium. These findings do not support the theory that macrophages may be converted to mesothelial cells by way of fibroblasts. Further, Ellis and others (1965) have shown that while macrophages which had been labelled with trypan blue were present during the first 48 hours, trypan blue could not be identified in the surface cells at 3 days. Also at this time there was marked proliferation in the underlying fibroblasts. They concluded that these appearances suggested a two-stage process: an initial wave of phagocytic cells responsible for clearing cell debris, followed by a second wave of fibroblasts responsible for the healing of the defects and differentiation of the new mesothelium. The present investigation supports the findings of Ellis and others (1965) in this respect. However, Eskeland (1966b) and Eskeland and Kjaerheim (1966b) have grown autologous peritoneal fluid cells in Millipore diffusion chambers implanted within the peritoneal cavity and have obtained fibroblasts and cells resembling mesothelial cells within the chamber. Since no cells resembling mesothelial cells were seen in sample smears of the peritoneal fluid of these animals they concluded that the most likely source of the mesothelial cells was from transformation of the peritoneal macrophages, either directly or via fibroblasts. Two main criticisms may be levelled at this work. First, if mesothelial cells become detached and float in the peritoneal fluid they would almost certainly lose their characteristic shape and it would be difficult to recognize them in smears of peritoneal fluid stained by routine methods. Secondly, it is likely that the peritoneal fluid could be contaminated with fibroblasts. Again, these may not be recognizable in smears stained by routine methods. Ross and

Lillywhite (1965) culturing buffy coat cells of blood in subcutaneous diffusion chambers have shown that 91 per cent of chambers containing blood obtained by cardiac puncture contained connective-tissue-forming cells and collagen, whereas only 6 per cent of chambers containing blood obtained by cannulation of the carotid artery did so. They explained this by contamination of the blood by connective-tissue cells picked up during puncture of the thick wall of the heart. Surely if this could occur in cardiac puncture it is even more likely that the peritoneal fluid would be contaminated with fibroblasts after a laparotomy wound. Also, although it has been claimed (Allgower and Hulliger, 1960; Ross and Benditt, 1961; Kouri and Ancheta, 1972) that macrophages and monocytes are capable of transformation into fibroblasts there is a body of evidence to refute this claim (Grillo, 1963; Ross and Odland, 1968; Ross, Everett, and Tyler, 1970). Ross and others (1970) have clearly shown in experiments on skin wounds in parabiotic animals that fibroblasts do not arise from haematogenous precursors and therefore must arise from connective-tissue cells adjacent to the wound. It seems unlikely if transformation of monocytes and macrophages to fibroblasts cannot take place in skin wounds that it would occur in peritoneal wounds since the source of peritoneal macrophages and monocytes is from haematogenous precursors (Volkman, 1966), which is the same as the source of these cells in skin wounds.

The healing of visceral peritoneum has been found to differ little from the healing of parietal peritoneum. The one difference is that wounds of the liver capsule appear to heal more rapidly than either caecum or parietal peritoneum. There are two possible reasons for this: first, the liver provides a fairly firm substrate for healing while the peritoneum of the anterior abdominal wall and, more so, the caecum are subject to distension. Secondly, and less likely, there is the possibility that the caecum and parietal peritoneum may be damaged by stretching when they are removed and pinned out after fixing.

Some discrepancy exists between the various authors on the time taken for regeneration of the mesothelial layer. Ellis and others (1965) and Hubbard and others (1967) have shown that healing occurs in 5–6 days in the case of parietal peritoneum, and Glucksman (1966) has shown that the visceral mesothelium covering the terminal ileum heals in 5 days, while Eskeland (1966a) has demonstrated that regeneration of the mesothelial layer of parietal peritoneum is not complete until 8 days. With the exception of Eskeland these investigators have used flattening of the surface layer of cells as a criterion for mesothelial regeneration, whereas Eskeland has used Häutchen preparations. Using Häutchen preparations it has been shown that when the surface cells become flattened, cell-to-cell contact, as shown by silver lines, has not necessarily occurred. The present study has confirmed the findings of Eskeland (1966a) that the parietal peritoneum of the rat is healed within 8 days, and also that while multiplication and migration of mesothelial cells from the margin of the wound may play a small part in the regenerative process it cannot play a major part, since new mesothelium develops in the centre of a large wound at the same time as it develops in the centre of a smaller one. It has not been possible to confirm the finding of Eskeland (1966a) and Eskeland and Kjaerheim (1966a) that macrophages are transformed into mesothelial cells by way of fibroblasts. The present study suggests that mesothelium is reconstituted by differentiation of subperitoneal fibroblasts. This problem is being investigated further with the electron microscope in this laboratory at the present time.

Acknowledgements.—I wish to thank Professor R. L. Holmes for his helpful criticism, Messrs. R. K. Adkin, R. H. Nettleton, P. McPhie, and V. C. Menys for technical assistance, and Mrs. Sandra Brougham for typing the manuscript.

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MAXIMAL GASTRIC SECRETION IN PATIENTS WITH CHRONIC AIRWAY OBSTRUCTION[*]

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SUMMARY

It has been suggested that patients with chronic obstructive chest disease have greater maximal gastric secretion than normal subjects. This problem was studied in 30 subjects using the histamine infusion test with phenol red as a marker to correct for pyloric loss. Clinical, radiological, and physiological criteria were used to define two groups: (1) 13 subjects with normal chests; (2) 14 subjects with unequivocal chronic airway obstruction.

The two groups did not differ significantly in maximal gastric secretion, and this conclusion was not altered by taking stature into account because stature was statistically comparable in the two groups. However, age was significantly different and correction of the secretory data for the diminution of maximal secretion with age improved the correspondence between the groups.

The failure to take stature and age into account may be responsible for conflicting evidence in the past.

THERE is a clinical association between chronic respiratory disease and peptic ulceration. First, there is an increased incidence of chronic obstructive airway disease in patients with peptic ulcer (Hirvonen and Perttila, 1951; Weber and Gregg, 1955). Secondly, peptic ulceration is a frequent, and often unexpected, finding at the post-mortem examination of patients dying from severe pulmonary emphysema (Fulton, 1933; Green and Dundee, 1952; Plotkin, 1957; Flint and Warrack, 1958). Thirdly, there are reports of an increased incidence of peptic ulceration during life in patients with chronic obstructive airway disease (Glick and Kern, 1964).

A possible connecting link between peptic ulceration and chest disease might be gastric hypersecretion of acid, which occurs commonly in patients with duodenal ulcer and has also been reported to occur in patients with chronic airway obstruction (Kramer and Markarian, 1960; Passi and Vasko, 1969). Evidence has recently been produced confirming that gastric acid output is correlated significantly with body stature (Baron, 1969; Hassan and Hobsley, 1969) and age (Hassan and Hobsley, 1971). The present paper reports the results of a study of maximal gastric secretion in patients with obstructive chest disease, taking age and lean body mass into account.

CLINICAL MATERIAL AND METHODS

Thirty volunteers including 14 subjects from the Chest Out-patients' Clinic at the Middlesex Hospital were investigated. None of these subjects had any clinical evidence to suggest the presence of gastroduodenal ulceration.

Assessment of Pulmonary Function.—This assessment was made in each subject clinically, radiologically, and by performing pulmonary-function studies. Using a closed-circuit double spirometer (Goodart Pulmotest), the following pulmonary-function studies were performed in each of the 30 subjects: forced vital capacity (F.V.C), forced expiratory volume in 1 second ($F.E.V._1$), functional residual capacity (F.R.C.), residual volume (R.V.), total lung capacity (T.L.C.), and transport factor (pulmonary diffusing capacity) using carbon monoxide ($T._LCO$). Conversion factors were used to correct gas volumes to standard conditions (B.T.P.S.) for a body temperature of 37° C. Predicted values according to the age, sex, and indices of body build of the subject were determined from nomograms. The final verdict as to whether the subject had a normal respiratory system or not was made by a neutral observer from the Respiratory Function Laboratory.

Calculated Lean Body Mass (L.B.M.).—This was calculated from the height (*H*) and weight (*W*) of each subject using the formulae described by Hume (1966):—

$$\text{For males, L.B.M.} = 0{\cdot}3281W + 0{\cdot}3392H - 29{\cdot}533.$$

$$\text{For females, L.B.M.} = 0{\cdot}29569W + 0{\cdot}4181H - 43{\cdot}2933.$$

Gastric Secretion Test.—The histamine-infusion test (Lawrie, Smith, and Forrest, 1964) was performed on each subject using histamine acid phosphate, 0·04 mg. per kg. per hour by continuous intravenous infusion. All the other technical details, including the use of phenol red as an inert marker to correct for pyloric loss, were as described by Hobsley and Silen (1969).

Phenol red was measured spectrophotometrically, correcting for contamination with bile and blood (Crawford and Hobsley, 1968) in each sample. The percentage recovery of phenol red was used to calculate the true total volume of gastric secretion corrected for pyloric loss.

RESULTS

As a result of assessing the respiratory system in each subject, two groups emerged (*Table I*). First, there was a group of 13 subjects with no evidence of respiratory abnormality. Of these, subjects Nos. 19

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[*] Based on a communication to the Surgical Research Society and the Society of University Surgeons in London in July, 1969.

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and 31 had abnormal values of R.V./T.L.C., being 43 and 41 per cent respectively. Nevertheless, as these findings were the only ones not in line with the clinical, radiological, and other pulmonary-function studies, these 2 subjects were considered to have normal chests. This group will be referred to as control subjects with normal chests. The second group consisted of 14 subjects with evidence of chronic airway obstruction. The remaining 3 subjects gave equivocal results and were, therefore, excluded.

Table I.—COMPARISON OF PULMONARY FUNCTION BETWEEN CONTROL SUBJECTS AND THOSE WITH CHRONIC AIRWAY OBSTRUCTION

SUBJECTS		V.C./P.N. (per cent)	F.E.V.$_1$/F.V.C. (per cent)	R.V. (litres)	T.L.C. (litres)	R.V./T.L.C. (per cent)	$\text{T}_\text{L}\text{CO}$/P.N. (per cent)
Controls (13)	Mean	109·0	80·5	1·92	6·2	31·0	94·5
	Range	80–123	71–94	0·95–2·50	4·4–8·8	16–43	78–116
	S.D.	12·48	7·04	0·65	1·47	6·89	9·37
	S.E.M.	3·46	1·95	0·18	0·41	1·91	2·60
Airway obstruction (14)*	Mean	94·8	48·3	2·55	6·0	42·9	80·5
	Range	51–126	18–100	1·60–4·40	3·6–8·8	23–70	56–124
	S.D.	23·33	22·36	0·87	1·30	13·30	18·22
	S.E.M.	6·24	5·97	0·23	0·35	3·55	5·05*

P.N., Predicted normal value. F.V.C., Forced vital capacity. F.E.V.$_1$, Forced expiratory volume in 1 second. R.V., Residual volume. T.L.C., Total lung capacity. T.$_\text{L}$CO, Carbon monoxide transfer factor.

* In one subject in the group with airway obstruction, T.$_\text{L}$CO was not measured.

Table II.—COMPARISON BETWEEN SUBJECTS WITH CHRONIC AIRWAY OBSTRUCTION AND THOSE WITH NORMAL CHESTS

	AGE (yr.)	CALCULATED L.B.M. (kg.)	WEIGHT (kg.)	HEIGHT (cm.)	SURFACE AREA (m.^{2})
Mean ± S.E.M. for 13 control subjects with normal chests	38·5 ± 4·0	49·9 ± 2·5	68·4 ± 4·0	171·6 ± 3·5	1·80 ± 0·067
Mean ± S.E.M. for 14 subjects with chronic airway obstruction	51·6 ± 3·3	47·8 ± 2·0	64·8 ± 2·9	168·2 ± 2·9	1·73 ± 0·058
Student's *t* test *P*	2·502 < 0·02	0·66 > 0·5	0·72 > 0·4	0·74 > 0·4	0·71 > 0·4

Table II compares the vital statistics in the two groups. Application of Student's *t* test demonstrated that there was no significant difference in the calculated lean body mass, weight, height, and surface area between the two groups. However, the control subjects with normal chests were significantly younger than those with chronic airway obstruction ($P < 0{\cdot}02$).

Comparison of maximal gastric secretion in the two groups showed that there was no significant difference in their secretory rate or acid output, even when corrected for pyloric loss (*Table III*). For the secretory rate the corrected figures were 75·7 (S.E.M. 6·9) ml. per 15 minutes for the control group, and 66·6 (S.E.M. 6·6) ml. per 15 minutes for those with chronic airway obstruction. While this difference was not statistically significant ($P > 0{\cdot}3$), a trend towards a *reduced* secretion in the group with abnormal chests might have been suspected.

However, the average ages of our two groups were significantly different, and there is quantitative confirmation that gastric secretion diminishes in a linear fashion with age (Hassan and Hobsley, 1971). Using the regression equation of Hassan and Hobsley (1971), the secretory rates of the present data, already corrected for pyloric loss, were standardized for differences in age by the formula:—

Standardized secretory rate (ml. per 15 min.)
= Phenol-red corrected secretory rate (ml. per 15 min.) − 34·1 + (0·75 × age in years).

The results of this calculation showed that the average standardized secretory rates were 71·0 ml. per 15 minutes for the control group and 71·6 ml. per 15 minutes for the group with chronic airway obstruction.

DISCUSSION

There is convincing evidence in the literature that patients with chronic chest disease suffer from peptic ulceration more frequently than subjects with normal chests. The aetiological factors responsible for this increased incidence are not understood clearly. Various suggestions have been advanced, such as increased corticosteroid activity (as a result of chronic stress), the injurious effect of hypoxia upon the gastric and duodenal mucosa (Passi and Vasko, 1969), and the possibility that endogenous histamine production may be increased as a result of cell damage. In this last respect, Eiseman (quoted by Passi and Vasko, 1969) believes that inactivation of histamine in these patients is reduced by the acidosis. Yet another suggested mechanism, applicable only to *gastric* ulcers, involves the competence of the pylorus: there is an association between gastric ulcer and duodenal regurgitation (reviewed by Delaney, Cheng, Butler, and Ritchie, 1970), and Beeley and Grech (1971) have reported a higher incidence of duodenal

Table III.—COMPARISON OF MAXIMAL GASTRIC SECRETION BETWEEN SUBJECTS WITH CHRONIC AIRWAY OBSTRUCTION AND THOSE WITH NORMAL CHESTS

	SECRETORY RATE (ml. per 15 min.)		ACID OUTPUT (mEq. per 15 min.)	
	Un-corrected	Corrected for Pyloric Loss	Un-corrected	Corrected for Pyloric Loss
Mean ± S.E.M. for 13 control subjects with normal chests	63·3 ± 6·61	75·7 ± 6·9	7·3 ± 0·99	8·6 ± 1·07
Mean ± S.E.M. for 14 subjects with chronic airway obstruction	55·7 ± 5·9	66·6 ± 6·6	6·8 ± 0·86	8·2 ± 0·91
Student's *t* test *P*	0·858 > 0·3	0·955 > 0·3	0·323 > 0·7	0·325 > 0·7

regurgitation into the stomach in patients with chronic non-specific lung disease than in normal control subjects. The unquestionable association between gastric acid hypersecretion and duodenal ulceration has encouraged the study of gastric secretion in patients with obstructive chest disease. Up to now the evidence, though not unanimous, has suggested that patients with chronic chest disease secrete more gastric acid in response to a given stimulus than do subjects with normal chests (Kramer and Markarian, 1960).

In producing this evidence, however, stature and age were not considered, and therefore the hypersecretion of acid described in patients with obstructive chest disease might have been due to differences in stature and/or age.

In the present study indices of stature in the two groups were comparable. The maximal gastric secretion in these two groups was not statistically significantly different. Any difference might have been masked by the fact that the mean age of the control subjects with normal chests was considerably less than that of the other group. However, age correction of the maximal gastric secretion did not alter this finding, but made the already non-significant difference in maximal gastric secretion even less conspicuous.

It can be concluded that chronic airway obstruction does not significantly influence maximal gastric secretion. This conclusion is confined to maximal gastric secretion and there remains the possibility that if basal or submaximal gastric secretion is studied in these two groups of subjects, a significant difference may emerge.

Acknowledgements.—We are grateful to Dr. F. H. Scadding for allowing us to study his patients and to Dr. Gabriel Laszlo for being our neutral observer. We also wish to thank the staff of the Respiratory Function Laboratory, the Middlesex Hospital, and Miss S. Godfrey for technical assistance.

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THE ASSOCIATION OF PEPTIC ULCER AND ABDOMINAL AORTIC ANEURYSM AND ITS SIGNIFICANCE

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SUMMARY

Twelve out of 51 consecutive patients who were operated on for unruptured abdominal aortic aneurysm were found to have, in addition, a peptic ulcer. Of these 12 patients, 7 developed complications (haemorrhage or perforation) in the immediate post-operative period. Eight of the 51 patients died following operation and the commonest cause of death (5 out of 8 patients) was either haemorrhage or perforation of a peptic ulcer.

On the basis of these observations it is suggested that in patients with both an aortic aneurysm and a peptic ulcer vagotomy and pyloroplasty with gastrostomy should be carried out at the same time as aortic reconstruction.

IN a study of 7044 necropsies Jones, Kirk, and Bloor (1970) found that of 99 subjects with an abdominal aortic aneurysm, 22 (22·2 per cent) also had a peptic ulcer, whereas in the series as a whole the incidence of peptic ulceration in a comparable age-group was 7·2 per cent.

A clinical study of patients presenting with the stenotic type of arteriosclerosis of the aorto-iliac segment revealed that 24 per cent of 300 consecutive patients had peptic ulceration (Bouhoutsos, Barabas, and Martin, 1972). These patients suffered an eventual amputation of one limb more than twice as often, and of both limbs four times as often, as those without an ulcer, although there was no difference in the distribution of disease, in the surgical management, or in the early results of the operation. In the same study, of 100 consecutive patients with an abdominal aortic aneurysm, an incidence of peptic ulcer similar to that found by Jones and others (1970) was recorded. It is with this group that this paper is concerned.

MATERIAL AND RESULTS

A retrospective study of 100 consecutive patients operated on before 1971 for abdominal aortic

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aneurysm at Hammersmith and Chelmsford District Hospitals revealed a peptic ulcer in 24 of the patients. There were 90 male and 10 female patients with an average age of 70 and 67 years respectively. Of the ulcers, 20 were duodenal and 4 were gastric. Twelve of the 24 patients had been operated on for ulcer before, mostly by vagotomy and pyloroplasty. The remaining 12 patients, in whom the diagnosis of ulcer had been made previously or at the time of operation on the aneurysm or at post-mortem examination, had received no surgical treatment for the ulcer at the time of the aortic reconstruction. Of these 12 patients, 8 suffered haemorrhage or perforation in the immediate postoperative period (*Table I*).

Fifty-one patients were operated on for uncomplicated aortic aneurysm and 7 of these developed ulcer complications shortly after operation. Five of the patients with ulcer complications died. Two others died from renal failure and 1 from graft leakage. The mortality of the group was thus 8 (15·6 per cent).

Forty-nine patients were operated on for ruptured aneurysm and in these it is almost certain that some peptic ulcers were undiagnosed because of the urgent clinical condition presenting on the patient's admission. Furthermore, complications of an associated peptic ulcer might well be forestalled by the death of the patient, and in only 1 patient in this group did ulcer complications occur after operation. Unfortunately an autopsy was not performed on all those dying after the operation. Because of these indeterminate factors the incidence of peptic ulcer and the complication rate after operation for a ruptured aneurysm were not estimated. It is difficult to imagine that the incidence of peptic ulcer in association with abdominal aortic aneurysm would be less in patients with a ruptured aneurysm than in those with an uncomplicated aneurysm.

Table I.—COMPLICATIONS OF PEPTIC ULCER AFTER RESECTION OF AN ABDOMINAL AORTIC ANEURYSM IN A SERIES OF 100 PATIENTS

CASE	AGE AND SEX	RESECTION	PEPTIC ULCER COMPLICATION	DAY AFTER OPERATION THAT COMPLICATION OCCURRED	OUTCOME
1	60 M.	Elective	Perforation of duodenal ulcer	2	Died
2	62 M.	Elective	Perforation of gastric ulcer	10	Died
3	63 M.	Elective	Haematemesis from duodenal ulcer	38	Died
4	57 M.	Elective	Haematemesis from duodenal ulcer	2	Died
5	58 M.	Elective	Haematemesis from duodenal ulcer	7	Died
6	73 M.	Elective	Haematemesis from duodenal ulcer	2	Successful conservative treatment
7	65 M.	Elective	Haematemesis and melaena from duodenal ulcer	5	Successful emergency gastrectomy
8	73 F.	Emergency for ruptured aneurysm	Melaena from duodenal ulcer	7	Successful conservative treatment

DISCUSSION

Schatz, Fairbairn, and Juergens (1962) reported the fate of a selected series of 139 patients with abdominal aortic aneurysm who were managed conservatively; 18 died of rupture of the aneurysm and 2 from bleeding duodenal ulcer. They did not report the total number of patients with peptic ulcer in this group nor did they make mention of patients who may have recovered after a haemorrhage or perforation and, of course, no patient was subjected to the stress of aortic replacement. In the necropsy study of Jones and others (1970) 22 of 99 subjects with abdominal aortic aneurysms also had a peptic ulcer. Of these 22 patients, 9 died as a result of the aneurysm, 6 of the peptic ulcer, and 7 from unrelated causes.

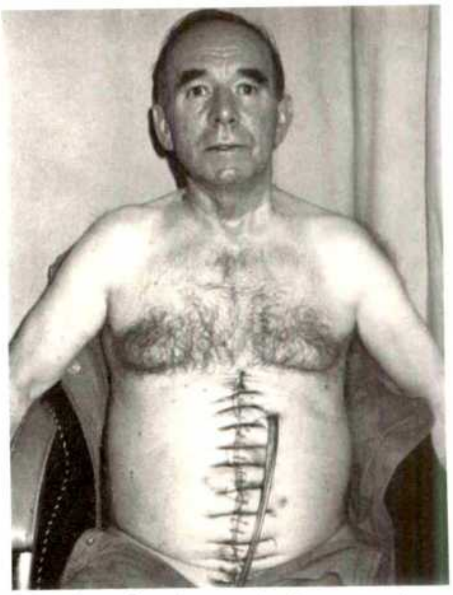
FIG. 1.—Patient 3 days after operation for a ruptured aneurysm. Note the distended abdomen and the gastrostomy drainage.

From our experience of ulcer complications in the immediate postoperative period after reconstruction of the aorta for aneurysm, the stress of such surgery is a very significant factor in the aggravation of the ulcer with consequent haemorrhage or perforation. Elective resection of an aortic aneurysm in a patient with a peptic ulcer is therefore hazardous, and ulcer complications were in fact the major cause of postoperative death. If this cause could have been excluded the mortality in our series after operation would have been reduced from 15·6 per cent to 5·9 per cent.

The high mortality of ulcer complications at this time may be due to a number of factors. First, diagnosis of some complications may be delayed, or even not made at all, because symptoms and signs are masked by the postoperative state and the ileus which is common after aortic surgery. Secondly, at the time that complications occur the patient is in a poor state to withstand further major surgery. Thirdly, if a pernasal intragastric tube has been used there is probably retention of secretions in the bronchi.

To prevent this prohibitively high complication rate all patients with abdominal aneurysm should be investigated for the presence of a peptic ulcer, and if an ulcer is found there appear to be two possibilities regarding management. Either the ulcer is dealt with first, in most cases by vagotomy and drainage, and the aorta resected at a later date, or both conditions are treated at the same time. If the first alternative is preferred then an often elderly patient is subjected to two major operations with the cumulative risk of each. In addition, the aneurysm may rupture in the waiting period. If the second alternative is adopted the magnitude of the operation is increased and the risk of sepsis possibly increased. As to the danger of sepsis, it has certainly been our practice that surgery of the colon or small intestine should never be undertaken when an aortic graft is to be used, and indeed we would abandon the operation if this part of the intestine were accidentally injured during exposure. When concerned with a duodenal ulcer, however, it seems to us safe to do a vagotomy and pyloroplasty at the time of operation on the aorta, particularly as such leakage as occurs from the pyloroplasty is probably not infective. We have in fact for some years been doing a gastrostomy in every patient after transperitoneal, aortic, or aorto-iliac surgery to avoid the use of a nasogastric tube and have had no cause to regret this measure (*Fig.* 1). In one instance some years ago we did a gastrectomy without complication, and recently in 3 patients with an aortic aneurysm and a duodenal ulcer, after completing the aortic reconstruction, we have carefully replaced the apron of the stomach, colon, and omentum to cover the operation field and have then done a vagotomy and pyloroplasty together with a gastrostomy using a balloon catheter. In these 3 patients convalescence was smooth. We admit that sometimes, because of difficulties during the aortic reconstruction, the surgeon may feel that the added risk of vagotomy and pyloroplasty would outweigh the risk of complication of the ulcer in the early period after operation, when he will act accordingly.

It is interesting that of the 300 operations for arteriosclerotic aorto-iliac stenosis which we have previously reported (Bouhoutsos and others, 1972), there were only 2 fatal complications from peptic ulcer, though the incidence of ulcer is the same in this group as it is in the aneurysm group. This may be because operations for stenosis are usually of a lesser magnitude than those for aneurysm, and indeed many are done by a retroperitoneal approach with little disturbance to the patient.

We believe, therefore, that it is necessary, and is at present our practice, to treat a patient with such dual pathology by vagotomy and pyloroplasty and a gastrostomy at the same operation as that for the aortic reconstruction, though we are hesitant in advising a gastrectomy in such circumstances.

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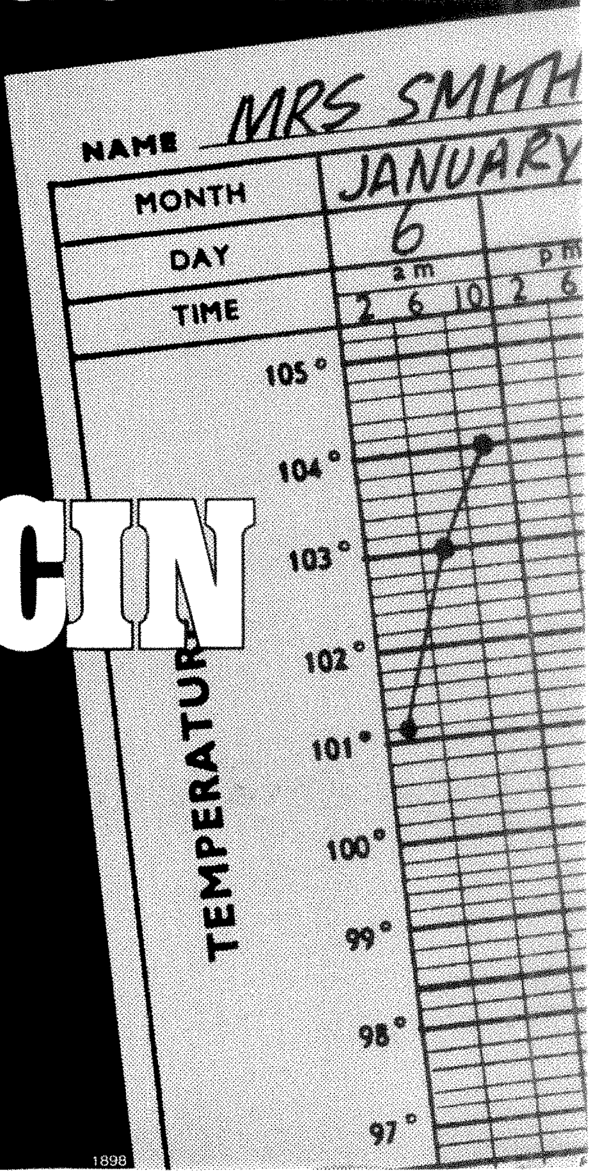

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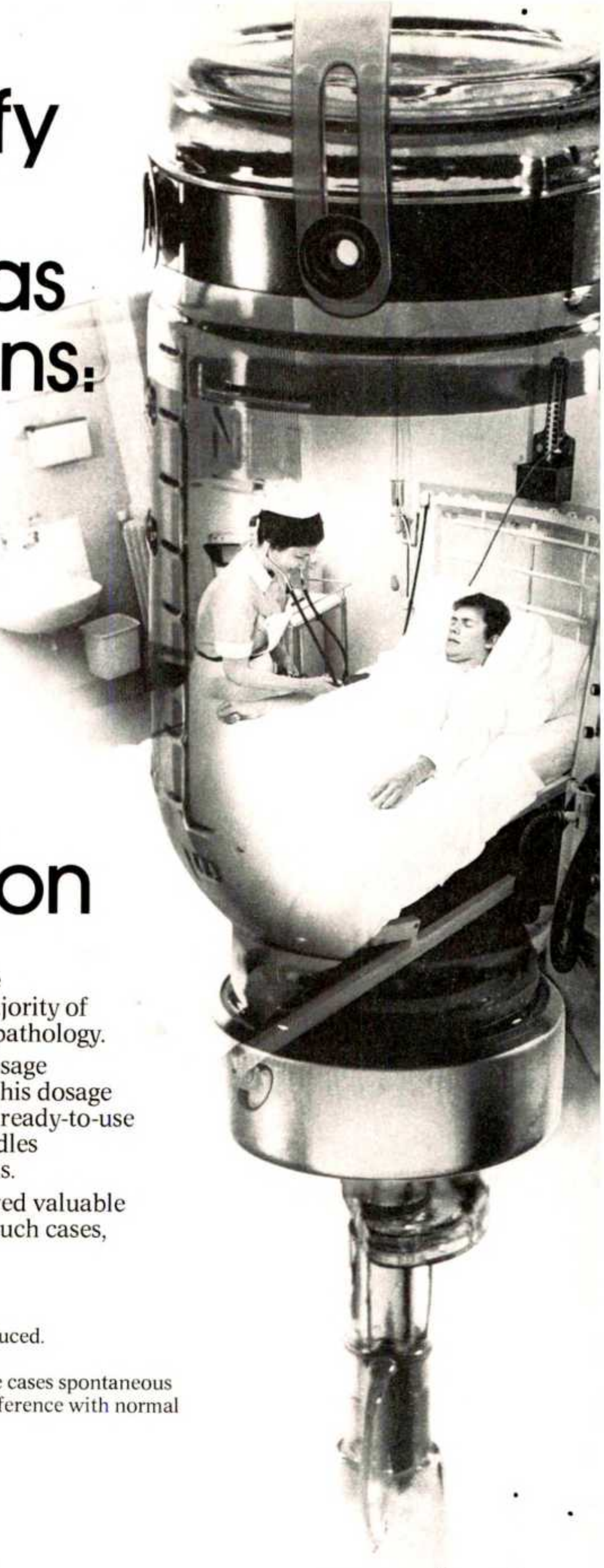

Pyopen infusion

In the published papers, Pyopen's success rate in chest infections is 65% even though the majority of the patients described had severe underlying pathology.

The best results have been achieved with a dosage of 20-30G. I.V. daily. Pyopen infusion makes this dosage simpler to administer by providing Pyopen in ready-to-use infusion bottles with diluent and transfer needles for the easier preparation of infusion solutions.

Pyopen is, of course, a penicillin, and has proved valuable in patients with known renal impairment: in such cases, however, dosage should be reduced.

Adult dosage: 20-30G. I.V. daily.
In patients with renal impairment dosage should be reduced.
Contra-indications: Penicillin hypersensitivity.
Side-effects: As with other injectable penicillins. In rare cases spontaneous skin and mucous membrane haemorrhages due to interference with normal clotting mechanisms have been reported.

Pyopen

Further information is available on request.
Pyopen* (carbenicillin sodium B.P.) is a British product originated by
Beecham Research Laboratories, Brentford, England. *regd.

SURGICAL RESEARCH SOCIETY

A meeting of the Surgical Research Society was held in the University College Hospital Medical School, London, on 5 and 6 January, 1973, with Professor L. P. LeQuesne (President of the Surgical Research Society) in the Chair. The following papers were presented:—

1. Effect of Aortocoronary By-pass Graft on Graded Anginal Symptoms, Exercise Performance, and Left Ventricular Function:

S. E. P. MILLER and W. D. JOHNSON (P. R. F. Bell), Medical College of Wisconsin, Milwaukee, and Western Infirmary, Glasgow.

Myocardial revascularization by reversed saphenous vein by-pass graft (R.S.V.B.G.) between the aorta and coronary arteries distal to atheromatous obstruction is reported to alleviate symptoms of angina pectoris. This study attempts to correlate changes in exercise performance, ventricular function, and graft patency with symptomatic improvement following surgery.

Seventy-eight patients with graded anginal symptoms were assessed pre- and postoperatively and symptomatic change was correlated with vein patency. Twenty-five of these patients were further studied by bicycle ergometry and left-heart catheterization, and assessed as to exercise performance and ventricular function.

Following R.S.V.B.G. 56 of the 78 patients (72 per cent) became asymptomatic and 21 improved. All the grafts were patent in 52 cases (67 per cent), all were closed in 6 (7·7 per cent), and in 20 patients (23·3 per cent) one or more but not all the grafts were closed. Of the 25 patients who were studied further, all showed increased exercise performance postoperatively. This was less pronounced in those with closed grafts, where angina was improved but fatigue and dyspnoea were marked.

The cardiac index (C.I.) increased at rest in some patients and with exercise in others, but no distinct pattern emerged. The left ventricular end-diastolic pressure (L.V.E.D.P.) which had been abnormally elevated in 6 patients at rest preoperatively returned to normal in 5 cases. With exercise, 23 patients had had an elevated L.V.E.D.P. which was reduced significantly in all cases. Systolic ejection fraction (S.E.F.) was significantly increased in 17 patients (68 per cent) postoperatively and reduced in 4 (16 per cent), all of whom had closed grafts.

2. Aberrant Positions of Central Venous Catheters:

A. O. B. JOHNSTON and R. G. CLARK, Department of Surgery, University of Sheffield.

Central venous catheters are used increasingly for monitoring central venous pressure and administering hypertonic nutritional solutions. It is known that incorrectly positioned catheter tips can cause serious complications—perforation of the myocardium (Brandt et al., 1970) and extensive thrombophlebitis. Langston (1971) stated that the catheter tip should be positioned in the superior vena cava or innominate veins if complications are to be minimized. All other positions are considered incorrect.

This study reports the radiological position of the catheter tip following 75 consecutive catheterizations performed by one operator under standard conditions. A radio-opaque 61-cm. Bardic Intracath was inserted via the cubital fossa. When the catheter was assessed clinically to be positioned correctly a radiograph was taken. In 39 patients the tip was found to be in the superior vena cava, and in the innominate vein in 8. Aberrant positions included 10 in the atrium, 12 in the internal jugular vein, and 4 in the subclavian vein. All the catheters found to be in an aberrant position were immediately repositioned. In this series no complication resulted from the catheter initially being positioned incorrectly.

It is concluded that radiographic control is essential for accurate positioning.

BRANDT, R. C., FOLEY, W. J., FINK, G. H., and REGAN, W. J. (1970), *Am. J. Surg.*, **119**, 311.
LANGSTON, C. S. (1971), *Radiology*, **100**, 55.

3. A Healing Bond between Tissues and a Smooth Synthetic Polymer:

M. E. B. JONES and DAVID ANNIS, University of Liverpool Medical School, Liverpool.

Since the normal process of healing does not result in the bonding of surrounding tissue to an implanted, smooth, synthetic surface the permanent location of internal prosthetic devices is dependent upon tissue ingrowth into porous or woven structures on the surface of the device. The object of this investigation was to look for surface factors of synthetic materials which could influence tissue bonding to smooth surfaces.

Contact-angle measurements on collagenous tissues, taken from various locations in a number of animals, showed that their surface energies (Y_s) differed in three important respects from the surface energies of conventional plastic materials used for the construction of implants:—

1. Tissue-surface energy is significantly higher.
2. The contribution of the two components of surface energy (Y_s^h and Y_s^d) is inverted, i.e., $Y_s^h > Y_s^d$ for collagenous tissues, and $Y_s^h < Y_s^d$ for most synthetic polymers.
3. Dehydration lowers the surface energy of these tissues.

A range of three copolymers was prepared from poly-(ethylene glycol) and poly(ethylene terephthalate) and the composition adjusted until the surface energy matched that of collagenous tissue. Across this range the effect of progressive changes in the surface energy of these copolymers on the healing/bonding process was examined by subcutaneous implants in rats. These showed that limited bonding occurred above a certain surface energy and that bond strength increased as it approached that of collagenous tissue.

The bond of living tissue directly to a synthetic polymer opens up many applications in prosthetic surgery.

4. A Clinical Trial of Treatment in Early Breast Cancer:

M. MAUREEN ROBERTS, MARION DAVIES, M. HENK, A. P. M. FORREST, L. H. BLUMGART, E. N. GLEAVE, C. W. JAMIESON, M. HULBERT, and H. CAMPBELL, Welsh National School of Medicine and St. Mary's Hospital, London.

Since 1967 a controlled, randomized clinical trial has been carried out to compare a conservative with a radical policy of treatment in early breast cancer.

Patients selected for conservative treatment underwent simple mastectomy with removal of the axillary tail of the breast and its associated pectoral nodes, but the contents of the axilla were left undisturbed. If the nodes did not contain tumour no further treatment was given. Those selected for radical treatment underwent mastectomy and axillary clearance, with radiotherapy when there was histological evidence of spread to the axillary nodes.

To date, 116 patients have been treated by the conservative method and 111 by the radical policy. Over the period of follow-up no differences have emerged between the treatment groups in terms of death or recurrence rates. Axillary recurrence was found in 5 of the 71 patients treated by simple mastectomy alone, giving a false-negative histological stage I of 5 per cent. This compares favourably with our clinical staging error of 40 per cent.

The low rate of recurrence together with the significantly decreased morbidity of conservative as compared with radical treatment already reported indicate that simple mastectomy alone is an adequate form of treatment for breast cancer when the tumour is known to be limited to the breast. We emphasize the need for histological proof of the state of the axillary nodes, as disease, if present, should be treated.

5. 'Early' Breast Cancer, Bone Scanning, and the Urinary Excretion of Hydroxyproline: D. S. Sumner, M. Baum, V. Parsons, and M. H. Edwards, Department of Surgery, King's College Hospital Medical School, London.

Galasko (1969) showed that many patients with apparently localized cancer of the breast had widespread unsuspected bony metastases which could be detected by scintiscanning of the skeleton. The technique unfortunately requires expensive equipment and is not universally available. A cheaper and simpler way to select these patients with disseminated disease and to save them from extensive radical treatment was suggested by Cuschieri and Felgate (1972). They found that urinary hydroxyproline was increased in some patients with breast cancer 2 years before metastases became apparent.

We have investigated bone scanning and its relationship to urinary hydroxyproline excretion in 112 patients. The patients were grouped as follows:—

Group I: 37 patients with benign breast disease.

Group II: 45 patients with early breast cancer and a normal scan.

Group III: 17 patients with early breast cancer and an abnormal scan.

Group IV: 11 patients with widespread disease.

The results were:—

Group	Total Hydroxyproline (mg. per 24 hr. ± S.D.)	Significance to Group above
I	22·4 ± 9·5	
II	20·8 ± 8·4	$P > 0·05$
III	32·3 ± 9·2	$P < 0·001$
IV	47·9 ± 12·6	$P < 0·001$

The urinary hydroxyproline level is elevated significantly when bony metastases are present.

Cuschieri, A., and Felgate, R. A. (1972), *Br. J. exp. Path.*, **53**, 237.

Galasko, C. S. B. (1969), *Br. J. Surg.*, **56**, 757.

6. The Relationship between Leg-vein Thrombosis and Pulmonary Emboli at Autopsy: M. Tessa Morrell, Nuffield Department of Surgery, Radcliffe Infirmary, Oxford.

Ignorance of the actual risk of pulmonary embolism in patients with venous thrombosis has resulted in some uncertainty in the need for treatment in every case.

The statistical relationship between thrombosis and embolism was studied at autopsy. The right lung and soft tissues of both legs were removed from each of 52 patients; the leg tissues were fixed in formol–saline, the lung was distended with and fixed in formol–saline, and both were sliced transversely at 1-cm. intervals. Suspected thrombi were examined histologically.

Of 33 patients with venous thrombi, 22 (66 per cent) had pulmonary emboli; 8 died of the emboli, 6 having had a good original prognosis. The incidence of embolism was greatest (18 in 23) when the longitudinal leg veins were thrombosed and least (4 in 10) when thrombi were confined to the calf tributaries. Death from embolism occurred in 6 out of 12 patients with femoro-iliac vein thrombosis but in none with only distal vein involvement. The relationship between thrombosis and embolism was independent of age and type of operation.

It is concluded that every patient with a diagnosis of thrombosis should be treated, as involvement of the longitudinal leg veins carries a high risk of pulmonary embolism.

7. The Action of Gastro-intestinal Polypeptide Hormones on the Isolated Perfused Gastro-oesophageal Sphincter: P. A. Thomas, and R. J. Earlam, Surgical Unit, the London Hospital.

An isolated preparation of the canine stomach and oesophagus perfused with autologous blood under controlled physiological conditions (Thomas and Earlam, 1972) has been used to study the direct effects of polypeptide gastro-intestinal hormones on the gastro-oesophageal sphincter. The hormones tested were gastrin I and II, cholecystokinin (CCK), caerulein, secretin, and glucagon. In the human, gastrin has already been shown to increase sphincter pressure and secretin to reduce it (Cohen and Lipshutz, 1971). The hormones were administered into an artery either as a bolus dose or as a continuous infusion. Bolus doses of gastrin I and II (1 μg.), CCK (10 Ivy units), and caerulein (12·5 μg.) all produced a rise in sphincter pressure as did a continuous intra-arterial infusion. These responses were abolished by atropine. Bolus doses of secretin (5 units) and glucagon (25 μg.) produced a fall in sphincter pressure. Continuous intra-arterial infusion had a similar effect. These results demonstrate that in this preparation the polypeptide gastro-intestinal hormones can be divided into two groups on the basis of their pharmacological action. The C-terminal related hormones produced a rise in sphincter pressure but secretin and glucagon reduced the pressure.

Cohen, S., and Lipshutz, W. (1971), *J. clin. Invest.*, **50** 449.

Thomas, P. A., and Earlam, R. J. (1972), *J. Eur. surg Res.*, **4**, 357.

8. The Bacterial Flora of the Upper Gastro-intestinal Tract in Relation to Gastric Secretion and to Bowel Habit following Vagotomy and Pyloroplasty: S. T. D. McKelvey, W. P. Ferguson and T. L. Kennedy, Department of Surgery Queen's University of Belfast.

Diarrhoea following vagotomy has been attributed to loss of the gastric acid trap, thus allowing passage of infective material into the intestine (Dragstedt, 1966) This paper reports quantitative bacterial counts of the gastric, duodenal, and jejunal juice following vagotomy.

Thirty-four patients were studied more than 1 year following vagotomy and pyloroplasty. Seventeen of these patients were undergoing investigation for episodic postvagotomy diarrhoea. The control group consisted of 17 patients with satisfactory bowel habit since vagotomy and pyloroplasty.

The resting juice in the stomach and duodenum wa cultured after aspiration through a double-lumen tub which had been positioned under fluoroscopic control. At the same intubation an insulin study was performed and analysed by the criteria of Hollander. On a separate occasion the resting juice in the upper jejunum was sampled using a specially devised capsule (Shiner, 1963).

The resting gastric juice contained heavy counts of nasopharyngeal organisms but colonic-type organisms were found infrequently. A similar pattern was found in duodenal and jejunal juice. Asymptomatic patients did not differ from those with diarrhoea. Colonization of the gut was heavier if the vagotomy was complete.

Vagotomy leads to colonization of the upper gastro-intestinal tract but this is not causally related to the occurrence of postvagotomy diarrhoea.

Dragstedt, L. R. (1966), *Surg. Clins N. Am.*, **46**, 1153.
Shiner, M. (1963), *Lancet*, **1**, 532.

9. Effects of Varying the Extent of Vagotomy on the Myoelectrical and Motor Activity of the Stomach in Man:

C. J. Stoddard, B. H. Brown, G. E. Whittaker, W. E. Waterfall, and H. L. Duthie, Medical Physics and Surgery Departments, University of Sheffield.

Transthoracic vagotomy in dogs is followed by temporary disorganization of the electrical activity in the stomach (Kelly and Code, 1969). The aim of this study was to assess the changes in electrical activity and gastric motility in man following truncal (T.V.), selective (S.V.), or highly selective vagotomy (H.S.V.) for the treatment of duodenal ulcer.

Nineteen conscious patients were studied 5 days post-operatively using electrodes mounted on a gastric tube and sucked on to the mucosa of the gastric antrum. Motility was measured via an open-tipped tube and gastric secretion was aspirated continuously. In 12 patients, after a control period of 1 hour, insulin, 0·2 U. per kg., was given intravenously. All the patients had a negative gastric secretory response to insulin.

The regular 3-per-minute rhythm of the electrical activity was maintained after H.S.V. with a normal peaked wave-form. After T.V. the rhythm was disorganized with occasional periods of 2–15 minutes of regular 3-per-minute activity with a sinusoidal wave-form. Patients after S.V. showed intermediate findings. Insulin hypoglycaemia did not alter these patterns except to increase the amplitude of the electrical waves and the incidence of action potentials. The disorganization of the electrical activity of the gastric antrum is related to the extent of vagal denervation.

Kelly, K. A., and Code, C. F. (1969), *Gastroenterology*, **57**, 51.

10. An Assessment of Clinical Tests of Gastric Emptying before and after Operation:

I. F. Gunn, K. D. Harding, Anne Brown, and J. Alexander Williams, The General Hospital, Birmingham.

In previous studies a correlation has been shown between dumping after vagotomy with pyloroplasty and rapid initial emptying from the stomach of a 10 per cent dextrose solution (Clarke and Williams, 1972). As the use of a fluid meal can be criticized in that it is unphysiological we have compared the emptying of a fluid meal with scintiscanning of a solid meal labelled with indium 113m (Harvey et al., 1970). Patients have been studied by both methods before and after different operations for duodenal ulcer.

Preoperatively the liquid meal had emptied more rapidly than the solid meal at 10 minutes ($P<0·01$) but by 20 minutes the emptying patterns were not significantly different. The regression line between the 50 per cent emptying times of the two methods shows good correlation ($r = 0·572$, $P<0·05$). Application of the paired *t*-test to 50 per cent emptying times shows there is no significant difference ($P>0·2$) between values for the two methods. After operation the rapid initial emptying found with a liquid meal is not reflected in the solid-meal patterns.

Although emptying of a solid meal after gastric operation is the more physiological, the fluid-meal test is better able to demonstrate differences between operations and may correlate better with the clinical symptoms of dumping.

Clarke, R. J., and Williams, J. A. (1972), *Br. J. Surg.*, **59**, 903.
Harvey, R. F., Mackie, D. B., Brown, N. J. G., Keeling, D. H., and Davies, W. T. (1970), *Lancet*, **1**, 16.

11. Gastric Emptying of a Solid Meal after Long and Short Pyloroplasties:

W. D. George, C. R. Royston, D. J. Cowley, and J. Spencer, Department of Surgery, Royal Postgraduate Medical School, London.

Symptoms of delayed gastric emptying commonly follow vagotomy and pyloroplasty, possibly owing to pyloric narrowing. Gastric emptying of solid meals has been studied in a randomized controlled clinical trial of selective or truncal vagotomy with either a short Heineke-Mikulicz pyloroplasty or a long Finney pyloroplasty, and compared with a control group of 17 patients with no gastro-intestinal disease. Emptying was measured by the modified gamma-camera technique (Cowley et al., 1972) and the results were expressed in half-emptying times ($T_{\frac{1}{2}}$).

The control group (17) had a mean $T_{\frac{1}{2}}$ of 85 ± 7·1 minutes.

Thirty-seven patients were studied; in 26 emptying times were measured 10–22 days after operation (mean 14 days), and in 24 at 4–6 months (mean 5·3 months). At 10–22 days after operation the mean $T_{\frac{1}{2}}$ was 364 ± 34 minutes in 15 patients with a Finney pyloroplasty and 332 ± 47 minutes in 11 patients with a Heineke-Mikulicz pyloroplasty. At 4–6 months postoperatively the mean $T_{\frac{1}{2}}$ was 146 ± 54 minutes in 13 patients with a Finney pyloroplasty and 150 ± 24 minutes in 11 patients with a Heineke-Mikulicz pyloroplasty. No difference in emptying was found between truncal or selective vagotomy. There was no relationship between the incidence of diarrhoea and abnormalities in gastric emptying. The slowing of gastric emptying was identical after long and short pyloroplasties.

Cowley, D. J., Vernon, P., Jones, T., Glass, H. I., and Cox, A. G. (1972), *Gut*, **13**, 176.

12. A Study of the Relationship between the Rate of Gastric Emptying and the Dumping Syndrome in Patients after Vagotomy and Drainage:

S. Haynes, J. P. S. Thomson, N. Brown, and D. H. Keeling (L. P. Le Quesne), The Department of Surgical Studies and Institute of Nuclear Medicine, The Middlesex Hospital Medical School, London.

Whilst it is widely accepted that the dumping syndrome is associated with rapid gastric emptying this relationship has not been clearly established. An investigation has been performed to determine the relationship between the rate of gastric emptying, the occurrence of dumping symptoms, and the changes in plasma volume following a hypertonic glucose meal (200 ml. of a 50 per cent solution). Gastric emptying was measured isotopically by labelling the meal with Indium 113m (1 m.c.) and using a gamma camera. The symptoms occurring during the test were noted and changes in plasma volume were indicated by serial measurements of the haematocrit.

Fourteen patients with duodenal ulcer were studied preoperatively and 29 after vagotomy (selective 16, truncal 13) and drainage (Heineke-Mikulicz pyloroplasty 14, gastroduodenal 5, gastrojejunal 10). The average initial (2–10 minutes) rate of gastric emptying in preoperative patients (0·8 per cent per minute) was not significantly different to that in 12 postoperative patients *without* dumping symptoms (1·2 per cent per minute), whereas the rate in 17 patients *with* dumping symptoms (5·2 per cent per minute) was significantly faster ($P < 0\cdot001$).

In the postoperative patients there was a significant correlation between the rates of initial gastric emptying and of plasma-volume fall ($r = 0\cdot67$, $P < 0\cdot001$).

13. Plasma Enteroglucagon and Plasma-volume Changes after Oral Hypertonic Glucose—Their Relationship to the Dumping Syndrome: J. P. S. Thomson, S. R. Bloom, S. Haynes, and O. Ogawa (L. P. Le Quesne), Department of Surgical Studies and Institute of Clinical Research, The Middlesex Hospital Medical School, London.

After partial gastrectomy (Marco et al., 1972) or vagotomy and drainage (Bloom et al., 1972) oral hypertonic glucose provokes a greater rise in plasma enteroglucagon than preoperatively. The magnitude of the rise is related to dumping symptoms (Bloom et al., 1972). To study these relationships further a hypertonic glucose meal (200 ml. of a 50 per cent solution) was administered and the plasma enteroglucagon was measured by radioimmunoassay and the plasma-volume changes were calculated from serial haematocrit estimations.

The mean rate of rise of plasma enteroglucagon in 14 duodenal ulcer patients preoperatively was 1·6 femtomole per ml. per minute. In studies in 42 postoperative patients (partial gastrectomy 13, vagotomy and drainage 29) the glucose provoked dumping symptoms in 26, the mean rate of fall in plasma volume in these patients (0·43 per cent per minute) being significantly greater than that in 16 patients without such symptoms (0·17 per cent per minute) ($t = 6\cdot76$, $P < 0\cdot001$). In the patients *without* dumping symptoms the rate of rise of plasma enteroglucagon (4·15 femtomole per ml. per minute) was significantly faster than in preoperative patients ($t = 2\cdot69$, $P < 0\cdot02$), while in patients *with* dumping symptoms the rate of rise (13·83 femtomole per ml. per minute) was significantly faster than in those without such symptoms ($t = 7\cdot21$, $P < 0\cdot001$).

In all the patients the rates of plasma-enteroglucagon rise and of plasma-volume fall correlated closely ($r = 0\cdot86$, $P < 0\cdot001$).

Bloom, S. R., Royston, C. M. S., and Thomson, J. P. S. (1972), *Lancet*, **2**, 789.

Marco, J., Baroja, I. M., Diaz-Fierros, M., Villanneva, M. L., and Valverde, I. (1972), *J. clin. Endocr. Metab.*, **34**, 188.

14. Mechanism of Raised Serum Alkaline Phosphatase in Some Liver Disorders in the Baboon: J. Jersky (D. J. du Plessis), Department of Surgery, University of the Witwatersrand, Johannesburg, South Africa.

Liver extracts were assayed for alkaline phosphatase (Engstrom, 1964). In orthotopic liver transplants an increase (from 4 to 20 King-Armstrong units per g. of liver tissue) in liver-type isoenzyme accompanied rejection and in auxiliary liver transplants similar increases were seen in both the donor and recipient livers when the former was rejected. As the rise in alkaline phosphatase in the recipient liver could be explained either by increased local production or by accumulation from the donor liver the following experiment was performed.

An auxiliary liver was removed 5 days after insertion, by which time it was being rejected. Radioactive leucine was then injected into the animal, which was killed 24 hours later. Using a specific antibody, alkaline phosphatase was extracted from the recipient liver; a fourfold increase in radioactivity confirmed increased local production.

In separate experiments a single hepatic duct of a normal liver was ligated. Both the obstructed and unobstructed lobes produced an excess of alkaline phosphatase.

Thus, in these two situations the increased serum alkaline phosphatase of liver disease is due to increased hepatic production of the enzyme and not to failure of excretion. A humoral stimulator seems to play a role in this phenomenon.

Engstrom, L. (1964), *Biochim. Biophys. Acta*, **92**, 71.

15. Rate of Blood-loss estimated by an Isotope-dilution Method: J. M. T. Griffiths, W. B. Clark, and A. N. Smith, Department of Clinical Surgery, University of Edinburgh, and Edinburgh Northern Hospital Group.

Serial blood-volume estimations using standard isotope-dilution methods are highly inaccurate in haemorrhage. Important factors are the loss of isotope, its sequestration in the circulatory bed, and its artificial dilution by simultaneous replacement therapy; repeated doses of isotope cause high background radiation which progressively increases the error. An equation was derived to overcome these difficulties, integrating mathematically the apparent blood-volume, for the theoretical measurement of the amount and rate of haemorrhage from a concealed source using a single dose of isotope:—

$$Vc = I_t \frac{1}{Vb/Va - 1},$$

where Vc = initial blood-volume minus the amount of blood loss in time t, Va the initial blood-volume, and Vb the apparent blood-volume after time t; I = infusion volume (ml.) in time t.

The validity of the method has been examined in two groups of experiments as follows:—

1. Using a model, a measured 'blood loss' was compared with a computed one; in 8 experiments, with initial 'blood-volumes' varying from 2·0 to 5·5 litres, the results verified the equation.
2. The method was applied to 6 female baboons under phencyclidine anaesthesia. Controlled measured haemorrhages were produced from the femoral artery. The error in the computed blood-volume (Vc) varied from 0 to 17·6 per cent with a mean overestimation of the initial volume remaining of 4·4 per cent.

16. A Circulating Myocardial Depressant Factor after Shock: W. D. Fisher, C. S. McArdle, M. Maddern, and I. McA. Ledingham, University Departments of Surgery and Orthopaedics, Western Infirmary, Glasgow.

A myocardial depressant factor has been demonstrated in the plasma of animals and patients following experimental and clinical shock respectively (Lefer, 1970; Lovett et al., 1971). The present study is an attempt to confirm this important observation using a modified assay with guinea-pig atrium.

Two groups of 6 greyhounds were subjected to haemorrhagic hypotension for 1 and 3½ hours. Plasma ultrafiltrates were prepared and were found to depress contractions of guinea-pig atrium from 15 ± 2 per cent preshock to 45 ± 4 per cent after 1 hour of hypotension ($P < 0\cdot001$). Following 3½ hours of hypotension significantly more depression was shown (73 ± 4 per cent; $P < 0\cdot005$), corresponding to the appearance of impaired cardiac function in the dogs. Further purification of plasma ultrafiltrates on gel chromatographic columns demonstrated the appearance of a peak of molecular weight 500–700 which appeared to contain most of the depressant activity.

The ultrafiltrates of plasma from 12 patients suffering from haemorrhagic endotoxic and cardiogenic shock were also assayed. Significantly greater depression ($P < 0\cdot05$) occurred in 7 patients dying from heart failure (56 ± 6 per cent) than in the 5 patients who survived (31 ± 11 per cent). These results support the view that a low-molecular-weight compound with cardiotoxic effects appears in the circulation after shock.

LEFER, A. M. (1970), *Fedn Proc. Fedn Am. Soc. exp. Biol.*, **29**, 1896.
LOVETT, W. L., WANGENSTEEN, S. L., GLENN, T. M., and LEFER, A. M. (1971), *Surgery, St Louis*, **70**, 223.

17. Urinary Losses of Intravenous Nutrients:

A. E. B. GIDDINGS, A. O. B. JOHNSTON, and R. G. CLARK, Department of Surgery, University of Sheffield.

Urinary losses of carbohydrate and amino acids were measured in 40 patients receiving parenteral nutrition during 4 postoperative days. In 20 patients (trial I) sorbitol and a *d*/*l*-amino-acid mixture (Trophysan Conc. 10) were given, while the other 20 patients received (trial II) sorbitol, fructose, and an *l*-amino-acid mixture (Vamin). A range of caloric intake from 12 to 51 Cal. per kg. per day was used within each trial. Nitrogen, fluid, and electrolyte intakes were related to body-weight.

Up to 8–13 per cent of infused sorbitol and 1–3 per cent of fructose were lost in the urine. Increased osmolar loading with sorbitol did not alter total urine osmolar output or volume. There was no change in sodium or potassium balance at higher osmolar intakes.

In trial I amino-acid losses were 7–12 per cent, and in trial II 2–6 per cent of the amount given was lost ($P < 0\cdot001$). In both groups the amounts lost were greater than those in control patients, who showed a small postoperative increase. Increased losses of infused amino-acids occurred in patients receiving the *d*/*l* mixture. The capacity of glycine to interfere with tubular reabsorption (Handler et al., 1949) may account for these higher losses.

Urinary losses reduced effective daily intake in a 70-kg. man by 210 Cal. and 2 g. of nitrogen per day.

HANDLER, P., KAMIN, H., and HARRIS, J. S. (1949), *J. biol. Chem.*, **179**, 283.

18. Insulin Secretion and Glucose Tolerance during and after Surgical Operation:

P. D. WRIGHT and I. D. A. JOHNSTON, Department of Surgery, University of Newcastle upon Tyne.

Glucose utilization becomes less efficient and plasma-insulin levels rise in the postoperative period or after injury (Bernard, 1877; Allison et al., 1969). A study was planned to examine the time of onset of these changes during surgery of varying degrees of severity. Plasma-glucose, insulin, and cortisol levels were measured in three groups of 6 patients undergoing (1) inguinal herniorrhaphy, (2) vagotomy and pyloroplasty, and (3) aortofemoral by-pass grafting.

Intravenous glucose-tolerance tests (25 g.) were performed before operation, during operation, and on four occasions in the first 8 postoperative days. Glucose-utilization coefficients (K values) were calculated and showed significant depression of glucose tolerance during the time of operation ($P < 0\cdot005$). Normal levels were restored by the eighth day. The depression of glucose tolerance was greatest on the third postoperative day in the major surgery group compared with the minor surgery groups ($P < 0\cdot025$). Insulin secretion was significantly depressed in all the groups during operation ($P < 0\cdot01$). Following operation secretion was enhanced ($P < 0\cdot025$), indicating insulin resistance.

Glucose tolerance is depressed following surgery, the degree of depression varying with severity of operation. Insulin secretion is suppressed during surgery and is later enhanced, suggesting later insulin antagonism.

ALLISON, S. P., CHAMBERLAIN, M. J., and HINTON, P. (1969), *Br. med. J.*, **4**, 776.
BERNARD, C. (1877), *Leçons sur le Diabété et la Glycogenèse Animal*, p. 210. Paris: Baillière.

19. The Effect of Thyroid Status on Nitrogen Balance and the Rate of Wound Healing after Injury in Rats:

J. LENNOX and I. D. A. JOHNSTON, Department of Surgery, University of Newcastle upon Tyne.

The relationship between post-traumatic changes in thyroid activity, the metabolic response (Harland et al., 1972), and wound healing is uncertain. Wound healing rates (Cuthbertson et al., 1941) and the tensile strength of wounds using Sandblom and Peterson's tensiometer were measured in rats with varying levels of thyroid activity.

Three groups of 10 rats were used. After total thyroidectomy one group was given thyroxine in high dosage; the second group received nothing and were hypothyroid. The third group underwent sham surgery and were used as controls.

Wound healing was accelerated by a mean of 2·5 days ($P < 0\cdot001$) in the hyperthyroid group and delayed by a mean of 2·0 days ($P < 0\cdot001$) in the hypothyroid group with reference to the control groups. The tensile strength of linear wounds was significantly greater at 10 days in the hyperthyroid group. The mean basal nitrogen turnover was 99·3 ± 8·9 mg. nitrogen per 100 g. rat in the hypothyroid group, 105·9 ± 4·4 mg. nitrogen in the control group, and 155·6 ± 8·8 mg. nitrogen in the hyperthyroid group. Following trauma the increase in nitrogen excretion was less in the hypothyroid group and greater in the hyperthyroid group compared with the control group.

There is a significant correlation between tensile strength of wounds and basal nitrogen turnover which may be related to thyroxine activity.

CUTHBERTSON, D. P., SHAW, G. B., and YOUNG, F. G. (1941), *J. Endocr.*, **2**, 475.
HARLAND, W. A., ORR, J.-S., and RICHARDS, J. R. (1972), *Scot. med. J.*, **17**, 92.

20. Coronary Vein Perfusion as an Alternative Method for ameliorating Ischaemic Changes in Experimental Animals:

I. A. SALLAM, W. H. BAIN, and W. J. KOLFF, Division of Artificial Organs, University of Utah, Salt Lake City, United States.

The possible augmentation of obstructed coronary blood-flow by utilizing the coronary vein instead of the artery was investigated. Studies were made in 10 anaesthetized animals. Myocardial ischaemia was established by ligating the left anterior descending coronary artery. In 8 animals ischaemic changes were evident electrocardiographically. Retrograde perfusion of the coronary vein with the internal mammary artery was accomplished either by direct end-to-side anastomosis or by the interposition of a Teflon cannula. The vein was ligated proximally. When perfusion of the coronary vein was begun signs of ischaemia disappeared over a period of 12–25 minutes but could be reproduced by clamping the internal mammary artery.

Previous attempts to utilize the coronary vein have been described by Beck in 1948, where a vein-graft was placed between the aorta and coronary sinus as a first stage, followed a month later by a second-stage operation in which the coronary sinus was removed. The high mortality-rate made such procedures unacceptable. The present approach differs in that it only utilizes the part of the vein involved in the ischaemic area and it establishes a retrograde perfusion. This may offer new prospects in patients in whom neither available surgical nor medical treatment proves to be of value and includes patients in whom the coronary artery is not suitable for coronary by-pass grafts owing to extensive diffuse narrowing or those patients presenting with cardiogenic shock after myocardial infarction.

Beck, C. S. (1948), *J. Am. med. Ass.*, **137**, 436.

21. Observer Variation in Clinical Diagnosis: Its Magnitude and Importance in Patients with Acute Abdominal Pain:

F. T. de Dombal, P. W. Gill, D. J. Leaper, Jane C. Horrocks, J. R. Staniland, and P. J. Guillou, University Department of Surgery, University of Leeds.

This report describes an evaluation of 'observer variation' in history taking and examination of patients with abdominal pain. Initial studies confirmed previous gloomy predictions. When 3 observers recorded data from a (fourth) clinician's patient interview there was a 20 per cent disagreement amongst them as to whether individual questions had been asked or not, and an 18 per cent disagreement as to whether the patient's response indicated any abnormality.

Following this initial experience a system of 'agreed definitions' was produced. Further studies using this system showed a rapid and considerable fall in the degree of observer variation between the data recorded by the same 3 observers, from just under 20 per cent to around 4 per cent in a series of 10 cases. Moreover, a fourth observer in a further series of cases rapidly achieved comparable levels of agreement with the original team. Finally, experience with a computer-aided diagnostic system using the same 'agreed definitions' scheme for entering data into the computer showed the rate of diagnostic error due to inadequate data acquisition to be low (4·8 per cent in a series of 500 cases).

It is suggested that observer variation in recording data from patients with acute abdominal pain is considerable, but that by using a system of carefully agreed definitions, 'faulty' data acquisition need not be the prime cause of errors in diagnosis.

22. Abnormal Detrusor Function in Asymptomatic Diabetes:

A. C. Buck, C. U. McRae, and P. I. Reed (G. D. Chisholm), Urological Unit, Department of Surgery, Hammersmith Hospital and Royal Postgraduate Medical School, London.

Abnormalities of bladder function in diabetes are considered to be a late manifestation of diabetic neuropathy. In a review of 3000 diabetic patients the incidence of neuropathy was 7 per cent, of which 25·6 per cent exhibited bladder dysfunction (Rundles, 1945). A higher incidence of bladder dysfunction is now recognized and in a selected group of asymptomatic juvenile diabetics the incidence was 87 per cent (Faerman et al., 1971).

In this study 25 diabetic patients who were free of urinary symptoms were studied by urodynamic techniques. The following measurements were made: (1) urinary flow rate, (2) residual urine volume, (3) cystometry, and (4) bladder capacity. Bladder sensation in relation to bladder capacity was recorded.

The results showed that 24 patients (90 per cent) had normal flow rates and residual urine volumes, but 17 patients (68 per cent) had atonic bladders with a low pressure curve and absence of detrusor contractions. Grossly abnormal bladder capacities (mean 817 ml.) were recorded. In addition, bladder sensation was diminished in 75 per cent of these patients, while in 6 patients there was complete loss of bladder sensation. There was a positive correlation between the severity of diabetes and bladder abnormalities ($P < 0{\cdot}04$).

The incidence of abnormal bladder function in asymptc matic diabetes is higher than suspected previously.

Faerman, I., Maler, M., Jadzinsky, M., Alvarez, E
Fox, D., Zilbervarg, J., Cibeira, J. B., and Colinas, I
(1971), *Diabetologia*, **7**, 168.
Rundles, R. W. (1945), *Medicine, Baltimore*, **24**, 111.

23. Neural Elements in the Medulla activate via C-fibres in Abdominothoracic Vagal Trunk

I. V. F. Fussey, J. F. B. Morrison, and H. I Duthie, Department of Surgery, University c Sheffield, and Department of Physiology, Universit of Leeds.

Using micro-electrodes, the spike activities of singl neural elements in the dorsal motor vagal nucleu (D.M.V.N.) have been recorded in 10 anaesthetized dog The units showed a characteristic low-frequency irregula discharge when spontaneously active and a single evoke spike when an electrical stimulus was applied to a vag trunk at the level of the diaphragm. The recording site were shown to be in the D.M.V.N. by examination c serial sections of each medulla.

The distribution of some of the fibres which activate D.M.V.N. units was demonstrated by electricall stimulating points along the nerve of Latarjet and vag branches which were followed to the wall of the stomacl The units were activated via vagal C-fibres as indicated b the high-stimulus intensities at threshold (6–10 V.) an the conduction velocities (0·95–1·50 m. per sec.) calculate from latency and approximate vagal conduction distanc Some units were shown to be efferent neurons by demor strating the abolition of the evoked spike during the tim that a spontaneous spike was passing in the opposi direction.

These results are the first direct evidence of effere gastric innervation from the D.M.V.N. and are consiste with the suggestion by Kerr and Preshaw (1969) that th nucleus mediates hypoglycaemia-induced acid secretion.

Kerr, F. W. L., and Preshaw, R. N. (1969), *J. Physiol Lond.*, **205**, 405.

24. Further Studies on the Response t Insulin after Three Types of Vagotomy in Mar

P. J. Lyndon, D. Johnston, R. B. Smith, C. S Humphrey, M. C. Mason, and J. C. Goligher University Department of Surgery, The Gener Infirmary, Leeds.

The vagotomies were truncal (T.V.), selective (S.V. and highly selective (H.S.V.). Studies were carried o before operation ($n = 30$), 1 week after operation (T.V 515; S.V., 150; H.S.V., 150), and more than 1 year aft operation (T.V., 35; S.V., 27; H.S.V., 56). Patien studied more than 1 year after operation were in goo health. The dose of insulin used was 0·2 U. per kg.

The incidence of incomplete vagotomy at 1 week w 16 per cent for T.V., 13 per cent for S.V., and 4 per ce for H.S.V., but after 1 year it was more than 50 per ce for each type of vagotomy. However, mean peak ac output to insulin (P.A.O.$^{\text{I}}$) at more than 1 year aft operation was only 3·0 mEq. per hour for T.V., 5·0 mE per hour for S.V., and 4·4 mEq. per hour for H.S.V preoperatively. Six serial studies of P.A.O.$^{\text{I}}$ in H.S. patients for up to 3 years suggest that P.A.O.$^{\text{I}}$ does n increase after 1 year.

After H.S.V. the vagotomy can be incomplete only (on the oesophagus or (*b*) at the antral end of the stomac It is shown, first, that incompleteness is usually on t oesophagus and not distally and, secondly, that incon pleteness distally is usually detectable at the early pos operative test.

Complete vagotomy of the parietal cell mass is obtai able in 96 per cent of patients by the use of H.S.V., and t P.A.O.$^{\text{I}}$ does not increase significantly 1 year after H.S.

25. An Assessment of the Insulin Test by Graded Vagotomy in the Dog: S. NUNDY and J. H. BARON, Department of Surgery, Royal Postgraduate Medical School, London.

Hollander postulated that the insulin test was qualitative, the rise in acidity affording no indication of the number of intact vagal fibres. The insulin test has therefore been assessed by graded vagotomy in the dog.

Three dogs with a chronic gastric fistula had four operations each. Approximately half the acid-secreting area was denervated by cutting nerves in the lesser omentum from the antral border to 1 cm. of the oesophagogastric junction, and this partial vagotomy was then followed by conventional proximal gastric vagotomy, selective vagotomy, and truncal vagotomy. Each dog had 8 insulin tests 3 weeks after each operation, the doses ranging from 0·125 to 1·0 U. per kg.

Although the mean rises in acidity after presumed total parietal-cell denervation were less than 20 mEq./l. (a Hollander-negative result), about 20 per cent of the results of individual tests were Hollander positive. Before vagotomy the highest rises in acidity occurred between 30 and 60 minutes after insulin injection. After partial vagotomy this rise occurred significantly later, between 45 and 90 minutes. The rise in acid output differentiated more completely between innervated and denervated stomachs and was more repeatable than the rise in acidity.

Our findings support the contention that the results of the insulin test should be reported in terms of the rise in acid output.

26. Effect of Proximal Gastric Vagotomy on Plasma-gastrin Response to Meat Extract in Duodenal Ulcer Subjects: J. H. WYLLIE, B. H. STAGG, M. R. LEWIN, and C. G. CLARK, Department of Surgery, University College Hospital Medical School, London.

In 16 patients treated by proximal gastric vagotomy the postoperative insulin test was positive in 8. Using a radio-immunoassay the ability of the antrum to release gastrin into the circulation in response to meat extract (Oxo) was studied before and 10 days after operation in all patients. The mean fasting plasma-gastrin level preoperatively was 92 pg. per ml., and was not significantly altered after vagotomy, when it was 77 pg. per ml. In the insulin-negative cases the plasma-gastrin response to meat extract was reduced postoperatively, being absent in 4 cases, so that the mean peak plasma-gastrin level fell from 237 to 135 pg. per ml. In contrast, mean plasma-gastrin responses were unchanged in patients with a positive insulin test.

This unexpected relationship between the vagus nerve and the release of antral gastrin by meat extract may be explained if preservation of the antral nerves is essential for gastrin release by Oxo. If so, it appears that a positive insulin test may be the result of residual antral rather than fundic innervation. This means that insulin tests after proximal gastric vagotomy may have less significance than positive tests in other types of vagotomy.

27. Gastric Secretory Response to Continuous Insulin Infusion in the Dog: R. R. DOZOIS, D. C. CARTER, and J. R. KIRKPATRICK, Department of Clinical Surgery, University of Edinburgh.

The gastric secretory response to a continuous insulin infusion was studied in 4 dogs which were each provided with a gastric fistula.

Following collection of two 15-minute samples of basal secretion, soluble insulin (0·025, 0·05, 0·15, and 0·30 U. per kg. per hour) was delivered intravenously for 3 hours by a slow-injection pump. Samples of gastric juice were collected every 15 minutes and samples of venous blood were drawn every 30 minutes after the start of the infusion. Volume, acid concentration, and acid output were measured and blood-glucose levels were determined.

Graded doses of insulin produced graded levels of hypoglycaemia and a graded acid response. The highest peak acid output (P.A.O.) and the highest total acid output were achieved with a dose of insulin of 0·15 U. per kg. per hour. No initial inhibitory phase of gastric acid secretion was seen, but a dose-related delay in the onset of the acid response was noted. A linear correlation between the P.A.O. and the lowest blood-glucose, the plateau blood-glucose, and the maximum fall of blood-glucose (Baron, 1970) was observed.

Our results further substantiate the recent hypothesis (Baron, 1970; Spencer and Grossman, 1971) that insulin provides a graded glycopenic stimulus producing a graded acid response.

BARON, J. H. (1970), *Gut*, **11**, 826.
SPENCER, J., and GROSSMAN, M. I. (1971), *Ibid.*, **12**, 891.

28. Gastric Secretion and Serum Gastrin after Intravenous Infusions of Insulin in Man: D. P. GIRVAN, J. H. BARON, J. SPENCER, and J. HANSKY, Department of Surgery, Royal Postgraduate Medical School, London, and Department of Medicine, Monash University, Melbourne, Australia.

Intravenous infusion of insulin produces plateau acid secretion with minimal side-effects (Carter et al., 1972). This infusion test has been compared with bolus injections of insulin and the relationships of hypoglycaemia, acid, and serum gastrin have been explored.

An insulin infusion of 0·04 U. per kg. per hour produced a mean lowest blood-glucose of 23·5 ± 9·2 mg. per 100 ml., which is significantly higher than the 16·1 ± 6·4 mg. per 100 ml. produced after a bolus injection dose of 0·2 U. per kg. The peak acid output and mean rise in acidity were comparable in the two procedures, and the Hollander status after vagotomy was identical. Unpleasant side-effects were fewer and milder in the patients undergoing infusion.

Serum gastrin (Hansky and Cain, 1969) was increased during infusion of insulin and inversely correlated with blood-glucose. The mean rise of serum gastrin in 6 unoperated patients with duodenal ulcer was 46·7 pg. per ml., which is almost identical with the mean rise of 48·7 pg. per ml. in 6 patients with positive Hollander tests after vagotomy.

The insulin-infusion test uses less insulin, avoids severe hypoglycaemia, has milder side-effects, and provides comparable acidities to the conventional insulin test. Measurements of serum gastrin after insulin infusion, as after single injections, gave no additional information of value in assessing vagotomy.

CARTER, D. C., DOZOIS, R. R., and KIRKPATRICK, J. R. (1972), *Br. med. J.*, **2**, 202.
HANSKY, J., and CAIN, M. D. (1969), *Lancet*, **2**, 1388.

29. Turbulence in the Classification of Varicose Veins: J. SOMERVILLE, P. BYRNE, and D. KING (W. G. Fegan), Department of Clinical Research, Sir Patrick Dun's Hospital, Dublin.

It has been suggested that turbulent retrograde flow is important in the production of superficial varicose veins (Kline and Byrne, 1972). To investigate the significance of turbulence 38 female patients were selected and tape recordings were made of the audio output of a Parks 806 Directional Doppler during retrograde flow in the long saphenous vein. The recordings were analysed using a Kay Sona spectrograph and the patterns were compared with those of known turbulent and laminar flows in *in vivo* and *in vitro* models. Retrograde flow was produced by having an upright person stand on her toes. Five of the patients investigated had medial malleolar ulcers.

Ten of the patients exhibited turbulence. Of these, none had ulcers but 2 (12·5 per cent) showed mild signs of calf-muscle-pump failure (oedema, pigmentation). Thirteen patients (81 per cent) showed gross varicosity. Of the 22 patients who did not show turbulence, 7 (31·4 per cent) showed signs of calf-pump failure. The remaining 15 patients (68 6 per cent) had no signs of calf-pump failure, had minimal symptoms and varices, and had only a short history.

These results show three distinct groups: (1) a group exhibiting turbulence, largely asymptomatic with gross varicosities, (2) an asymptomatic non-turbulent group with a short history, and (3) a symptomatic non-turbulent group showing evidence of calf-pump dysfunction.

KLINE, A. L., and BYRNE, P. (1972), *Br. J. Surg.*, **59**, 915.

30. The Use of Venous Pressure Measurements and Directional Doppler Recordings in Distinguishing between Superficial and Deep Valvular Incompetence in Patients with Deep Venous Insufficiency: J. D. LEWIS, D. C. S. PARSONS, T. N. NEEDHAM, J. N. DOUGLAS, J. LAWSON, J. T. HOBBS, and A. N. NICOLAIDES, Surgical Unit, St. Mary's Hospital, London.

It has been suggested recently that cinephlebography will distinguish between superficial and deep valvular incompetence in patients with venous insufficiency (Field et al., 1972). In the present study a simple technique based on the reduction of venous pressure during exercise has been developed which can also achieve this.

The pressure in a superficial vein on the foot was recorded with the patient standing still and walking. The measurements were repeated after occluding the superficial veins only, with a 5-cm. wide pneumatic cuff on the ankle.

Fifty patients (80 limbs) have been studied. In 27 clinically normal limbs pressure measurements were normal. Of the 53 clinically abnormal limbs, 6 had normal pressures and in these lymphoedema was confirmed by lymphangiography, 16 had abnormal pressures on walking which became normal when the ankle cuff was inflated ('superficial insufficiency only'), and 31 had abnormal pressures on walking whether the cuff was inflated or not ('deep venous insufficiency').

Ascending phlebography was performed on all the patients. The state of the valves in the deep veins was assessed by recording the effect of respiration and the Valsalva manœuvre on the blood velocity using a directional Doppler. This confirmed the presence of reflux in the popliteal vein in all 31 limbs with 'deep venous insufficiency'. With the exception of 2 limbs no reflux was detected in the remaining limbs.

FIELD, E. S., KAKKAR, V. V., STEPHENSON, G., and NICOLAIDES, A. N. (1972), *Br. J. Surg.*, **59**, 304.

31. The Influence of a Temporary Arteriovenous Fistula in maintaining the Patency of Venous Replacements by Autografts, Allografts, and Dacron Prostheses in the Dog: D. C. S. PARSONS and J. T. HOBBS, St. Mary's Hospital, London.

Venous replacement distal to the diaphragm has not been successful. The problems are the replacement of occluded proximal veins and the insertion of valves to correct valvular insufficiency in the deep veins.

The effect of a temporary distal arteriovenous fistula on the patency rate of grafts placed in canine iliac veins was investigated. Bryant et al. (1958) suggested the use of a fistula during venous replacement.

In 13 dogs 1½-cm. segments of knitted Dacron tu were inserted into both common iliac veins, and a femor arteriovenous fistula was constructed on one side. T fistula was later closed and the dogs were observed 10 months. Patency of the grafts was monitored venography. On the side with the arteriovenous fistu 10 of the 13 grafts were patent, as compared with t contralateral side with no fistula where 10 grafts we occluded and 3 stenosed. The fate of the graft w related to the volume flow and the diameter.

In a further series of 9 dogs 2½-cm. allografts a autografts which contained a patent valve and we vitally preserved were inserted in the iliac veins. temporary arteriovenous fistula was again constructed one side. The patency rate was shown to be more th 90 per cent at 7 months. Valvular function was present 4 of the 9 autografts; no valve function was seen in t allograft veins.

BRYANT, M. F., LAZENBY, W. D., and HOWARD, J. (1958), *Archs Surg., Chicago*, **76**, 289.

32. The Risk of Deep-vein Thrombosis Surgical Patients: A. NICOLAIDES, D. IRVIN M. PRETZELL, P. DUPONT, J. LEWIS, S. DESAI, J. DOUGLAS, V. V. KAKKAR, and E. S. FIELD, Surgi Unit and Department of Epidemiology, St. Mar Hospital, and Department of Surgery, Kin College Hospital, London.

Factors such as age, severity of operation, previo history of deep-vein thrombosis (D.V.T.), obesi malignancy, varicose veins, and infection may be associat with a high incidence of D.V.T. (Kakkar et al., 197 Nicolaides et al., 1972).

In a prospective series of 390 general surgical patie factors believed to predispose to D.V.T. have be studied by linear logistic analysis. The patients had be screened with the ^{125}I-fibrinogen test in two differe hospitals using the same criteria for diagnosing D.V. The two groups of patients were comparable with resp to the incidence of the various factors studied.

A standard computer program was used to obtain t maximum-likelihood estimates of the coefficients for t various factors studied. The most important fac appeared to be the hospital ($P<0{\cdot}001$). Severity operation, infection, previous history of D.V.T., and a were also important ($P<0{\cdot}01$); malignancy and p medication with opiates were the least important of t significant factors ($P<0{\cdot}05$).

Using the coefficients for the significant factors equation was obtained of the form:—

$$\begin{aligned} y = -0{\cdot}28 &- (0{\cdot}92 \times \text{hospital}) \\ &+ (0{\cdot}72 \times \text{severity of operation}) \\ &+ (0{\cdot}70 \times \text{previous history of D.V.T.}) \\ &+ (0\ 60 \times \text{infection}) \\ &+ (0{\cdot}024 \times \text{age}) + (0{\cdot}38 \times \text{malignancy}) \\ &+ (0{\cdot}38 \times \text{premedication with opiates}). \end{aligned}$$

The value of factors other than age was 0 or 1. For a patient y can be expressed as a percentage risk of devel ing D.V.T. and is useful in determining which patie will need preventive measures.

KAKKAR, V. V., HOWE, C. T., NICOLAIDES, A. N., RENN J. T. G., and CLARKE, M. B. (1970), *Am. J. Surg.*, 1 527.

NICOLAIDES, A. N., KAKKAR, V. V., FIELD, E. S., a SPINDLER, J. (1972), *Br. J. Surg.*, **59**, 303.

33. The Effect of Dextran 40 on Venous Fl Changes in the Leg induced by Abdomi Operations: D. H. LEWIS and H. JANSEN (Matheson), Department of Surgery I, University Gothenburg, Gothenburg, Sweden.

In 34 patients the venous flow pattern of the leg was investigated immediately before and after abdominal operations. All the patients were operated upon under general anaesthesia and with muscle relaxation. Isotope injections were made via a short plastic cannula in the dorsal vein of the great toe. Time-concentration curves were registered with a scintillation detector over the groin and, in several cases, simultaneously over the calf. Twenty-two patients received glucose only during operation (control group) and 12 received 500 ml. of 10 per cent dextran 40 (Rheomacrodex). The patients in the dextran group were operated upon for gall-stones and were compared with 12 in the control group undergoing the same operation. In the control group the time of appearance of the isotope at the groin was *shorter* after operation than before. Preoperatively the curve rose slowly to a broad, low peak and declined slowly. Postoperatively the curve rose quickly to a peak of short duration. The difference between the pre- and postoperative curves was most marked over the calf. In the dextran group the pre- and postoperative curves were identical both with regard to appearance time and pattern.

It is suggested that the changes in the curves in the control group are due to a decrease in the vessel volume available for venous return from the leg, especially in the calf. This is prevented by the administration of 500 ml. of dextran 40 during operation. These observations could account, at least in part, for the anti-thrombotic action of a single infusion of dextran 40 during operation.

34. An Improved Electrical Impedance Technique for the Detection of Deep-vein Thrombosis: K. W. Johnston, V. V. Kakkar, T. P. Corrigan, D. P. Fossard, and J. J. Spindler, Department of Surgery, University of Toronto, and Department of Surgery, King's College Hospital Medical School, London.

Several studies have recently confirmed the inadequacy of clinical examination in diagnosing deep-vein thrombosis (D.V.T.) in the legs. In addition, the ^{125}I-fibrinogen test and the Doppler ultrasound technique have limitations. In this paper a simple non-invasive method is described which can be used to detect clinically significant thrombi.

The technique is based on the measurement of the change in calf electrical impedance following deep inspiration. Wheeler et al. (1972) first applied this method to the diagnosis of D.V.T. In the present study 100 limbs with suspected D.V.T. were examined by Wheeler's technique and also by ascending venography. Thirty per cent of the patients studied were unable to co-operate sufficiently to allow the measurement of electrical impedance changes. Also, 50 per cent of the thrombi in the popliteal and femoral veins were missed.

Wheeler's technique has been improved by using a thigh pressure cuff instead of relying on deep inspiration to produce calf-impedance changes. Fifty patients with suspected D.V.T. were studied. In contrast to Wheeler's method it was possible to use this new technique in all patients and it clearly delineated between those with and those without clinically significant D.V.T., and may prove a simple, safe, and non-invasive method for detecting significant thrombi.

Wheeler, H. B., Pearson, D., O'Connell, D., and Mullick, S. (1972), *Archs Surg., Chicago*, **104**, 164.

35. Isografts and Allografts of Pancreatic Islets in Rats: W. F. Ballinger, P. E. Lacy, D. W. Scharp, C. B. Kemp, and M. Knight (A. W. Kay), Departments of Surgery and Pathology, Washington University School of Medicine, St. Louis, United States.

Viable islets of Langerhans can be transplanted in rats as isografts (inbred Lewis strain) and allografts (Wistar to Lewis). The need for the development of such techniques is indicated by the discouraging results of whole-organ pancreatic transplantation in humans.

Streptozotocin-induced diabetic rats lose weight and die in 4–8 weeks; they secrete, on average, 130 ml. of urine containing approximately 14 g. of glucose per day and have blood-sugars over 400 mg. per 100 ml. Diabetic rats receiving approximately 600 islets of Langerhans intraperitoneally or into a muscle pouch in the thigh gain weight, produce 50–60 ml. of urine containing 6–8 g. of glucose per day, and their hyperglycaemia is reduced to approximately 200 mg. per 100 ml. Allografted rats receiving azathioprine are remarkably similar to the isograft series.

Preliminary studies indicate: (1) dialysed, layered Ficoll solutions permit rapid separation of islets, (2) preparations containing acini as well as islets do not survive when transplanted, (3) intact rat islet preparations can be successfully stored for at least 24 hours at 4° C. with evidence of continued viability, (4) tissue-culture techniques may permit long-term survival of islet cells, and (5) human islets have been prepared as in rats with preservation of synthesis and production of insulin.

36. Transplantation of Interstitial Cells of the Testis: Pauline F. Boyle and M. Fox, Department of Urology, Royal Hospital, Sheffield.

The first successful testicular transplant showing vascularization of the graft and subsequent changes of secondary sexual development was reported by Berthold in 1849. The testis has usually been transplanted as a whole and major problems were associated with vascular supply and allograft rejection.

Experiments were designed to investigate the effect of transplantation of homogenates of the testis under conditions in which the allograft response could not occur. The fate of the transplanted cells was followed histologically and effects on secondary sexual development were observed.

Bilateral orchidectomy was performed in groups of F 1 mice (CBA/T6XC57BL) at the age of 3 weeks and 3 months, and the testes were cut up finely with scissors and transplanted into ear pinnae, under the skin of the snout and back, and under the parietal peritoneum. The animals were weighed at regular intervals and killed after 3 months. The grafts were removed and examined histologically, and the seminal vesicles and penises were weighed and also examined.

Castrated mice gained weight more slowly than control and transplanted animals. Weight-gain was similar in transplanted and control animals. Cells indistinguishable from interstitial cells were found in ear pinnae and under the peritoneum at 3 months. After orchidectomy the seminal vesicles and penis atrophied in adult mice and did not develop in adolescent animals. Following transplantation nearly normal results were obtained.

Berthold (1849), *Arch. Anat. Phys. Wiss. Med., Berlin*, 42.

37. The Early Diagnosis of Rejection by the Leucocyte Migration Test in Cadaveric Renal Transplantation: R. J. Williams, H. McFarlane, N. P. Mallick, G. Taylor, and W. McN. Orr, Renal Transplantation Unit, Manchester Royal Infirmary and University of Manchester.

Experience of the leucocyte migration test as a means of providing an early diagnosis of rejection in cadaveric renal transplantation has been reported (Williams et al., 1971). The method has now been evaluated in an additional 22 patients using whole foetal kidney and glomerular basement membrane from homologous kidney as sources of antigen.

A high degree of reproducibility of migration indices (Mx/M_0) was obtained using these antigens in 50 normal subjects (range 0·80–1·10; mean 0·93; S.D. 0·075).

In the transplanted patients 33 episodes of inhibition of migration (M.I. < 0·75), with or without initial stimulation (M.I. < 1·15), were observed and were followed in 25 instances by clinical and biochemical evidence of rejection within 2–5 days. Antirejection doses of prednisolone were already being given in 6 of the 8 instances where inhibition of migration was not followed by evidence of rejection.

WILLIAMS, R. J., DOYLE, ANNE, MACFARLANE, H., MALLICK, N. P., and ORR, W. MCN. (1971), *Br. J. Surg.*, **58**, 868.

38. Measurement of Lymphocyte Activity in Response to a Renal Allograft: R. W. BLAMEY, RITA NICOL, and THELMA BAXTER, St. Vincent's Hospital, University of Melbourne.

Measurement of immune activity against a renal transplant would be of use in the management of antirejection therapy. Synthesis of DNA (measured by the uptake of ^{3}H-thymidine) and of RNA (^{3}H-uridine) by lymphocytes of recipients of renal allografts has been measured in 2-hour cultures at intervals after transplantation.

Two rat transplant systems have been studied in 39 DALF$_1$ to MAB grafts, and 23 transplants within the MAB (closed) strain; the former gives consistent acute rejection, the latter variable rejection. ^{3}H-thymidine uptake to recipient lymphocytes is significantly raised at 4 days when there is little evidence of rejection and at 7 days when rejection occurs in the former system. Rise in uptake is proportional to the histological degree of rejection in the latter system. Recipient lymphocyte ^{3}H-uridine incorporation is not raised at the time of rejection.

In 15 patients following transplantation a fivefold increase in thymidine uptake accompanied 6 out of 7 definite rejection episodes. However, uptakes of these levels have also occurred on 10 other occasions, some being associated with infection. Acute tubular necrosis and problems from urinary obstruction did not give raised thymidine uptakes. Uridine uptake did not correlate with rejection.

Incorporation of ^{3}H-thymidine to recipient lymphocytes offers some measure of the immune activity against an allograft.

39. The Mechanism of Enhancement of Rat Renal Allografts. The Nature of Enhancing Antibody: S. DESAI and M. RUSZKIEWICZ (C. W. Jamieson), St. Mary's Hospital, London.

The rejection of rat renal allografts between Lewis × Brown Norway F$_1$ hybrid to Lewis across a strong histocompatible barrier can be markedly delayed by prior intravenous administration of donor-strain bone-marrow cells to the recipients; this delay is due to immunological enhancement rather than to tolerance. This study has now been extended by attempting to reproduce the delay in rejection by passive transfer of allo-antiserum, by demonstrating cytotoxic effects *in vitro* of the active serum on donor-strain lymphocytes by a modification of the cytotoxic test using ^{51}Cr (Lance et al., 1968), and by identification of the types of antibodies involved by a modification of the method described by Deutsch and Morton (1957).

These studies show that passive transfer of allo-antiserum produces delay in rejection similar to that in animals treated with bone-marrow. The degree of abrogation of rejection is related to the levels of cytotoxic allo-antibody; the cytotoxic antibodies have been identified as belonging to 19S(IgM) and 7S(IgG) classes of immunoglobulins.

DEUTSCH, H. F., and MORTON, J. I. (1957), *Science, N.Y.*, **125**, 600.
LANCE, E. M., FORD, P., and RUSZKIEWICZ, M. (1968), *Immunology*, **15**, 571.

40. Antibody-induced Enhancement of Cardiac Allografts in Mice: R. A. SELLS and J. BRADLEY, Departments of Surgery and Haematology, University of Liverpool.

Hearts were removed from HALB/C mouse foetuses and transplanted to pockets created beneath the dorsal ear skin of adult CBA mice. Using a modification of the technique of Judd and Trentin (1971) initial failure of grafts was 12 per cent. Graft function was evaluated using E.C.G. electrodes implanted on either side of the graft, with an indifferent electrode placed in a hind-limb muscle.

Recipients and grafts were treated with antibodies prepared in CBA mice by injecting donor thymocytes and spleen cells with adjuvant (group III) and by two donor skin-grafts (group IV). The cytotoxic titres of both groups of sera were similar.

In group I (isografts; $n = 28$) 80 per cent of the grafts survived beyond day 90. In group II (control allografts; $n = 36$) 50 per cent of the grafts ceased to function by day 7 (range 5–11 days). In group III (allografts + adjuvant-induced antibodies; $n = 16$) 50 per cent of the grafts ceased to function by day 10·5 (range 8–13 days). In group IV (allografts + skin-graft induced antibodies; $n = 20$) 50 per cent of the grafts ceased to function by day 25 (range 11–70 + days).

Prolongation of mouse foetal heart allograft survival may be produced by using antibodies directed at the donor antigens. The ability to prolong graft survival does not appear to be related to the titre of the cytotoxic antibodies.

JUDD, K. P., and TRENTIN, J. J. (1971), *Transplantation*, **11**, 298.

41. The Character of Effector Cells and the Accumulation of Macrophages in rejecting Heart Allografts in the Rat: N. L. TILNEY (P. R. F. Bell), Sir William Dunn School of Pathology, University of Oxford.

The morphologic simplicity of the myocardium makes the heterotopic cardiac transplant in the inbred rat an attractive model for defining events and patterns of cellular rejection. The rapid destruction of allografts transplanted between animals of major genetic differences was studied.

Cells in normal hearts and in isografts and effector cells infiltrating allografts were harvested. Grafts were removed serially from groups of recipients. Pieces of myocardium were digested enzymatically, the cell infiltrate was removed, and total counts and differential counts were performed. Cell populations and their varying rates of accumulation were compared and related to histological and autoradiographical observations. Increasing cell numbers were correlated with weight-gain of the heart grafts which were being rejected.

Macrophages may destroy allografts following specific activation by host lymphocytes (Mackaness, 1969). Following intravenous administration, particles of colloidal carbon were noted to adhere selectively to the vascular endothelium of transplanted hearts. Circulating macrophages phagocytoze these particles upon entering the myocardium. The distribution and rate of accumulation of the labelled cells were documented.

Small lymphocytes which rapidly infiltrate allografts undergoing acute rejection are followed by increasing numbers of macrophages. Primitive cell forms are present. Few cells enter isografts, and those which do are predominantly medium and large mononuclear cells.

MACKANESS, G. B. (1969), *J. exp. Med.*, **129**, 973.

42. The Immunosuppressive Effect of Surgery—A Possible Mechanism: J. BANCEWICZ, AILEEN C. GRAY, and G. LINDOP (P. R. F. Bell), University Department of Surgery and Pathology, Western Infirmary, Glasgow.

Lymphocyte responsiveness to mitogens is decreased following operation (Riddle and Berenbaum, 1967; Park et al., 1971). The leucocyte-migration-inhibition test, which is a good *in vitro* correlate of cell-mediated immunity *in vivo*, was used to demonstrate a period of postoperative immune depression.

The reactivity of 9 patients to tuberculoprotein (PPD) was studied. All the tests were positive preoperatively and became negative postoperatively. In 2 patients recovery of the response occurred within 10 days, but in the others recovery was slower.

In the morphological studies the size of the lymphocytes appeared to increase postoperatively. A sevenfold increase in the spontaneous uptake of ^{14}C-labelled thymidine which was maximal on the fifth postoperative day was also found. This observation indicates an increased synthesis of DNA following surgery. Similar changes were seen in 1 patient who suffered trauma but did not undergo anaesthesia.

The increase in DNA synthesis plus the observed increase in lymphocyte size may indicate an activation of lymphocytes following trauma which renders them unresponsive to further immune stimulation.

Park, K. S., Brody, J. I., Wallace, H. A., and Blakemore, W. S. (1971), *Lancet*, **1**, 53.
Riddle, P. R., and Berenbaum, R. C. (1967), *Ibid.*, **1**, 746.

43. **Properties of Somatosensory Cells in the Human Thalamus:** J. Hankinson and P. Wilson (I. D. A. Johnston), Regional Neurological Centre, Newcastle upon Tyne, and the University of Newcastle upon Tyne.

Following the studies of Guiot et al. (1962) thalamic recording is regarded as the most precise localizing technique available for stereotaxic operations within the thalamus, but there is little quantitative information concerning the properties of human thalamic somatosensory cells.

One hundred and ninety-three somatosensory cells were studied in 80 patients, most of whom suffered from Parkinson's disease. The majority of these cells probably lay within the ventrocaudalis and ventro-intermedius nuclei. One hundred and thirty-seven of the cells responded to cutaneous stimulation of either the contralateral hand or face. Most of the receptive fields on the face were situated near the mouth and nose, and the tips of the digits were usually represented. Cells giving non-adapting discharges usually had larger fields than those giving rapidly adapting responses. For the former the mean areas of receptive fields were $5{\cdot}0 \pm 0{\cdot}9$ cm.^{2} on the face and $3{\cdot}9 \pm 0{\cdot}8$ cm.^{2} on the hand. For the latter the corresponding values were $0{\cdot}8 \pm 0{\cdot}1$ cm.^{2} on both the face and hand. Forty-four cells responded only to either flexion or extension of single joints in the contralateral hand. Following electrical stimulation of the median nerve, somatosensory cells discharged with latencies between 13 and 19 mseconds.

Guiot, G., Hardy, J., and Albe-Fessard, D. (1962), *Neurochirurgia*, **5**, 1.

44. **Effect of Carotid Ligation on Cerebral Blood-flow in the Baboon:** D. Sengupta, A. M. Harper, and W. B. Jennett, Wellcome Surgical Research Institute, University of Glasgow, and Institute of Neurological Sciences, Southern General Hospital, Glasgow.

Following carotid ligation there is a risk of ischaemia of the cerebral hemisphere during or after the operation. Experiments were made on anaesthetized baboons to test the effects of ipsilateral carotid ligation on cerebral blood-flow (C.B.F.) and on the normal physiological responses of cerebral circulation to hypercapnia, hypoxia, and hypotension. The C.B.F. was measured following intracarotid injection of ^{133}Xe and calculated from the height/area equation (Høedt-Rasmussen et al., 1966).

The results showed that, at steady state, C.B.F. did not alter following ipsilateral carotid ligation. Before carotid ligation there was a 123 per cent rise in the C.B.F. at hypercapnia, and an 81 per cent rise at hypoxia. C.B.F. was maintained until the mean blood-pressure fell below 70 per cent of the normal value (autoregulation). Following ipsilateral carotid ligation there was only a 41 per cent rise in the C.B.F. at hypercapnia, a 20 per cent rise at hypoxia, and the C.B.F. fell steadily with a fall in the blood-pressure (autoregulation impaired).

It is inferred that although C.B.F. may be normal following carotid ligation, it is likely that the circulatory reserve of the brain is insufficient to meet physiological challenges such as hypercapnia, hypoxia, or hypotension and that this may be the reason for the development of delayed neurological complications.

Høedt-Rasmussen, K., Sveinsdottir, E., and Lassen, N. A. (1966), *Circulation Res.*, **18**, 237.

45. **Ventilatory and Intracranial Pressure Responses to CO_2 Stimulation:** M. Briggs and A. P. Adams (W. B. Jennett), Radcliffe Infirmary, Oxford.

An attempt has been made to analyse some aspects of the relationship between intracranial pressure (I.C.P.) and respiration in man. The I.C.P. end tidal CO_2 and ventilation were monitored continuously in 14 patients during a CO_2 challenge, using a rebreathing circuit adapted from Clark et al. (1966).

Within the P_{CO_2} range studied (40–60 mm. Hg) the relationship between I.C.P. and P_{CO_2} was always linear in one group of 5 patients and was always alinear in a second group of 6 patients. No common factors have been found linking the patients in these groups. The rate of pressure change observed with increasing P_{CO_2} was not significantly related to the mean resting I.C.P.

Regression slopes for ventilation versus P_{CO_2} revealed, as expected, a wide variation between patients (Bulow, 1963) which was unrelated to the resting I.C.P. One patient, however, who was tested before surgery, when the mean I.C.P. was 13 mm. Hg, and after the insertion of a ventriculo-atrial shunt (with a valve opening pressure of 5·3 mm. Hg) showed an increased respiratory responsiveness to CO_2 postoperatively, the slope improving from 1·62 to 2·91 litres per mm. Hg increase.

The results establish base-line patterns of responses to CO_2 stimulation, and those observed in 1 patient indicate that respiratory sensitivity may be depressed by levels of I.C.P. not previously considered to be pathological.

Bulow, K. (1963), *Acta physiol. scand.*, **59**, suppl. 209.
Clark, T. J. H., Clarke, B. G., and Hughes, J. M. S. (1966), *Lancet*, **2**, 368.

46. **Measurements of Breathing in Brain-damaged Patients:** J. B. North and Sheila Jennett (W. B. Jennett), Institute of Neurological Sciences, Glasgow, and Departments of Neurosurgery and Physiology, University of Glasgow.

Recent reports of abnormal breathing in brain-damaged patients indicate an area for study. Hyperventilation is associated with a poor prognosis after head injury (Vapalahti and Troupp, 1971); different abnormal respiratory patterns may be of localizing value in brain damage; hypoxaemia without obvious lung pathology is common after head injuries.

A system has been developed for detecting abnormal breathing in neurosurgical patients using impedance pneumography (North and Jennett, 1972). Of the first

150 patients who were screened, 86 showed some abnormality, but no close association was found between particular disorders and sites of lesions.

Patients with abnormal breathing patterns were studied quantitatively, measuring ventilation volume and frequency by pneumotachygraphy, together with arterial blood-gases and end tidal CO_2, during breathing of air, 100 per cent oxygen, and CO_2. This provided information about pulmonary gas exchange and respiratory centre chemosensitivity. More than 25 per cent of the patients studied showed an abnormal ventilatory response to CO_2; hyperventilation was not uncommon, but was often associated with hypoxaemia.

NORTH, J. B., and JENNETT, SHEILA (1972), *Lancet*, **2**, 212.

VAPALAHTI, M., and TROUPP, H. (1971), *Br. med. J.*, **3**, 404.

47. A Clinical Study of Intracranial Volume/Pressure Relationships:

J. D. MILLER, J. GARIBI, and J. D. PICKARD, University Department of Neurosurgery, Institute of Neurological Sciences, Glasgow.

In experimental animals inflation of an intracranial balloon causes little increase in intracranial pressure (I.C.P.) at first, but eventually uniform increases in volume cause progressively greater increases in I.C.P.; there is thus an exponential relationship between balloon volume and I.C.P. (Langfitt et al., 1965). The purpose of this study was to test whether the same relationship was valid for changes in C.S.F. volume in patients with increased I.C.P.

In 20 patients, during continuous monitoring of the I.C.P., a constant volume of 1 ml. was withdrawn from or injected into the lateral ventricles, and the resulting change in I.C.P. was measured. This was repeated at different times and at differing levels of resting I.C.P., so that 371 observations were made.

There was a positive correlation between the resting I.C.P. and the increase in I.C.P. produced by the injection of fluid ($r = 0{\cdot}41$; $P < 0{\cdot}001$), and between the resting I.C.P. and the reduction in I.C.P. produced by withdrawal of fluid ($r = 0{\cdot}45$; $P < 0{\cdot}001$). The results support the concept of an exponential intracranial volume/pressure relationship in patients with several different causes for increased I.C.P. Induction of small changes in C.S.F. volume gave useful information in individual patients concerning the compensatory capacity available in the presence of intracranial space-occupying lesions.

LANGFITT, T. W., WEINSTEIN, J. D., and KASSELL, N. F. (1965), *Neurology, Minneap.*, **15**, 622.

48. Early Intracranial Pressure and Blood-flow Measurements in Cerebral Gunshot Wounds:

H. A. CROCKARD and D. S. GORDON (H. W. Rodgers), Department of Neurosurgery, Royal Victoria Hospital, Belfast.

Studies of intracranial pressure (I.C.P.), blood-pressure, cerebral blood-flow by radiocirculography, and blood-gas analysis have been used in the management of bullet wounds of the brain in 24 patients within 1 hour of injury.

Intracranial Pressure.—Three groups were recognized.

1. Low intracranial pressure (0–10 mm. Hg): These patients had a very low I.C.P. associated with low blood-pressure. After massive transfusions the blood-pressure and I.C.P. rose. In 2 cases with severe brain damage the I.C.P. reached very high levels before death.

2. High intracranial pressure (60–80 mm. Hg): This response occurred with 'through-and-through' high-velocity injuries. The blood-pressure was also high and the patients required little resuscitation.

3. Moderate intracranial pressure (20–30 mm. H Two groups displayed moderate hypertension: (low-velocity missile injuries usually affecting one hem sphere and (*b*) tangential impacts with high-veloc missiles.

Routine controlled ventilation (I.P.P.V.) controlled t intracranial pressure. Inattention to the state of the airw caused an irrevocable increase in the I.C.P.

Cerebral Blood-flow.—Estimations of the cerebral bloo flow within the first hour after injury helped the progno and confirmed animal experiments (Grauber and Mood 1971). Patients with a blood-flow reduction of over 40 p cent of normal within the first hour died.

GRAUBER, S. E., and MOODY, D. (1971), *J. Neurosurg.*, 568.

49. A New Approach to the Treatment Brain Oedema: Mineralocorticoids:

SCHMIEDEK, W. OETTINGER, A. BAETHMANN, and ENZENBACH, Institute for Surgical Research, Depar ments of Surgery and Neurosurgery, University Munich, West Germany.

The use of adrenal steroids for the prevention reduction of brain oedema is confined to glucosteroi However, from previous studies (Koczorek et al., 196 mineralocorticoids may also exert a beneficial effect brain oedema. The results from neurosurgical patien treated with high doses of aldosterone are reported.

In 20 patients with brain tumours aldosterone w given pre- and postoperatively for several days in a dose 5–10 mg. per day. During the operation samples fro perifocal brain tissue, including cortex and subcortic white matter, were obtained and analysed for: (*a*) wat content and tissue electrolytes (Na, K), (*b*) tissue enzym (GAPDH, CE, IDH, MDH, GLDH, GOT), and (labile metabolites (CP, ATP, ADP, AMP, Pyr., Lact When compared with 20 unpretreated patients, tiss analysis revealed: (1) a significant reduction of wat content in both the cortex and white matter ($P < 0{\cdot}002$ (2) a concomitant decrease of Na ($P < 0{\cdot}005$) and a slig increase in K, (3) little but insignificant changes of tiss enzymes, and (4) an almost identical pattern of lab metabolites in the two groups. Aldosterone medicati was well tolerated in all the patients without any sid effects.

KOCZOREK, KH. R., ANGSTWURM, A., BAETHMANN, ENGELHARDT, D., REULEN, H. J., SCHMIEDEK, VOGT, W., SIMON, B., FRICK, E., and BRENDEL, (1968), in *Postoperative Störungen des Elektrolyt- u Wasserhaushaltes* (ed. BÜCHERL, E. S.). Stuttga Schattauer.

50. A Chronic Experimental Model for t Production of Subarachnoid Haemorrhag

E. W. PETERSON, R. SEARLE, F. MANDY, R. LEBLAN and MIRIELLE BOSC (W. G. Waddell), Departme of Neurosurgery, Faculty of Medicine, University Ottawa, Canada.

A Rickham reservoir was implanted subcutaneously the neck of macaque Rhesus monkeys and connected by catheter to the subarachnoid space anterior to the brai stem. Several days after recovery the animals we anaesthetized and control angiograms of the carotic vertebral circulation were performed by the transbrach route. Subarachnoid haemorrhage was induced injecting 2·5 ml. of the animal's blood by transcutaneo puncture of the reservoir. Repeat angiography demo strated marked arterial spasm of the intracerebral vesse Reversal of this vasospasm was accomplished by injecti the reservoir with theophylline and/or dibutyryl cyc AMP. Serial post-treatment angiograms showed prolonged drug reversal effect. Radiographic subtracti technique applied to the angiograms accentuated the appearance of the vasospasm and of the vasodilatation as a result of treatment (Rickham, 1964).

The experimental model permits long-term survival and repeated production of subarachnoid haemorrhage. The tolerance to drug modification of vascular tone suggests that this may have clinical application in the control of cerebral vasospasm, and in the prevention of ischaemic sequelae following subarachnoid haemorrhage.

RICKHAM, P. P. (1964), *Br. med. J.*, **2**, 173.

51. The Effect of Ovariectomy on Experimental Mammary Carcinoma in the Rat with Portacaval Shunt: J. F. O'GRADY, MARGOT GRUENSTEIN, and F. A. REICHLE (P. Fitzgerald), Department of Surgery, University College, Dublin, and Temple University Hospital, Philadelphia, United States.

End-to-side portacaval shunt (P.C.S.) significantly reduces the incidence of experimental mammary carcinoma in the rat (Reichle et al., 1969). The mechanism of this inhibition is unknown. The major circulatory, metabolic, and hormonal changes which occur after portasystemic by-pass may be related to this tumour inhibition (Reichle et al., 1972).

Ten mg. of 7,12-dimethylbenz-(α)-anthracene (DMBA) were given in a single intragastric instillation to 105 Holtzman rats (150 g.). After 2 weeks P.C.S. (77 rats) and sham operations (28 rats) were performed. When palpable mammary tumours had developed bilateral ovariectomy was performed. A total of 19 rats (10 with shunts, 9 having had sham operations) with breast tumours underwent bilateral ovariectomy and survived long enough for adequate follow-up. Average increase in tumour size at death or 1 year after DMBA was $2\cdot48 \pm 0\cdot57$ cm. in sham-operated rats and $0\cdot82 \pm 0\cdot39$ cm. in rats with shunts ($P < 0\cdot05$). The average time of death after ovariectomy was $85\cdot7 \pm 11\cdot8$ days in sham-operated rats and $92\cdot7 \pm 18\cdot2$ days in rats with shunts (not significant). Approximately equal weight-gain following the sham or shunt operation was observed in both groups.

Following bilateral ovariectomy the suppression of DMBA-produced carcinoma growth is significantly greater in animals with a portasystemic by-pass. This may be due either to an altered hormonal response of the tumours in the shunted animals or to an effect of the P.C.S. on the hormonal changes associated with ovariectomy.

REICHLE, F. A., GRUENSTEIN, M., MERANZE, D. R., ROSEMOND, G. P., and SHIMKIN, M. B. (1969), *J. surg. Res.*, **9**, 559.
— — — — REICHLE, R. M., MERANZE, D. R., ROSEMOND, G. P., and SHIMKIN, M. B. (1972), *Archs Surg., Chicago*, **104**, 206.

52. *In vivo* Binding of Tritiated Oestradiol in Benign and Malignant Lesions of the Human Breast: N. O'HIGGINS, N. DESHPANDE, and J. I. BURN, Breast Unit, Department of Surgery, Royal Postgraduate Medical School, London, and the Imperial Cancer Research Fund.

Previous workers have examined the uptake of tritium-labelled hormones by mammary cancers (Braunsberg et al., 1967). The capacity to bind tritiated oestradiol-17 *in vivo* was determined in 8 benign and 13 malignant mammary cancers. Uptake was measured in whole-tissue slices and nuclear preparations.

A loading dose of 9 μc. of tritiated oestradiol was given intravenously. This was followed by a continuous slow infusion of 64μc. of tritiated oestradiol, which was started at least 3 hours before operation and continued until the lesion had been removed. Serial venous blood samples were examined to confirm that a steady state of oestradiol had been achieved. Radioactivity levels in the excised specimens were measured in a well counter.

The uptake in the benign lesions ranged between 808 and 2530 disintegrations per minute (d.p.m.) per mg. of wet tissue (mean 1229 d.p.m.). Levels in the malignant cancers ranged between 1456 and 12,563 d.p.m. (mean 2196 d.p.m.). There was a complete separation between postmenopausal patients with benign and malignant disease.

BRAUNSBERG, H., IRVINE, W. T., and JAMES, V. H. T. (1967), *Br. J. Cancer*, **21**, 714.

53. Macrophage Activity and Hormonal Responsiveness in Mammary Cancer: W. D. GEORGE, WENDY PARTRIDGE, and J. I. BURN, Breast Unit, Department of Surgery, Royal Postgraduate Medical School, London.

Changes in reticulo-endothelial macrophage activity occur in patients with cancer and may reflect the host's resistance to the disease (Old et al., 1961). Hormone therapy in advanced breast cancer should theoretically stimulate macrophage activity. Hepatic macrophage activity was studied serially in 14 patients with advanced mammary cancers before and after endocrine therapy. Activity was measured by the rate of clearance of radio-iodine labelled micro-aggregates of albumin given intravenously (Ilio and Wagner, 1963).

Seven patients received oestrogen therapy. Four responded successfully to treatment and all showed an increase in macrophage activity as therapy continued. Of 3 patients who failed to respond to oestrogens, 2 showed a decrease in macrophage activity whilst the third showed no change.

Seven patients underwent major endocrine ablations. Two responded successfully and both showed increase in macrophage activity. Of the 5 non-responders, macrophage activity decreased in 4 and remained unchanged in the other patient.

These results suggest that in patients with advanced mammary cancer successful endocrine therapy is related to the stimulation of reticulo-endothelial macrophage activity.

ILIO, M., and WAGNER, H. N. (1963), *J. clin. Invest.*, **42**, 417.
OLD, L. J., BENACERRAF, B., CLARKE, D. A., CARSWELL, E. A., and STOCKERT, E. (1961), *Cancer Res.*, **21**, 1281.

54. A New Method of determining the Hormone Dependence of Human Breast Cancer: H. FLAX (H. Ellis), Tumour Biology Group, Westminster Hospital, London.

A new technique has been developed to determine the hormone dependence of individual breast cancers (Salih et al., 1972) involving the 24-hour maintenance at 37° C. of tumour slices in Trowell's T8 medium with two near-physiological concentrations each of 17-β-oestradiol, testosterone, and prolactin. The technique has been successful for soft-tissue metastases as well as for the primary tumour. Results are determined by a histochemical reaction demonstrating the total dehydrogenase activity of the pentose shunt (Chayen et al., 1970) as well as by conventional haematoxylin and eosin staining (which showed 96 per cent correlation on independent histopathological assessment). The tumour is classed as dependent if it appears more active with a particular hormone or hormones than both the initial untreated biopsy and the medium control.

In the 100 patients studied so far, dependences have been as follows: prolactin only, 14 per cent; prolactin and oestradiol, 10 per cent; testosterone only, 12 per cent; prolactin and testosterone, 8 per cent; oestradiol only, 8 per cent. Where appropriate, endocrine-ablative surgery was advised for the dependent cases. In the 48 per cent of cases that were independent the results, by indicating whether any particular hormone was strikingly inhibitory to the tumour, were helpful for selecting hormones for administration. Correlation with the clinical progress of these patients (only at 9 months so far) has been encouraging.

Chayen, J., Altmann, F. P., Bitensky, L., and Daly, J. R. (1970), *Lancet*, **1**, 868.
Salih, H., Flax, H., and Hobbs, J. R. (1972), *Ibid.*, **1**, 1198.

55. The Effect of Vagotomy on the Exocrine Pancreatic Secretory Response to Pentagastrin and to a 400-g. Meat Meal in Dogs: M. Davis, Saroj Gupta, and J. B. Elder, University Department of Surgery, Royal Infirmary, Manchester.

It has been stated that the pancreas becomes more sensitive to humoral stimulation after truncal vagotomy but the evidence is controversial (Konturek et al., 1971; Moreland and Johnson, 1971). The effect of truncal vagotomy on the exocrine secretory response to a 400-g. meat meal and to intravenous pentagastrin infusion at a dose maximal for acid secretion before and after vagotomy in 2 dogs with chronic pancreatic and gastric fistula (G.F.) has been studied.

With the G.F. closed the mean bicarbonate output after pentagastrin (8 μg. per kg. per hour) increased from 22·98 ± 1·1 mEq. to 33·1 ± 4·6 mEq. ($P < 0·05$) after vagotomy; protein output to pentagastrin increased from 1898 ± 422 mg. to 3520 ± 342 mg. ($P < 0·01$) after vagotomy. Bicarbonate output to the meat meal decreased significantly ($P < 0·001$) after vagotomy but protein output was not significantly altered ($P < 0·4$).

These results may be explained on the basis of an increased sensitivity of the pancreas to hormonal stimulation after vagotomy.

Konturek, S. J., Popiela, T., and Thor, P. (1971), *J. dig. Dis.*, **16**, 1087.
Moreland, H. J., and Johnson, L. R. (1971), *Gastroenterology*, **60**, 425.

56. Does the Vagal Nerve-supply to the Pancreas matter in Man? R. B. Smith, J. P. Edwards, and D. Johnston, University Department of Surgery, The General Infirmary, Leeds.

Reports on the function of the pancreas after severance of its parasympathetic nerve-supply in man (as in truncal vagotomy (T.V.)) are conflicting. These nerves are preserved in highly selective vagotomy (H.S.V.). The pancreatic response to insulin (0·2 U. per kg.) has been studied in 9 preoperative patients with duodenal ulcer (D.U.), and in patients more than 1 year after T.V. (6 patients) or H.S.V. (12 patients). The three groups of patients were matched for age and weight. Gastric acid was aspirated continuously and the duodenal *p*H remained greater than 7.

Outputs of amylase were found to increase significantly after insulin in D.U. and H.S.V. patients (from a mean of 9·1 to 20·5 kilo units in D.U. patients and from 6·0 to 16·5 kilo units in H.S.V. patients), whereas no significant increase was found in patients after T.V. (3·8 to 4·5 kilo units). Similarly, outputs of trypsin increased significantly in D.U. patients (from 16·0 to 31·1 I.U.) and in patients after H.S.V. (from 14·1 to 27·6 I.U.), whereas no such increase was observed after truncal vagotomy.

These results are in agreement with previous reports of impaired (Pfeffer et al., 1952) or absent (Dreiling et al., 1952) pancreatic response to insulin after T.V. in man. After H.S.V. significant increases in enzyme output still occurred in response to vagal stimulation.

Dreiling, D. A., Druckerman, L. J., and Hollander, F. (1952), *Gastroenterology*, **20**, 578.
Pfeffer, R. B., Stephenson, H. E., and Hinton, J. W. (1952), *Ann. Surg.*, **136**, 585.

57. Disappearance of Acid from the Duodenum: N. J. Dorricott and W. Silen (G. Slaney), Department of Surgery, Queen Elizabeth Hospital, Birmingham, and Harvard Medical School, Beth Israel Hospital, Boston, United States.

Experiments were carried out to investigate the poorly understood mechanism by which the duodenal mucosa contributes to the disappearance of hydrogen ions in the duodenum in the absence of pancreatic juice and bile.

In 7 standing awake dogs distal duodenal pouches were perfused by a constant-circulation technique with isotonic solutions ranging from 60 to 120 m*M* HCl (Dorricott and Silen, 1972). Fluxes of H^+, Na^+, K^+, and Cl^- were related to the initial concentration of H^+ and Na^+ and load of H^+ exposed to the duodenal mucosa per unit of time.

In all the experiments there was a loss of H^+ from the perfusate and a gain of Na^+, K^+, and Cl^-. A higher initial concentration of H^+ was associated with a greater rate of disappearance of H^+, e.g., 667 ± 70 μEq. per 30 minutes from 120 m*M* HCl and 312 ± 30 μEq. per 30 minutes from 60 m*M* HCl ($P < 0·001$). Alteration of load of H^+ and initial concentration of Na^+ did not produce significant change in the rate of disappearance of H^+. An excess of cations over measurable anions, closely related to H^+ loss, entered the pouch, which can best be explained by a process of bicarbonate neutralization.

These experiments show a relationship between disposal of H^+ by the duodenal mucosa and intraluminal H^+ concentration, and not load of H^+ as found by Meyer et al. (1970).

Dorricott, N. J., and Silen, W. (1972), *Surg. Forum*, **23**, 391.
Meyer, J. H., Wong, L. W., and Grossman, M. I. (1970), *Am. J. Physiol.*, **219**, 971.

58. Human Duodenal Electrical Activity: W. Waterfall, B. Brown, and H. L. Duthie, University Department of Surgery, Royal Infirmary, Sheffield.

Stainless-steel electrodes (0·25 mm. in diameter) were mounted on a gastric tube and attached to the mucosa of the second part of the duodenum by suction in 16 subjects. Unipolar records of the electrical activity of the duodenum were obtained with the subjects in the resting state and also during intravenous infusion of pentagastrin (1·0 and 6·0 μg. per kg. per hour in 8 tests) and of secretin (0·25 and 2·0 U. per kg. per hour in 6 tests).

In the fasting subject a regular waveform of 11–12 cycles per minute was present all the time (pacesetter potential; basal electrical activity) with an amplitude of 0·2–1·6 mV. When motor waves were present (16 per cent of the time) they were accompanied by bursts of action potentials superimposed on the pacesetter potentials which then had their maximal amplitude. The frequency of the pacesetter potential was not affected by the infusion of pentagastrin or secretin. Action potentials and motor activity were increased significantly with pentagastrin and decreased with secretin. The contrasting actions of these hormones on the motor action of the duodenum have been confirmed and their effects on the electrical activity displayed.

59. *Ex vivo* Perfusion of Canine Jejunal Loop: Electrical and Mechanical Activities: C. Mendel, D. Jaeck, J. C. Schang, J. Kachelhoffer, M. R. Eloy, and J. F. Grenier (H. L. Duthie), Service d'Investigations Chirurgicales et Unité de Recherches de Biophysiopathologie Digestive de l'I.N.S.E.R.M. Pavillon Chirurgical B, Hôpital Civil de Strasbourg.

Controversy remains concerning bioelectrical potentials and motility of intestinal smooth muscle (Hiatt and Goodman, 1971). Using extracorporeal perfusion with pulsatile blood-flow, bioelectrical activity and motility were studied simultaneously in isolated loops of dog jejunum. Twenty experiments have been performed. Six silver electrodes were spaced 2·0 cm. apart on the antimesenteric border of the intestine. In each dog serial bioelectric and motility recordings were obtained from the intact loop *in vivo*, then from the isolated loop *in vivo*, and finally from the perfused isolated loop.

Electro-enterographic tracings demonstrate similar bioelectric activity *in vivo* and under *ex vivo* perfusion. Independent slow wave activity was initiated at all recording sites on the jejunum and propagation occurred regardless of a duodenal pacemaker. Immediate and consistent intestinal contraction occurred with each slow-wave electrical potential. Such contractions persisted despite the absence of spike activity. Augmented amplitude of contraction was associated with increased frequency of spike activity.

Thus, for the first time correlation between the mechanical and bioelectrical activities of the jejunum has been determined under *ex vivo* conditions in the absence of extrinsic nervous control and the duodenal pacemaker.

HIATT, R., and GOODMAN, I. (1971), *J. surg. Res.*, **11**, 454.

60. Is there Impaired Immunity in Patients with Crohn's Disease?

P. M. BOLTON, S. L. JAMES, and L. E. HUGHES, University Department of Surgery, Welsh National School of Medicine, Cardiff.

One of the popular theories of the aetiology of Crohn's disease is that there is an abnormal immune response to either intestinal contents or components of the gut wall. Evidence for this concept has been produced by the demonstration of impairment of cellular immunity in Crohn's disease (Parent et al., 1971). Contrary results have also been reported (Röpke, 1972), and the immunological competence of Crohn's patients remains undecided. In order to investigate this question, immunological profiles (lymphocyte count, immunoglobulin level, DNCB response, Mantoux test and lymphocyte transformation to phytohaemagglutinin) have been measured in patients with Crohn's disease and compared with those of control subjects, matched for degree of illness.

The patients with Crohn's disease were studied in two groups, 21 being ill and 15 in remission. Ill patients with Crohn's disease had significantly elevated IgG and IgA levels and an increased rate of Mantoux negativity. The immunoglobulin changes were probably non-specific and the Mantoux responses were related to steroid therapy. Other parameters were similar in the ill patients and the control subjects. There was no significant difference between the patients with Crohn's disease in remission and the control subjects in any parameter.

The results do not confirm an immunological abnormality associated with Crohn's disease.

PARENT, K., BARRETT, J., and DODD WILSON, I. (1971), *Gastroenterology*, **61**, 431.
RÖPKE, C. (1972), *Scand. J. Gastroent.*, **7**, 671.

61. A Study of Lymphocyte Function in Crohn's Disease using the Mitotic Index:

D. CAVE and B. N. BROOKE, Professorial Surgical Unit, St. George's Hospital, London.

When studying cellular immunity in Crohn's disease, it has been found that lymphocyte transformation, though widely accepted as an indication of cell-mediated immunity, presents problems as regards quantification owing to difficulty of recognizing transformed cells. Mitosis is an easily recognized event to which transformation proceeds. Mitotic lymphocytes are accumulated using colchicine. By recording the percentage of lymphocytes in mitosis a mitotic index is obtained.

Ten consecutive patients with Crohn's disease of the large and/or small intestines, unselected for age or sex, were used in the study. The mitotic index for this group was highly significantly lower ($P < 0{\cdot}001$) than for a control group (mean mitotic index for Crohn's group 4·8, control group 15·8).

Doubt still remains regarding the immunological abnormality contributing to Crohn's disease (Brooke, 1972). The evidence regarding cellular immunity is equivocal using both lymphocyte migration and lymphocyte transformation.

The present results lend support to the evidence that the ability of lymphocytes to transform is reduced in Crohn's disease, which may therefore represent a state of anergy.

BROOKE, B. N. (1972), *Surg. Clins N. Am.*, **52**, 971.

62. Objective Measurements in Anal Control after Surgery for Imperforate Anus:

I. TAYLOR, H. L. DUTHIE, R. B. ZACHARY, and R. H. SMALLWOOD, Royal Infirmary and Children's Hospital, Sheffield.

Measurements of force in the anal canal, electrical activity of the internal anal sphincter, and rectal pressure have been made in 20 children after operations for varying degrees of imperforate anus. The degree of continence was compared with the following parameters: (1) the force in the anal canal on voluntary squeezing, (2) the response of the internal anal sphincter to rectal distension, (3) the presence of a functioning puborectalis sling, (4) sensation on rectal distension, and (5) rectal pressure on distension. The normal inhibitory response in the anal canal on rectal distension was found in 6 patients who had good continence. An abnormal response of an increase in force in the anal canal was found in 6 patients who had moderate or poor continence. By giving numerical values to the changes in the above five parameters a multifactorial assessment was made which correlated well with the degree of continence. In any such assessment sensory, motor, and reflex factors should be combined.

63. Gastrin and Recurrent Ulcer after Vagotomy:

C. G. CLARK and J. H. WYLLIE, Department of Surgery, University College Hospital Medical School, London.

Recurrent ulceration after vagotomy and pyloroplasty is usually associated with incomplete vagotomy, but incomplete vagotomy occurs in 50 per cent of patients. Byrnes et al. (1970) have shown that fasting plasma-gastrin levels in patients with recurrent ulcer are significantly higher than in asymptomatic postvagotomy patients, suggesting a specific involvement of gastrin in the aetiology. An investigation of gastrin levels and gastric secretion was therefore made in 12 patients with recurrent ulceration. Vagotomy was incomplete in all cases as judged by the insulin test. Plasma gastrin was measured by radioimmunoassay (Wyllie et al., 1972). The basal plasma-gastrin level did not differ from that in unoperated patients. Similarly the plasma-gastrin response stimulated by meat extract (Oxo) or insulin was either normal (truncal vagotomy) or slightly reduced (selective vagotomy).

These results suggest that gastrin does not play a major role in the aetiology of recurrent ulcer after vagotomy and drainage.

BYRNES, D. J., YOUNG, J. D., CHISHOLM, D. J., and LAZARUS, L. (1970), *Br. med. J.*, **2**, 626.
WYLLIE, J. H., BOULOS, P. B., LEWIN, M. R., STAGG, B. H., and CLARK, C. G. (1972), *Gut*, **13**, 887.

64. Inactivation and Degradation of Synthetic Human Gastrin I by Homogenates of Intestinal Mucosa: H. R. HUNZIKER (J. H. Wyllie), Department of Surgery, University College Hospital Medical School, London.

The bioassay technique of Smith et al. (1970) was used to demonstrate inactivation of synthetic human gastrin I (S.H.G. I) during its incubation at *p*H 6·8 with homogenates of rat intestinal mucosa. Chemical analysis showed that the inactivation process was characterized by deamidation of the C-terminal phenylalanine amide residue. Sequential hydrolysis of the peptide bonds followed.

This inactivation of S.H.G. I was carried out most actively by lysosomal and microsomal fractions of the homogenates which inactivated respectively 1·22 ± 0·10 and 3·31 ± 0·24 nmol. of S.H.G. I per 10 minutes for each mg. of protein. Treatment of the microsomal fraction with 0·26 per cent sodium deoxycholate did not disrupt the endoplasmic reticulum but it completely solubilized the enzyme which deamidates S.H.G. I. This enzyme was found to have similar properties to lysosomal cathepsin-C.

It thus appears likely that S.H.G. I is degraded by lysosomal enzymes and not by specific enzyme systems; this would explain the ability of homogenates from a variety of tissues to degrade gastrin *in vitro*. Since only certain organs appear to inactivate gastrin *in vivo* (Temperley et al., 1971) the existence of specific gastrin receptors or transport systems on the cell membrane may be inferred.

SMITH, G. M., LAWRENCE, A. J., COLIN-JONES, D. G., and SCHILD, H. O. (1970), *Br. J. Pharmacol.*, **38**, 206.

TEMPERLEY, J. M., STAGG, B. H., and WYLLIE, J. H. (1971), *Gut*, **12**, 372.

65. An Important Duodenal Role in Gastrin Release: J. R. HAYES, T. L. KENNEDY, JOY ARDILL, and K. D. BUCHANAN, Departments of Medicine and Surgery, Queen's University, Belfast.

The plasma-gastrin response to a standard protein meal has been studied in normal subjects and in patients with duodenal ulceration before and after surgery. The peak gastrin level following stimulation and its timing were noted.

In control subjects the mean peak gastrin level was 2·5 times the basal level and occurred after 30 minutes. In subjects with duodenal ulceration the mean peak gastrin level was 3·5 times the basal level and occurred after 45 minutes. However, in patients with pyloric stenosis the peak gastrin level was only 1·5 times the basal level and was markedly delayed, occurring at 60 minutes.

Two groups of postoperative patients were studied. In patients with vagotomy and no drainage procedure the peak gastrin level was 2·5 times the basal level and occurred at 45 minutes, whereas in patients with vagotomy and a gastro-enterostomy a much smaller peak which was only 1·4 times the basal level occurred at 45 minutes. A group of patients with the dumping syndrome following vagotomy and pyloroplasty had peak gastrin levels after only 15 minutes.

These results suggest that the passage of food into the duodenum plays an important role in the normal release of gastrin.

66. Histamine Release in Man and Acute Gastroduodenal Ulcers: W. SEIDEL, W. LORENZ, A. DOENICKE, G. MANN, and R. UHLIG, Surgical Clinic and Department of Experimental Surgery and Pathological Biochemistry, University of Marburg/Lahn, Germany.

Exogenous histamine causes acute erosions and ulcers in the gastro-intestinal tract of man and animals (Katz and Siegel, 1968). Since acute gastroduodenal ulcers are often observed after operations the release of endogenous histamine could be important in their pathogenesis. For this reason the plasma-histamine concentrations were measured fluorometrically in 60 male probands (10 for each drug) after anaesthetics (thiopentone 5 mg. per kg., methohexitone 2·5 mg. per kg., propanidid 7 mg. per kg.) and plasma substitutes (dextran-60, gelatin, Ringer's solution, 500 ml. per test person), and in 20 patients before and on the first 3 days following intra-abdominal operations.

After thiopentone, methohexitone, and propanidid, the plasma-histamine concentrations rose from 0·7 ± 0·4 ng. per ml. to 4·2 ± 3·1, 2·0 ± 0·9, and 3·8 ± 2·1 ng. per ml. respectively ($P < 0{\cdot}01$). Following dextran and gelatin in 2 and 8 cases respectively the plasma histamine reached values of 3 ng. per ml. Ringer's solution was without effect. In 3 patients histamine concentrations of 2 ng. per ml. were measured 2 days following operation. During the histamine infusion a half-maximum gastric secretion was correlated to 3 ng. per ml. of plasma histamine.

Since acute erosions were observed after histamine tests on gastric secretion, histamine release probably facilitates the development of 'stress' ulcers following surgery.

KATZ, D., and SIEGEL, H. J. (1968), *Prog. Gastroenterol.*, **1**, 67.

67. The Effect of Locally Administered 15(R) 15 Methyl-E_2 Methyl Prostaglandin on Basal and Pentagastrin-induced Acid Secretion in Man: D. C. CARTER, S. M. M. KARIM, D. BHANA, and P. A. GANESAN (A. P. M. Forrest), University of Edinburgh and Makerere University, Kampala, Uganda.

The inhibition of acid secretion in man by orally administered prostaglandin has not been described previously. In 19 tests in male volunteers 100, 150, or 200 μg. of 15(R) 15 methyl-E_2 methyl prostaglandin (PG) in 10 ml. of saline were instilled via the nasogastric tube after a 30-minute basal period. Aspiration was recommenced 30 minutes later and continued for 12 × 15 minute collections. Control tests where saline alone was instilled were performed in the same individuals. In 12 tests the maximal acid output (M.A.O.) in response to pentagastrin (6 μg. per kg. I.M.) was compared to the M.A.O. in 10 paired tests in which 200 μg. of PG were instilled 30 minutes prior to pentagastrin injection.

Inhibition of unstimulated acid secretion was seen in all the cases after 150 and 200 μg. of PG. The reduction in 3-hour output after 200 μg. of PG ranged from 98·5 to 37·3 per cent (mean 75·2 per cent) of the corresponding control values, and the inhibition was statistically significant ($P < 0{\cdot}01$). The M.A.O. after pentagastrin was lowered in all but 1 case by 200 μg. of PG, and the mean reduction of 64·8 per cent for the 12 paired tests was significant ($P < 0{\cdot}05$).

It is concluded that this PG analogue inhibits basal and pentagastrin-induced acid secretion when administered locally.

68. Isolation of a Gastric Secretory Hormone from Pig Intestinal Mucosa: R. C. KESTER, J. G. CHANDLER, H. ROSEN, and M. J. ORLOFF (Professor Sir Donald Douglas), The Departments of Surgery, Dundee Royal Infirmary, and University of California, San Diego, United States.

Previous studies have demonstrated that the intestinal phase of gastric secretion and portacaval shunt-related gastric hypersecretion are due to a jejunal hormone (Orloff et al., 1970). This study was directed at isolating this hormone from pig intestinal mucosa, using similar principles to those employed by Gregory and Tracy

(1964) for the isolation of gastrin. Assuming that the hormone is a small heat-stable peptide similar to other digestive hormones, 500-gallon batches of intestinal mucosa were boiled and centrifuged, and the supernatant was incubated with DEAE cellulose to absorb the active agent. After removing the active material from the cellulose with sodium hydroxide the *p*H was adjusted to 4, precipitating a substance which returned to solution at *p*H 7 and was soluble in isopropanol. This material was redissolved in saline and sterilized. Twenty-five extracts were tested by intravenous infusion into fasting dogs with Heidenhain pouches. Control studies using diluent were done before each test. A threshold response of 397 μEq. was elicited by a dose of approximately 1 g. Above 2 g. there was a highly significant mean total acid secretory response of 1115 μEq. and there was a typical dose–response relationship. The gastric stimulatory substance extractable from pig intestinal mucosa by a method that selectively isolates heat-stable acidic peptides is thought to be the hormone responsible for the intestinal phase of gastric secretion and for portacaval shunt-related gastric hypersecretion.

GREGORY, R. A., and TRACY, H. J. (1964), *Gut*, **5**, 103.
ORLOFF, M. J., VILLAR-VALDES, H., ABBOTT, A. G., WILLIAMS, R. J., and ROSEN, H. (1970), *Surgery, St Louis*, **68**, 202.

69. Pyloric Reflux in Duodenal Ulceration and Its Relationship to Smoking: R. FIDDIAN-GREEN, R. C. G. RUSSELL, and M. HOBSLEY, Department of Surgical Studies, The Middlesex Hospital, London.

The possibility that pyloric reflux may be excessive in patients with duodenal ulcer has been investigated in 59 patients and 50 control subjects. Gastric aspirates were collected during a plateau of maximum secretion (histamine diphosphate 0·04 mg. per kg. per hour), and reflux was estimated in terms of sodium concentrations. Details of smoking habits and length of history of symptoms were recorded.

The mean volume of reflux in the duodenal ulcer group was significantly greater than in the control group ($t = 3{\cdot}24$, $P < 0{\cdot}005$). There was a positive correlation between reflux and both length of history and average daily number of cigarettes smoked. Adjustment for length of history enhanced the correlation between reflux and smoking ($r = 0{\cdot}684$, $P < 0{\cdot}01$).

Abnormal reflux may be a factor in producing duodenal ulceration. Smoking may be a factor in producing reflux.

70. Pyloric Reflux and Gastritis in Man: R. FIDDIAN-GREEN, P. A. J. BALL, R. C. G. RUSSELL, and M. HOBSLEY, Department of Surgical Studies, The Middlesex Hospital, London.

Benign gastric ulceration occurs in an area of gastritis. If pyloric reflux is the cause of this gastritis the concentration of reflux within the stomach contents must be the critical factor, since a certain amount of reflux is a normal event.

Reflux concentrations are related to sodium concentrations. In 50 control subjects, 59 duodenal ulcer (D.U.) patients, and 28 gastric ulcer (G.U.) patients gastric aspirates were obtained during a plateau of maximal stimulation, and the sodium concentration was measured. The sodium concentration was significantly higher in G.U. patients than in D.U. patients or control subjects ($P < 0{\cdot}001$), 20 mEq./l. being the intermediate concentration between the level in G.U. patients and that in the other two groups.

Similar studies were performed in 17 further patients (G.U. or D.U.) who were subsequently subjected to gastrectomy. The specimens were examined histologically by two independent observers for the presence or absence of gastritis. No patient with a sodium concentration in the gastric juice of less than 15 mEq./l. had gastritis, while all the patients with a concentration exceeding 15 mEq./l. had gastritis.

High concentrations of reflux juice in gastric contents are associated with gastritis. In this series *all* the patients with a benign G.U. had such high levels of reflux.

71. The Effect of o-(β-Hydroxyethyl)-rutosides (HR) on Cutaneous Digital Xenon Clearance in Patients with Peripheral Atherosclerosis: J. C. MILLIKEN, G. D. KEYE, and M. J. FOX (W. G. Fegan), Department of Clinical Research, Sir Patrick Dun's Hospital, Dublin.

A method of estimating digital cutaneous blood-flow by an atraumatic isotope-labelling technique has been described (Fox and Milliken, 1972). McEwan et al. (1970) suggested that local rather than regional blood-flow insufficiency is the cause of skin lesions in peripheral vascular disease and that in patients with less than optimum capillary blood-flow or tissue perfusion HR could significantly improve tissue perfusion and oxygenation.

In 15 patients with severe foot ischaemia arteriography using the ^{131}I-albumin technique for visualization of the popliteal branches showed that 38 of a possible 45 infrapopliteal vessels were stenosed or occluded. Of the patients who responded clinically to the oral administration of HR, 1·0 g. daily, xenon-clearance studies were carried out in 7 before and after 4 weeks' treatment. The clearance data were expressed as K values, where $K = 0{\cdot}693/T_{\frac{1}{2}}$ and $T_{\frac{1}{2}}$ represents the biological half-life of the isotope in minutes. Pretreatment K values averaged 0·397 (range 0·301–0·630) and post-treatment values averaged 0·811 (range 0·630–1·155). These findings indicate that cutaneous xenon-clearance values provide useful evidence of clinical progress in chronic ischaemia.

FOX, M. J., and MILLIKEN, J. C. (1972), *Br. J. Surg.*, **59**, 312.
MCEWAN, A. J., STALKER, C. G., and LEDINGHAM, I. MCA. (1970), *Br. med. J.*, **3**, 612.

72. The Relationship between Ultrasound Assessment and Angiography in Occlusive Arterial Disease of the Lower Limb: J. CHAMBERLAIN (A. I. S. Macpherson), Royal Infirmary, Edinburgh.

The Doppler ultrasound technique has been used to assess the haemodynamics of the peripheral circulation in patients with arterial disease (Yao et al., 1969). Using this method the resting pressure index (ankle systolic pressure/brachial systolic pressure) and the response after exercise of the systolic pressure at the ankle were determined in 62 limbs. The angiograms in all the patients were assessed and graded according to the occlusions present (Morton et al., 1967).

Following exercise four types of abnormal response of the ankle systolic pressure were found (curves grade 1–4). In patients with a single aorto-iliac lesion a normal or slightly lowered pressure index was found, with a grade 3–4 post-exercise curve. In patients with localized femoropopliteal disease a low-pressure index usually accompanied a grade 1–2 post-exercise curve. In multiple occlusions there was a lower pressure index with a more severe grade of curve. If the profunda circulation was involved angiographically, then this resulted in a lower resting pressure index with a grade 3–4 curve. These results correlated well with the numerical assessment of the angiograms.

It is concluded that in patients who have a very low resting pressure index and with a grade 3–4 post-exercise curve the profunda circulation is impaired, even though clinical examination may not suggest this.

MORTON, D. L., EHRENFIELD, W. K., and WYLIE, E. J. (1967), *Archs Surg., Chicago*, **94**, 952.

YAO, S. T., HOBBS, J. T., and IRVINE, W. T. (1969), *Br. J. Surg.*, **56**, 676.

73. The Prediction of Organ Viability: K. C. Calman and P. R. F. Bell, Department of Surgery, Western Infirmary, Glasgow.

The techniques and clinical applications of organ preservation would be extended considerably if a simple and reliable method for the prediction of organ survival was available. During investigations of organ storage the changes in adenine nucleotide content in the rat kidney have been studied.

Both kidneys were clamped for 0–120 minutes at normothermia. One kidney was removed for estimation of ATP, ADP, and AMP; the clamp on the other kidney was released and survival was determined. The total kidney adenine nucleotide content (ATP+ADP+AMP) was plotted according to whether the animal survived or died; on this basis there was a good separation between the two groups ($P<0{\cdot}001$). If the renal adenine nucleotide contents were below 0·8 µmol per g. the animals died and when the nucleotide contents were above this level the animals survived.

The total adenine nucleotide level in organs may be used to predict survival. Two corollaries follow: (1) variations in adenine nucleotide levels should occur when an organ is perfused with different solutions, and this has been confirmed; (2) increasing the ATP content of organs (e.g., by perfusion with insulin, intermediary metabolites of Persantin) should effectively increase the storage time and this has also been confirmed.

74. The Influence of Serum and Cellular Factors in the Depression of Phytohaemagglutinin (PHA)-induced Transformation of Lymphocytes in Gastro-intestinal Carcinoma: R. M. Grant, C. Harris, W. Mathieson, and J. N. Norman, Department of Surgery, University of Aberdeen.

Depression of PHA-induced lymphocyte transformation in cases of carcinoma may be due to the presence in the serum of a factor produced by the tumour. Such a factor would occur in the highest concentration in the venous blood draining a tumour.

In 6 cases of gastro-intestinal carcinoma the PHA-induced transformation of peripheral venous blood lymphocytes cultured in media containing sera derived from autologous peripheral venous blood, autologous inferior mesenteric venous blood from close to the tumour, and homologous group AB blood has been studied.

Maximal lymphocyte transformation occurred where the serum was derived from pooled homologous AB blood. By comparison, depression of lymphocyte transformation occurred where the serum was derived from either of the autologous sources. This depression was greatest where serum from the inferior mesenteric venous blood had been incorporated. Further depression in transformation was noted where lymphocytes from the inferior mesenteric venous blood were cultured in serum from the same source.

These results, while suggesting the presence of a factor in the serum causing depression of lymphocyte reactivity, also indicate that changes in the lymphocytes themselves might be important.

75. Phytohaemagglutinin Transformation of Peripheral and Lymph-node Lymphocytes in Patients with Gastro-intestinal Cancer: P. J. Guillou, T. G. Brennan, and G. R. Giles, University Department of Surgery, Leeds (St. James's), and University Hospital, Leeds.

Regional lymph-nodes draining experimental tumours show enhanced immunological activity (Alexander et al., 1967) and this response is considered to be important in the control of tumours such as breast cancer (Deodhar et al., 1972). The phytohaemagglutinin-induced transformation of peripheral and mesenteric lymph-node lymphocytes has been compared in 8 patients with gastro-intestinal cancer and 7 patients with benign abdominal disease.

When cultured in autologous serum, 39·7 ± 3·8 per cent of peripheral lymphocytes from patients with cancer transformed, compared with 50·4 ± 4·6 per cent from control subjects. Culture of these lymphocytes in homologous AB serum resulted in transformation rates of 41·7 ± 5·9 per cent in patients with cancer (4 increased, 2 decreased) and 50·1 ± 6·4 per cent in control subjects (all essentially unchanged).

In control subjects the mean transformation rates in nodes from small-bowel mesentery was 41·2 per cent and in paracolonic nodes was 45·6 per cent. Similar studies in patients with cancer produced mean transformation rates of 27·7 per cent for mesenteric lymph-nodes and 29·7 per cent for cells from nodes directly draining the neoplastic lesion. Culture of lymph-node cells in homologous AB serum resulted in increased transformation rates.

The mesenteric lymph-nodes of patients with gastro-intestinal cancer showed depressed rather than enhanced immunological competence.

ALEXANDER, P., BENSTED, J., DELORME, G. J., HALL, J. G., and HODGETT, J. (1967), *Proc. R. Soc.*, B, **174**, 237.

DEODHAR, S. D., CRILE, G., and ESSELSTYN, C. B. (1972), *Cancer, N.Y.*, **29**, 1321.

76. The Measurement of Growth Rate in Rectal Carcinoma: G. Bone and R. Camplejohn (I. D. A. Johnston), Departments of Surgery and Pathology, University of Newcastle upon Tyne.

It is suggested that tumour growth depends upon an increased proliferation of malignant cells as compared with adjacent normal cells. Fourteen patients with carcinoma of the rectum were studied. The relative growth rates of the tumours and normal rectal mucosa were measured by an *in vivo* stathmokinetic technique (Refsum and Berdal, 1968). Vincristine, 0·045 mg. per kg. body-weight, was given to produce mitotic arrest. Biopsies were taken from the tumour and normal rectal mucosa before and up to 4 hours after the intravenous injection of a single dose of vincristine. The mitotic index rose after the administration of vincristine and the rate of increase was determined from the biopsy specimens, and using this information the potential doubling time and mitotic duration were calculated.

The mean potential doubling time for the rectal carcinoma was 250 hours, and for normal rectal mucosa 90 hours. The mean mitotic duration for rectal carcinoma was 3 hours, and for normal rectal mucosa 2·1 hours.

It is concluded that in rectal carcinoma the growth rate is slower than that of normal rectal mucosa. Tumour growth must therefore be due to a reduced cell loss compared with normal mucosa.

REFSUM, S. B., and BERDAL, P. (1968), *Tidsskr. norske Lægeforen.*, **12b**, 1224.

77. Skin Disinfection—A Cause of Coliform Wound Infection? D. Shaw (Sir Donald Douglas), Department of Surgery, University of Dundee.

Miles predicted in 1942 that infections due to Gram-negative bacilli would become more prevalent after the suppression of Gram-positive cocci. Preoperative skin disinfection, the reduction or elimination of normal skin flora, and postoperative wound sepsis caused by coliform organisms have not been studied. The aim of this work was to elucidate any adverse relationship.

Skin preparation in the operating theatre followed the recommendation of the Medical Research Council Sub-committee Report (1968). A skin biopsy was taken from the wound edge immediately the incision was complete and was placed in nutrient broth containing a chlorhexidine inhibitor. After culture the organisms were identified.

Specimens were taken from 244 patients having elective surgery; all had clean operations. There was growth of organisms from 40·2 per cent. The wound-infection rate for coliform organisms was 5·1 per cent in patients whose specimens grew skin flora and 11·6 per cent in patients whose specimens had no growth. The difference is statistically significant.

The killing of resident flora by skin disinfection appears to be a factor in some cases of wound infection due to coliform organisms.

MEDICAL RESEARCH COUNCIL SUB-COMMITTEE REPORT (1968), *Lancet*, **1**, 831.
MILES, A. A. (1942), *Ibid.*, **1**, 809.

78. Intraperitoneal Noxytiolin as an Experimental Chemotherapeutic Agent: S. DESAI and C. W. JAMIESON, Surgical Unit, St. Mary's Hospital, London.

Following claims that local instillation of noxytiolin (Noxyflex) has chemotherapeutic value in bladder tumours (Garrett, 1969) it was reported (Jamieson, 1970) that noxytiolin inhibits the growth of tumour cells in culture at very low concentrations (0·0025 per cent). The present study was designed to detect any local or systemic chemotherapeutic effect of noxytiolin *in vivo*.

Four groups of 10 BALB/C mice received intraperitoneal injections of 1×10^5 Ehrlich's ascites tumour cells; this dose of tumour cells consistently produced ascites. The tumour growth rate was measured by daily weighings of the animals and the duration of their survival after injection. Intraperitoneal injections of 5 and 15 mg. of noxytiolin per kg. body-weight were given on days 1 and 7 after the injection of tumour cells. Identical groups of control mice received a sham injection of TC 199 on the same days. Fifteen mg. of noxytiolin per kg. body-weight produced a highly significant slowing of the growth of tumours when compared with the control mice.

The experiments were repeated using the same dose of noxytiolin, but the noxytiolin and the control injections were given subcutaneously. No difference in the growth of tumours was observed in 40 mice.

Local instillation of noxytiolin has a chemotherapeutic effect, supporting its toxicity *in vitro*, but systemic administration has no such value in this tumour model.

GARRETT, M. J. (1969), *Br. J. clin. Pract.*, **23**, 10.
JAMIESON, C. W. (1970), *Br. J. Surg.*, **57**, 863.

SHORT NOTES OF RARE OR OBSCURE CASES

PNEUMOMEDIASTINUM IN A CASE OF PERFORATED RETROPERITONEAL HERNIA

BY P. G. RANSLEY
HAROLD WOOD HOSPITAL, ROMFORD, ESSEX

THE unusual association of a pneumomediastinum and small-bowel obstruction was explained with the finding of a perforated retroperitoneal hernia. This complication of a retroperitoneal hernia does not appear to have been reported previously.

CASE REPORT

Mr. H. G., aged 74 years, was a gipsy of relatively fixed abode who had been under the care of physicians for several years with chronic bronchitis and emphysema. He was a very cachetic patient, never exceeding 45 kg. in weight owing to a combination of alcoholism and a malabsorption state following a partial gastrectomy 25 years previously. He was breathless at rest.

On 14 Jan., 1971, he was admitted to hospital at his general practitioner's request. At that time he showed little change from his normal state and a chest radiograph showed no change from previous examinations. While in hospital he developed slight abdominal distension with normal but active bowel-sounds, but on 25 Jan. he suddenly collapsed with a rigid distended abdomen. His blood-pressure was 90/60 mm. Hg. and his pulse was 110 per minute. Erect abdominal films demonstrated multiple small-bowel fluid levels and the chest radiograph now showed a pneumomediastinum (*Figs.* 1 and 2).

Following resuscitation the patient underwent emergency laparotomy. The appearances at operation were of long-standing small-bowel obstruction. The collapsed and distended jejunal segments met in a mass of inflammatory tissue just lateral to the duodenojejunal flexure. Closer examination revealed a loop of bowel herniated into the left lateral paraduodenal fossa. On freeing the herniated loop a ragged perforation was visible at the apex. The bowel recovered sufficiently to be considered viable, the perforation was closed, and the walls of the fossa were apposed. He made an excellent immediate recovery but his chest condition deteriorated over several days and he died 1 week postoperatively.

DISCUSSION

Spontaneous mediastinal emphysema or pneumomediastinum was probably first described by Laennec in 1879 (quoted by Hamman, 1939) but it has received scant attention in the medical literature, being usually associated with trauma or rupture of an emphysematous bulla. Air in the mediastinum can track downwards into the retroperitoneal tissues (Hamman, 1939) and the reverse is sometimes seen following presacral insufflation.

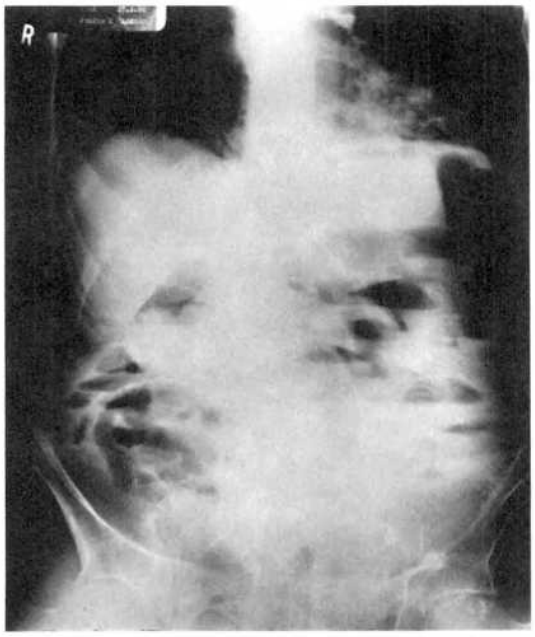

FIG. 1.—Erect radiograph of the abdomen, showing small-bowel obstruction.

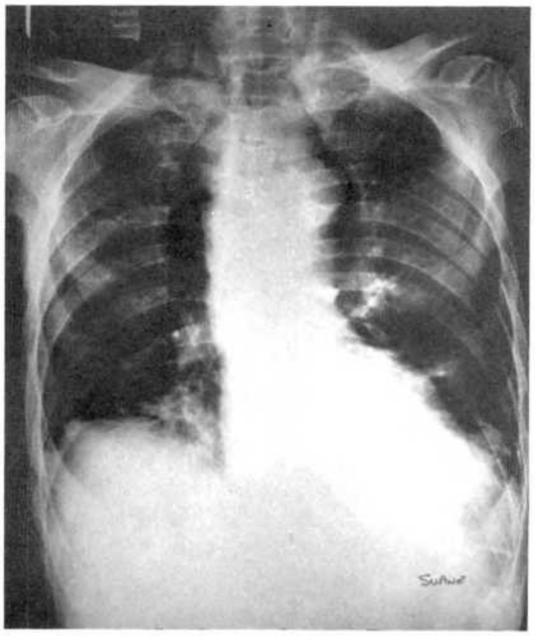

FIG. 2.—Chest radiograph, demonstrating pneumomediastinum.

Paraduodenal fossa hernia is a surgical rarity which was well described by Moynihan (1906) and is usually a diagnosis made at laparotomy. It is probably a congenital abnormality dependent upon disorders of midgut rotation and not a 'herniation' (Andrews, 1923). Preoperative suspicion may be raised by a long atypical history of subacute obstruction, or the finding of an unusual pattern of obstructed loops on radiographic examination, but it is rare for the diagnosis to be made prior to exploration.

The interest in the present case lies in the fact that although a diagnosis of perforation of an obstructed intestinal loop was made preoperatively, the complete diagnosis was missed. The presence of air in the mediastinum with small-bowel obstruction should have suggested a retroperitoneal perforation, with air tracking upwards into the chest.

Acknowledgement.—I would like to thank Mr. J. E. Talbot, F.R.C.S., for permission to publish this case who was admitted under his care.

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AN UNUSUAL METASTASIS OF CARCINOMA OF RECTUM

By J. C. B. PENFOLD and C. V. MANN
ST. MARK'S HOSPITAL, LONDON

THE following case history is presented to draw attention to the possibility of metastases from carcinoma of the rectum developing in unusual situations when early ligation of the vascular pedicle is employed as part of the operative technique.

CASE REPORT

At a routine follow-up examination Mr. W. B. was found to have a 1·5-cm. asymptomatic nodule in the position of the right posterior internal haemorrhoidal venous plexus. The anal mucosa moved freely over the module.

A restorative resection for a moderately well-differentiated adenocarcinoma of the upper third of the rectum had been performed 9 months previously. At operation early ligation of the vascular pedicle had been performed and the rectal stump had been irrigated with a 1-in-400 perchloride of mercury solution prior to anastomosis. The anal sphincters had been stretched to four fingers at the conclusion of the operation.

Examination of the specimen had shown an adenocarcinoma of the ulcerating type, 7 cm. in diameter and nearly circumferential. There had been 7 cm. of normal bowel below the growth. Microscopic examination of the specimen had shown it to be an adenocarcinoma of average grade. It had spread through the rectal wall and had invaded the perirectal fat (Dukes's B case). Twelve lymph-nodes had been examined and found to be tumour free. Some growth had been found in the adjacent extramural veins.

Because of the position of the nodule and the operative anal stretch, it was considered most likely to be a thrombosed internal haemorrhoid. However, at review 3 months later the nodule was 2 cm. in size. The patient was admitted for a wide excision on a clinical assumption of malignancy.

The lump together with at least 2·5 cm. of uninvolved surrounding tissue was locally excised; this excision totally divided the external sphincter but some of the internal sphincter and puborectalis sling remained. The wound was left open.

Postoperatively the patient was at first completely incontinent, but control gradually improved. At discharge from hospital 3 weeks later he was continent to solid faeces.

The excised tissue proved to be an average-grade adenocarcinoma of similar histology to that of the original tumour.

It is now considered that the patient has had optimal curative treatment for the recurrence and no further surgery is indicated.

PATHOGENESIS OF THE SECONDARY GROWTH.—This appears to be an example of embolic retrograde venous spread. The presence of extramural venous invasion in the original operative specimen and the early ligation of the vascular pedicle were probably the causative factors. The growth was not due to direct spread, as there were 7 cm. of normal bowel below the excised original tumour and rectal examination of the rectal stump is still completely normal, nor is it an example of implantation, as the nodule was situated below the anal mucosa which moved freely over it. There has never been any haemorrhoidal wound to facilitate local penetration and the rectal stump was irrigated at the time of operation.

DISCUSSION

This is a most unusual site of secondary spread of carcinoma of the rectum. A search of the records of St. Mark's Hospital was only able to demonstrate similar haemorrhoidal venous involvement in 3 cases and all these were in very advanced carcinoma of the rectum. Anal metastases from rectal cancers have been reported before, but those appeared to have arisen by different modes of spread compared with this case (Killingback, Wilson, and Hughes, 1965).

Recent reports have suggested that early vascular pedicle ligation is followed by an increased incidence of systemic metastases (Hughes and Cuthbertson, 1962). The present case supports this view that retrograde vascular flow occurs following pedicle ligation, thereby allowing systemic tumour embolism to take place.

It has been noted before that the presence of extramural venous invasion is a common finding in those who have or develop hepatic metastases (Bussey, 1971).

Careful examination of the operative specimen has enabled us to determine the pathogenesis of this secondary deposit and to encourage us to believe that local excision will be sufficient treatment.

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TORSION OF A GASTRIC LEIOMYOMA

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SUMMARY

A patient with an extraluminal gastric leiomyoma, which presented as an emergency because of torsion, is reported. This is thought to be the first report of such an occurrence. The diagnosis was not made preoperatively in spite of intensive investigation.

EXTRALUMINAL gastric leiomyomas are uncommon and usually present as a mass. The following case report is of a patient who presented as an acute abdominal emergency but with no evidence of gastro-intestinal bleeding.

CASE REPORT

Mrs. I. C., aged 59 years, was admitted to the University Hospital of the West Indies, Jamaica, with a 12-hour history of peri-umbilical and left hypochondrium pain and vomiting. The pain had been sudden in onset, having woken her up. The vomitus consisted of bile. There was no significant previous gastro-intestinal history.

On examination the patient was distressed because of severe pain, and the significant findings were confined to the abdomen. A large tender mass was palpated in the left hypochondrium, and an enlarged uterus with fibroids was palpated on vaginal examination. She was admitted to the medical wards with a diagnosis of splenomegaly. Investigations on admission showed a haemoglobin of 13·5 g. per 100 ml. and a white-cell count of 12,400 per c.mm. with a polymorph leucocytosis. She continued to vomit bile after admission and her abdomen became more distended. A diagnosis of perinephric abscess was suggested but an intravenous pyelogram was normal. Surgical consultation was sought 48 hours after her admission and at that time it was noted that she was anaemic and that the femoral pulses were unequal; the abdominal mass was smooth and tender and did not move on respiration. A diagnosis of ruptured aortic aneurysm or haemorrhage into a pancreatic cyst was considered. An emergency aortogram showed a normal aorta displaced to the right by an avascular mass. A barium-meal examination showed the stomach to be displaced anteriorly but otherwise normal.

At laparotomy the abdomen contained 2 litres of dark blood; the mass was palpated in the lesser sac and was exposed through the gastrocolic omentum. It was oval in shape, measuring 20 × 10 cm., and haemorrhagic, and was attached to the posterior wall of the antrum of the stomach by a pedicle on which the tumour had twisted in a clockwise direction (*Fig.* 1). The tumour was excised with a cuff of normal stomach to reveal ulceration of the stomach mucosa over the base of the pedicle. The patient made an uneventful recovery. Histological examination confirmed an infarcted leiomyoma, with cells containing clear cytoplasm in many areas.

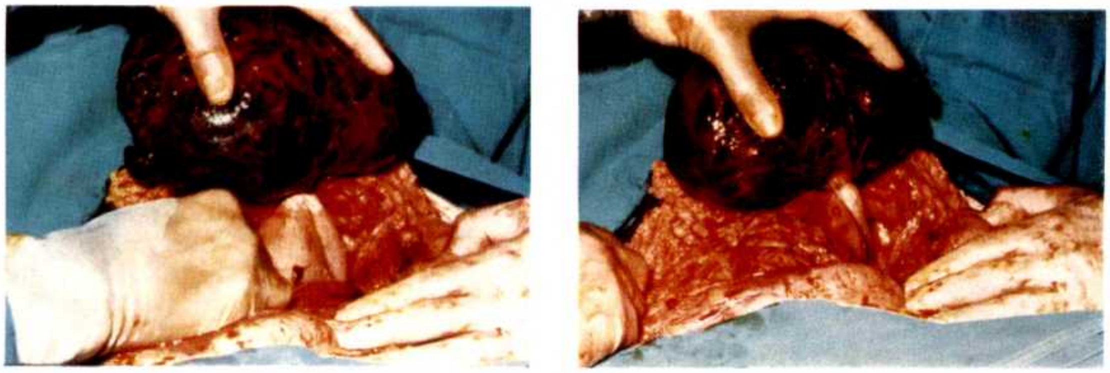
A B

FIG. 1.—Operative photographs of the exogastric leiomyoma (A) twisted and (B) untwisted.

DISCUSSION

Leiomyomas constitute 1·6 per cent of all gastric tumours which present clinically (Marshall, 1955). They usually project into the lumen of the stomach and have an associated ulcer on the mucosal surface. The patients frequently have peptic-ulcer-type symptoms or evidence of upper gastro-intestinal bleeding. Extraluminal gastric leiomyomas are very unusual and few are pedunculated; they may present clinically because of a large mass. The diagnosis of extraluminal gastric leiomyomas is difficult. Schofield and Fox (1965) and Smithwick, Beisecker, and Leand (1969) described separate cases in which the tumour enlarged into the lesser sac and a diagnosis of pancreatic pseudocyst was made. Salmela and Kohler (1969), in reviewing the radiographic appearances of 59 mesenchymal tumours of the stomach, mentioned an exogastric leiomyoma which had displaced other organs. Wolf (1968), in describing a massive exogastric leiomyoblastoma, found that barium-meal examination was unhelpful, and the diagnosis was made on noting a large right gastro-epiploic artery on selective coeliac axis angiography. Seinnreich, Freidman, Dacso, and Stern (1966) described a large exogastric leiomyoblastoma which simulated a uterine fibroid; no abnormalities were shown by the barium meal examination. Arsac, Martin, Tocquet, and Delavierre (1967) investigated extensively a case which had presented with a pleural effusion, the diagnosis only being made at an exploratory operation.

The patient described here presented as an acute abdominal emergency with a painful tender mass. It became evident that she was bleeding into the peritoneal cavity. The diagnosis was not made after extensive investigations including aortography and a barium meal. In essence investigations showed an avascular tumour in the lesser sac displacing other organs. An aortic aneurysm was excluded, but the clinical progress was not typical of a pancreatic lesion. We have been unable to trace any other case of exogastric leiomyoma in the literature which presented with torsion in this way. However, there are 3 reports of exogastric leiomyomas or leiomyoblastomas which presented with bleeding into the peritoneal cavity owing to ulceration of the peritoneal surface of the tumour (Secher, 1968; Smithwick and others, 1969).

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TETRAPLEGIA IN RHEUMATOID ARTHRITIS WITH COMPLETE RECOVERY AFTER SURGERY

By A. J. POLYZOIDES and J. R. PEARSON

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SUMMARY

1. A patient with tetraplegia caused by subluxation of the lower cervical spine in rheumatoid arthritis is presented. The clinical history, early complication, and delayed diagnosis are described.
2. Compression of the dura mater by rheumatoid granulation tissue and vertebral subluxation are suggested to be responsible for the cord damage.
3. Failure of conservative treatment after a week is a strong indication for surgery.
4. Posterior decompression of the cervical spine and splitting of the dura mater are recommended.

Tetraplegia caused by subluxation of the lower cervical spine in rheumatoid arthritis was first described by Hauge in 1958.

Recognition of the onset of tetraplegia is not easy because of the deformities of rheumatoid arthritis and the difficulty in eliciting neurological signs which involve joints such as the elbow and knee.

Sharp and Purser (1961) described the atlanto-axial subluxation in rheumatoid arthritis in detail but this subluxation, despite its high incidence of 25 per cent in rheumatoid patients, rarely produces neurological complications.

The number of patients reported with complete tetraplegia caused by lower cervical rheumatoid subluxation remains very small and complete neurological recovery is unusual. Hopkins (1967) reported 4 patients, 2 of whom had a partial recovery while 2 died. Crellin, Maccabe, and Hamilton (1970) described 1 patient with tetraparesis who had complete recovery after 1 year following anterior cervical fusion.

The present case is interesting because of the development of tetraplegia and subsequent complete recovery following decompression of the cervical spine and splitting of the dura mater.

CASE REPORT

A man aged 51 years, who was a fitter in the car industry, was transferred to the Royal Orthopaedic Hospital on 16 June, 1970, with complete tetraplegia below the fifth cervical root level.

The clinical history started in 1945 when at the age of 26 the patient was admitted to an Army hospital complaining of severe burning pain in both heels.

In 1958 he complained of low-back pain and a diagnosis of ankylosing spondylitis was made in another hospital and the patient was sent to have spa treatment. In the same year, swelling in the proximal interphalangeal joints of the right middle and left index fingers was noticed by the patient and the diagnosis was changed to rheumatoid arthritis.

In January, 1970, neck pain with paraesthesia in the right hand became a serious complaint. In May, 1970, the patient complained of weakness in both arms and the right leg; he was sent to St. John's Hospital, Droitwich, for physiotherapy. The visiting physician diagnosed tetraparesis and radiographs showed cervical rheumatoid subluxation of C.V.4 over C.V.5 (*Fig.* 1).

The patient was immediately transferred to a general hospital and skull traction was applied to immobilize the neck in extension. As there was neurological deterioration to complete tetraplegia after 1 week he was transferred to the Royal Orthopaedic Hospital and surgery was undertaken the following day.

On admission the patient was comfortable in a cervical plastic collar. He was orientated in time and space and his cranial nerves were normal. Respiration was entirely diaphragmatic and he had no bladder or bowel control; an indwelling catheter was draining urine satisfactorily.

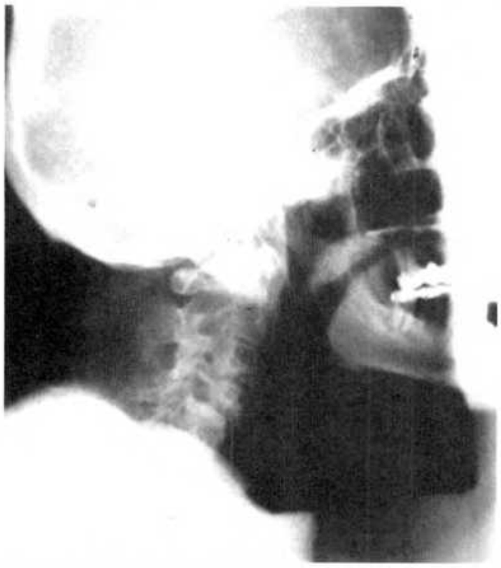

FIG. 1.—Lateral radiograph of the cervical spine, showing moderate subluxation of C.V.4 over C.V.5.

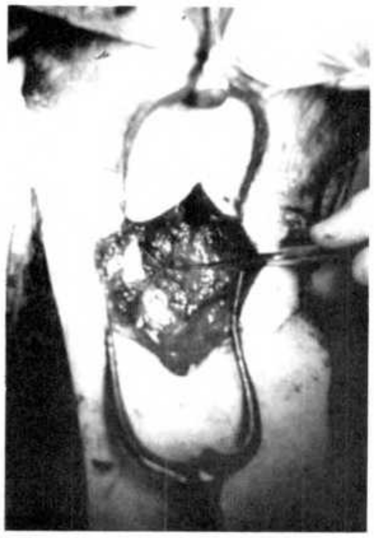

FIG. 3.—Photograph taken during the operation, showing the probe pointing to a circumferential band of granulation tissue constricting the dura.

Both wrists and hands showed chronic rheumatoid changes.

Muscle power was charted according to the Medical Research Council muscle grading and only the deltoid muscles were graded 4, all the other muscles in both the upper and lower limbs being graded 0 and 1.

Deep reflexes were exaggerated in the upper limbs and absent in the lower limbs. Abdominal reflexes were absent and the superficial plantar responses were extensor. The patient was anaesthetic from the fourth intercostal space downwards. The clinical picture was that of complete tetraplegia below the fifth cervical nerve-root.

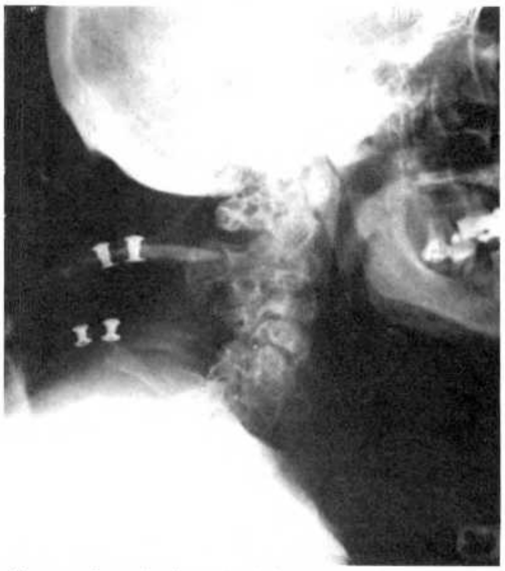

FIG. 2.—Lateral radiograph of the cervical spine with the neck immobilized in a collar with extension, showing reduction of the subluxation.

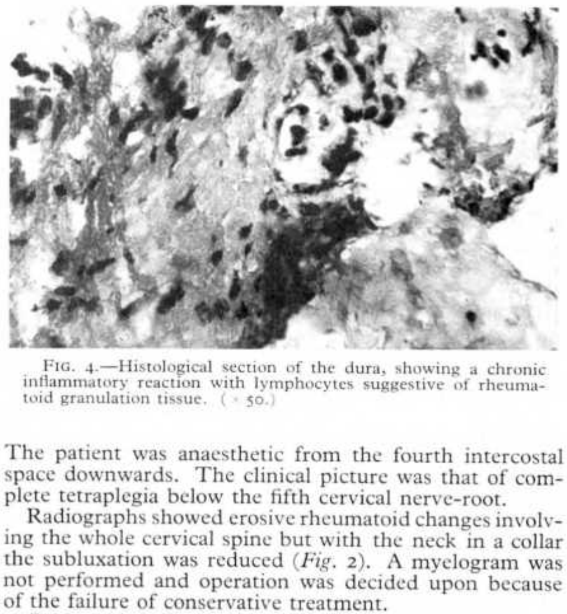

FIG. 4.—Histological section of the dura, showing a chronic inflammatory reaction with lymphocytes suggestive of rheumatoid granulation tissue. (× 50.)

Radiographs showed erosive rheumatoid changes involving the whole cervical spine but with the neck in a collar the subluxation was reduced (*Fig.* 2). A myelogram was not performed and operation was decided upon because of the failure of conservative treatment.

OPERATION.—The patient was intubated and halothane gas and oxygen were administered. He was placed prone with a head-rest extending the neck, the anterior part of the collar being retained to provide support.

Radiographs on the operating table showed complete reduction of the subluxation of C.V.4 over C.V.5 and with the aid of a marker the site of the fourth cervical vertebra was identified. A midline incision was made over the spinous processes. The third and fourth cervical

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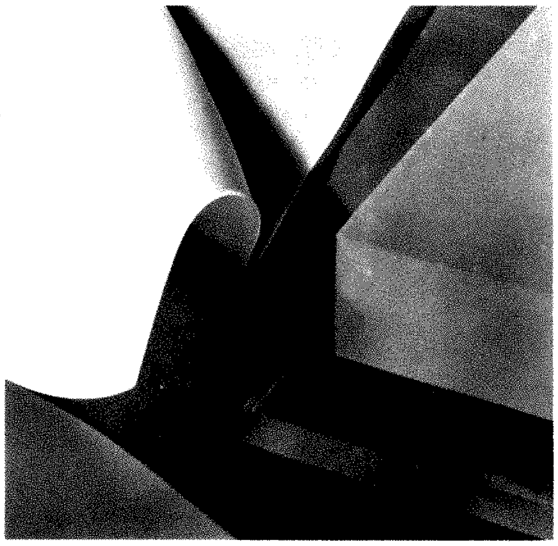

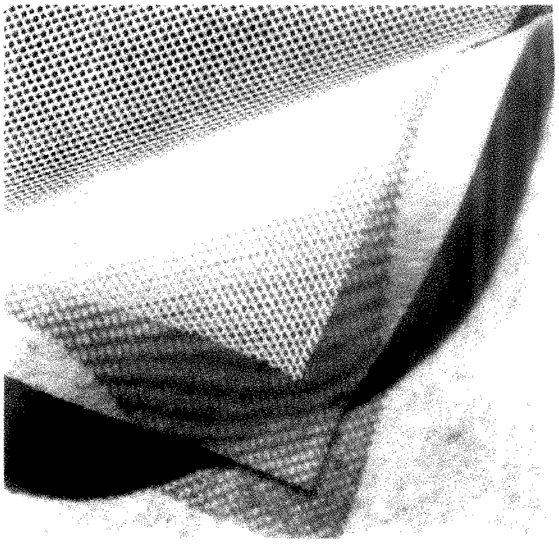

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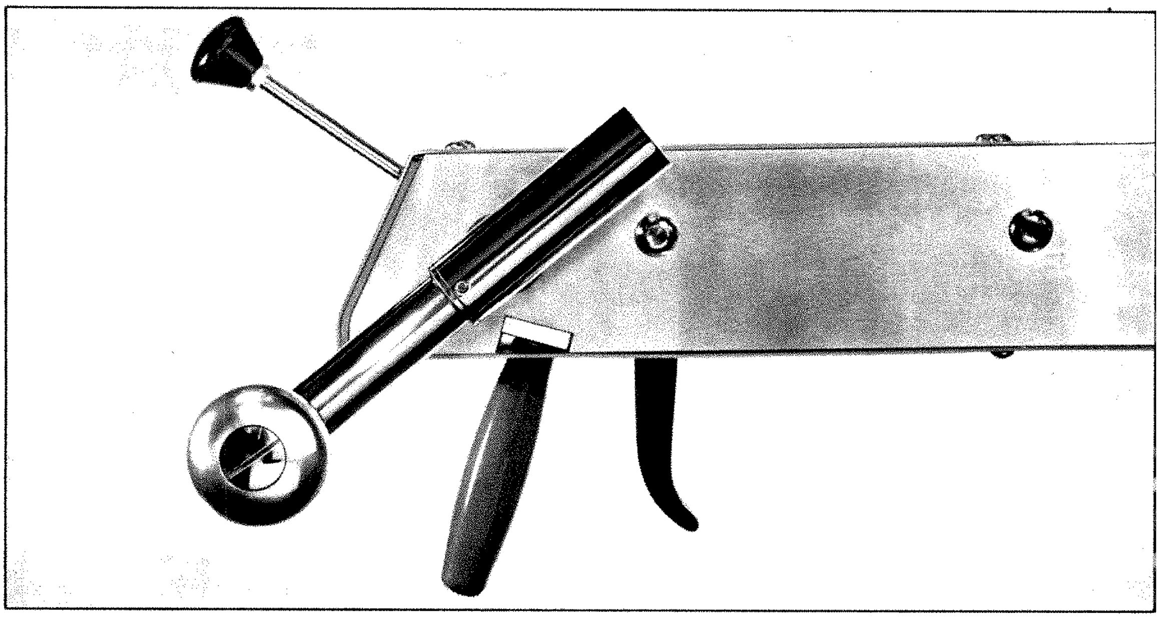

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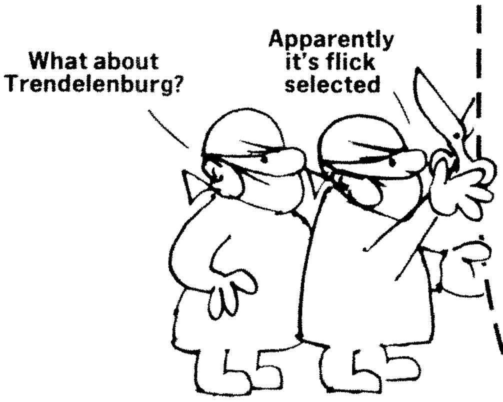

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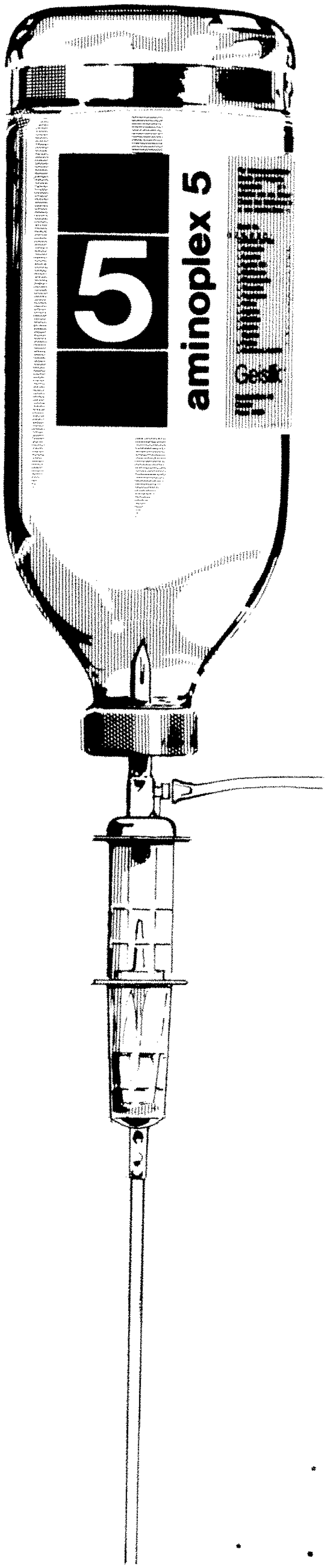

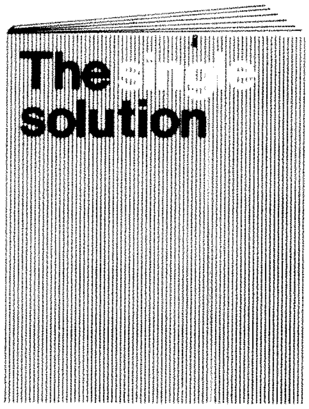
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segments were found to be hypermobile. Excision of the spinous processes of C.V.3 and C.V.4 with the medial half of the laminae was carried out, preserving a lateral laminar ridge.

The spinal cord was non-pulsatile and constricted at the level of C.V.4; proximally there was a circumferential infiltration of granulation tissue constricting the dura mater (*Fig.* 3). The dura sheath was opened without incising the arachnoid membrane and therefore there was no leakage of cerebrospinal fluid. A strip of dura mater, 1 cm. long and 0·5 cm. wide, was sent for histological examination to establish the presence of rheumatoid granulation tissue (*Fig.* 4). No attempt was made to excise the remaining granulation tissue as the cord was adequately decompressed and was pulsating.

PROGRESS.—Postoperatively the polythene collar was reapplied. On the fourth postoperative day, muscle grading showed signs of recovery. The muscles of the upper and lower limbs were graded 2 and 3. The superficial plantar responses were flexor. In the following weeks the patient showed steady improvement; by 6 weeks he had bladder sensation and control was returning to normal; in the fourth month his muscle power was graded 4 and he was fully mobilized.

Spinal fusion was not performed as radiographs of the cervical spine in flexion and extension 7 months after operation showed no evidence of the previous subluxation, and spontaneous fusion of the body and apophysial joints was obvious. Spontaneous fusion is anticipated in rheumatoid diseases of the cervical spine (Marmor, 1967).

Seven months after operation the patient was discharged home. At present he is enjoying a leisurely home life, feeding himself, and walking with sticks. A return to his previous job as a fitter is not anticipated but suitable employment will be found as he is very determined to start working again.

DISCUSSION

Lower cervical rheumatoid subluxation is not so well recognized as atlanto-axial subluxation and particular care should be paid to the clinical history of the patient and to early neurological complaints. Repeated radiographs in flexion and extension of the cervical spine should be taken of patients with rheumatoid arthritis, as 40 per cent have involvement of the cervical spine (Sharp, 1957), and more recently Weiss and Freehafer (1964) reported an even greater incidence of 50 per cent. A great number of patients will show atlanto-axial subluxation, and some will show lower cervical subluxation or both (Crellin and others, 1970); the precise incidence is still not known. In the present patient the diagnosis was made after tetraparesis and immobilization of the neck showed deterioration to tetraplegia. Marmor (1967) and Crellin and others (1970) stated that reduction of the subluxation is sufficient for cord recovery; this did not occur in the patient reported here. The operative findings clearly showed that infiltration of the dura mater with rheumatoid tissue is an added cause of compression of the spinal cord which can only be relieved surgically. This added pathology involving the dura mater has been described by Hopkins (1967) but has not been stressed sufficiently to be recognized and documented.

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INTERNAL PUDENDAL ARTERIOGRAPHY AFTER PRIAPISM

BY I. LYNN EVANS AND A. E. YOUNG
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SUMMARY

A case of postpriapic impotence which was investigated by internal pudendal arteriography is described and the possible therapeutic application of intra-arterial vasoconstrictors in the management of priapism is considered.

LONG-continuing priapism is almost invariably succeeded by impotence. The prognosis in individual cases must be judged clinically and on the basis of the duration of the priapism, but the clinician can usually do no more than meet his patient's anxious inquiries with reassurance and optimism. The postpriapic patient has normal penile sensation and ejaculatory reflexes, but may be impotent because he is unable to develop an erection and is thus incapable of intromission.

Arteriography, by showing irreversible arterial inflow occlusion, could avoid a futile search for a cure and perhaps indicate patients who would be suitable for a prosthetic penile implant (Pearman, 1967). This paper reports a case of postpriapic impotence which was investigated by internal pudendal arteriography.

CASE REPORT

The patient, a 39-year-old West Indian, was admitted in October, 1970, 24 hours after the onset of priapism. He had been seen 8 months previously when he had complained of headaches and had been found to be hypertensive. No cause was found to explain his hypertension, and his blood-pressure was controlled on guanethidine and Navidrex-K. One month prior to admission a transient episode of priapism had responded to treatment with diazepam.

On examination no abnormality was detected apart from priapism. The blood-pressure was 130/88 mm. Hg and the haemoglobin genotype was AA. Medical treatment using sedation and intravenous heparin was instituted, and the priapism settled over the next month.

At subsequent out-patients' clinics he complained of inability to develop an erection; the poor prognosis was explained, but he was none the less referred again on two occasions, and eventually to one of the present authors at whose instigation bilateral pudendal arteriography was performed. A catheter was introduced through the right femoral artery and manipulated through each internal iliac artery to each internal pudendal artery, using a Müller catheter guide system. The radiographs thus obtained (*Fig.* 1) displayed a normal pelvic arterial pattern, with the exception of the internal pudendal arteries which were seen to be occluded at the level of the perineal membrane. No arterial filling of the penis was apparent.

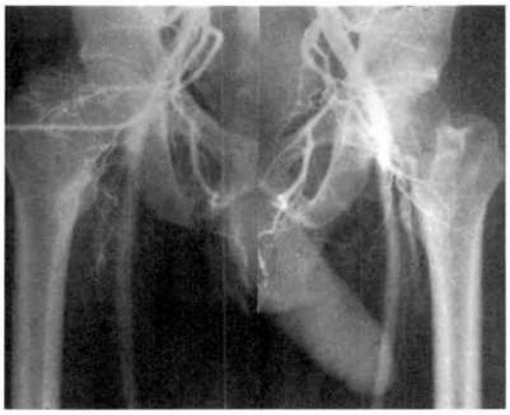

FIG. 1.—Composite right and left pelvic arteriograms, showing the internal pudendal arteries occluded at the level of the perineal membrane.

DISCUSSION

The erectile tissue of the penis draws its arterial supply almost exlusively from the internal pudendal arteries. In normal erection the primary haemodynamic event is active arteriolar dilatation, allowing filling and turgidity of the corpora cavernosa. Restriction of the venous outflow is less important. The return to flaccidity is initiated by arteriolar constriction and shunting into arteriovenous anastomoses.

Priapism may be symptomatic of a variety of diseases or may be 'idiopathic'. Neurological disease, especially spinal cord damage and disseminated sclerosis, may be responsible, as may venous obstruction by malignant disease of the bladder, rectum, or prostate, sickle-cell disease, leukaemia, prostatitis, or trauma. It has also been reported in patients taking anticoagulants or phenothiazines (Dawson Butterworth, 1970). 'Idiopathic' priapism often succeeds prolonged erection or vigorous intercourse.

The account of the genesis of priapism which has gained widest acceptance is that propounded by Hinman (1960):—

1. Prolonged erection allows stasis to develop in the corpora cavernosa.
2. An increased CO_2 tension locally produces a rise in viscosity of the blood in the corpora.
3. Relative venous congestion is produced at the junction of the cavernous spaces with the collecting veins.
4. In addition, oedema of the trabeculae fills the corpora and further impedes venous outflow.
5. Eventually arteriolar occlusion occurs.
6. Trabecular fibrosis develops, irreversibly disrupting the arteriolar supply mechanism.

The fibrosis subsequent upon trabecular oedema occludes the arterial inflow, thus allowing resolution of the priapism but with the penalty of associated impotence. This arterial occlusion has been demonstrated by Lipsky (1970), using direct puncture of the dorsalis penis artery, but to our knowledge pudendal arteriography has not previously been employed in this context. Its demonstration of occlusion of the internal pudendal artery at the perineal membrane suggests that the fibrosis is active throughout the corpora cavernosa. This fibrosis does not necessarily extend as far proximally as the perineal membrane in all cases, as erection of the base of the penis is sometimes maintained (Hinman, 1960).

We hope that this report will stimulate further angiographic studies of priapism, particularly in the acute phase. Baum and Nusbaum (1971) have successfully controlled gastro-intestinal haemorrhage by selective mesenteric arterial infusion of vasopressin, and the same method might be used to treat acute priapism by infusion directly into the internal pudendal arteries.

Acknowledgements.—We wish to thank Dr. J. D. Irving, who performed the arteriography, and Mr. D. Thomas of the Photographic Department.

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AN UNUSUAL CASE OF SPONTANEOUS PERFORATION OF THE OESOPHAGUS

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SUMMARY

An unusual case is reported of spontaneous per-ration of the oesophagus in which there was a arked absence of initial symptoms. It is suggested ıat this condition be considered in the differential agnosis of extensive hydropneumothorax. The nportance of early diagnosis as a prerequisite to ıccessful treatment is emphasized.

HIS report describes a 60-year-old woman who resented 8 days after rupturing her oesophagus ıring a bout of vomiting. Her only symptoms at ıe time of the incident were of mild dyspnoea and ıgue discomfort in the left chest. A search of the terature has failed to reveal a similar case.

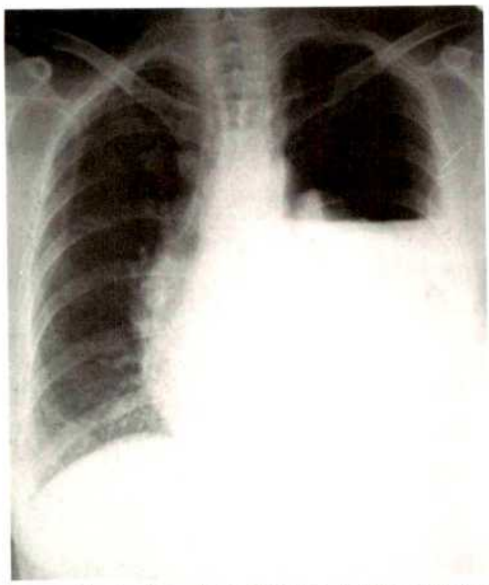

FIG. 1.—Chest radiograph on admission, showing a left-sided hydropneumothorax.

CASE REPORT

Mrs. K. B., a 60-year-old woman, was admitted with history of being perfectly well until 8 days prior to lmission. She had been caring for her family, all of hom had been suffering from gastro-enteritis, when she ıd developed symptoms of severe vomiting and diarıoea. The episodes of vomiting had lasted for 5 hours. s she recovered from the last bout of vomiting, the atient had noted that she had become slightly short of breath and 2–3 hours later had developed a vague aching pain in the left chest and hypochondrium, which radiated through to the back. The pain was not affected by breathing or by coughing.

She had remained in bed at home for 8 days following the onset of her symptoms, during which period there had been a slow deterioration in her general condition with increasing dyspnoea and anorexia.

On admission to hospital her general condition was fair; she was flushed and dyspnoeic although not clinically dehydrated. Her temperature was 36·8° C., the pulse was 104, regular, and of good volume, and the blood-pressure was 140/90.

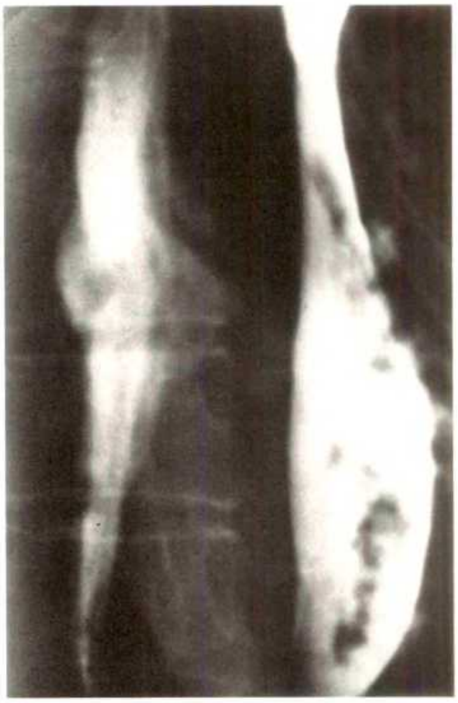

FIG. 2.—Gastrografin-swallow film, showing an oesophagopleural fistula.

On examination of the chest the trachea was deviated to the right with signs of a left-sided hydropneumothorax. There was no evidence of surgical emphysema. There were no other abnormal physical signs. The chest radiograph performed on admission (*Fig.* 1) confirmed the presence of an extensive left-sided hydropneumothorax with complete collapse of the left lung. There was no evidence of mediastinal emphysema.

At this time there was nothing to indicate the underlying pathology. The hydropneumothorax was treated by the insertion of intercostal drains and at the initial drainage procedure 600 ml. of purulent opalescent fluid were obtained. Following thoracentesis the patient's general condition improved although the volume of drainage remained in excess of 450 ml. per 24 hours for the next 4 days. A follow-up chest radiograph performed 2 days after the initial drainage procedure showed almost complete re-expansion of her left lung with only a small residual penumothorax and effusion. On the fifth day after admission the patient's general condition deteriorated further with anorexia and an inability to take fluids by mouth, associated with increasing dehydration. An intravenous fluid replacement régime resulted in a gradual improvement in the patient's general condition, although the inability to take fluids orally continued. On the seventeenth day after admission, in view of the continuing drainage from the left chest (150 ml. per 24 hours), formal drainage of the empyema was carried out with rib resection and insertion of two intercostal drains. Following this procedure there was a marked reduction in the drainage volume, although a small air leak continued. On the nineteenth day after admission the patient began to take fluids orally, and this was followed by a marked increase in the pleural drainage. It became apparent that an oesophagopleural fistula was present. This was confirmed by a gastrografin-swallow examination (*Fig.* 2).

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In view of the long interval since perforation and the continuing satisfactory general condition of the patient during this period, it was decided that conservative management should be continued. On the twenty-second day after admission a feeding jejunostomy was performed; at this procedure the only intra-abdominal abnormality found was a chronic duodenal ulcer. Following this operation the patient's condition deteriorated; she developed a bilateral bronchopneumonia and sputum culture demonstrated the presence of *Pseudomonas pyocyanea*. Despite appropriate antibiotic and supportive therapy, the patient continued to deteriorate and she died on the twenty-fourth day after admission, 32 days after rupture of the oesophagus.

At post-mortem examination the left pleural cavity was found to contain 500 ml. of purulent fluid. The left lung showed confluent bronchopneumonia; a 7-cm. longitudinal rupture of the lower third of the oesophagus was demonstrated with free communication into the left pleural cavity. There was no evidence of mediastinal abscess; at the site of the rupture the adjacent oesophageal wall was normal.

DISCUSSION

Since the original description by Boerhaave (1724) the dramatic nature of the symptoms following spontaneous perforation of the oesophagus is well known. Barrett (1946) in his now classic and often-quoted paper highlights the symptomatology and the difficulties in diagnosing this condition. The clinical manifestations and diagnostic problems of this condition have been well documented in a series of reports in the world literature (Eliason and Welty, 1946; Kinsella, Morse, and Hertzog, 1948; Moore and Murphy, 1948; Samson, 1951; Moynihan, 1954; Starkey, 1955; Hugh, 1965; McKeown, 1965; Movsas, 1966; Toghill, Raut, and MacGuire, 1968; Callaghan, 1972). Barrett (1947) reported the first cases of spontaneous perforation of the oesophagus which were successfullly treated by direct suture. Since then there have been increasing numbers of reports of similarly successful cases (Starkey, 1955; Hamilton, 1967; Tidman and John, 1967; Toghill and others, 1968; Callaghan, 1972). In the majority of the cases which have been managed successfully, early diagnosis was of crucial importance. In their extensive and detailed paper, Derbes and Mitchell 1965) point out that in their series, in the absence of treatment, only 35 per cent of cases survived for 2 hours, 11 per cent to the end of the second day, an no case lived longer than 1 week. They draw attention to the fact that 83 per cent of the cases occurre in old men; however, no age-group is exempt, rupture of the oesophagus has been reported i neonates (Hohf, Kimball, and Bellenger, 1962).

The mechanism of pressure rupture of the oesophagus, as many authors prefer to call this conditio has been dealt with in remarkable detail by Derbe and Mitchell (1956). They studied the mechani of the process and also the pressures required t produce rupture of the oesophagus. The majorit of perforations of the oesophagus occur in the lowe one-third and into the left side of the chest. Th anatomical siting for this condition is due to a weakness in the wall of the oesophagus in its lower one third, as was first demonstrated by McKenzie (1884 A number of other workers have experimented o cadaveric oesophagi to establish the pressures required to produce a rupture. McKenzie in h original work (1884) found that a pressure of 5 lb per sq. in. was required, Burt (1931) 4·91 lb. pe sq. in., Kinsella and others (1948) 3·69 lb. per sq. in Mackler (1952) 5 lb. per sq. in., while Tidman an John (1967) found that 2·3 lb. per sq. in. was required to rupture the isolated oesophagus but 4·6 lb per sq. in. was necessary for the oesophagus left i situ.

The process of spontaneous perforation of th oesophagus depends on violent contracting of th abdominal muscles during vomiting associated wit a failure of the cricopharyngeus to relax. This produces a rapid rise in pressure within the oesophagu which is stressed beyond its physical limits, resultin in rupture. Mackler (1952) observed in his experimental series that the mucosa ruptured after th muscular wall of the oesophagus had given way.

Bates (1969) points out that in cases where th mediastinal pleura ruptures at the time of perforatio of the oesophagus there is no mediastinitis or resulting toxaemia, and therefore the prognosis is ver much better. This author also emphasizes that i cases which are diagnosed late a conservative régim with antibiotics and chest drainage should be undertaken. Several reports are recorded in the literatur of patients surviving perforation of the oesophagu in which the diagnosis was missed, the resultin empyema being treated by drainage and antibioti (Frink, 1947; Lynch, 1949; Sanderson, 1965 Harma, Koskinen, and Suurkari (1968) reported case in which drainage of the mediastinum wa attempted endoscopically with some success. Bradham, Bridgman, Scott, and Betts (1967) reported cases of spontaneous perforation of the oesophagu in which treatment was delayed with a satisfactor outcome.

The case reported here is most unusual, firs because of the remarkable absence of symptoms the time of perforation and, secondly, the long dela before the patient's general condition deteriorate sufficiently to warrant hospitalization. Both thes manifestations can be explained by the fact that the time of perforation the stomach was probabl empty following repeated episodes of vomiting an therefore little, if any, soiling of the pleura or mediastinum occurred. It is also highly likely that th ıediastinal pleura ruptured at the same time as the esophagus hence avoiding mediastinitis. Only 1 ther case (Bradham and others, 1967) could be found ı the world literature in which the patient survived long delay (18 days) before treatment was started.

The case reported here presented more than the sual diagnostic problems associated with spon- aneous perforation of the oesophagus. In addition, ıere was no radiological evidence of mediastinal mphysema, which is a useful and early diagnostic ign (Naclerio, 1957). The importance of early iagnosis and treatment of spontaneous perforation f the oesophagus cannot be overemphasized if this ondition is to be treated successfully.

Acknowledgement.—I wish to thank Mr. A. G. Norman for permission to publish details of his atient.

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REVIEWS AND NOTICES OF BOOKS

Surgical Emergencies in the Newborn. By J. Alex Haller, jun., M.D., Baltimore, and James L. Talbert, M.D., Florida. 11 × 8½ in. Pp. 153 + ix. Illustrated. 1972. London: Henry Kimpton. £6·30.

T is symptomatic of the growing increase of the scope of paediatric surgery that yet another book on surgical mergencies in the newborn should be produced, this ime from the Johns Hopkins Hospital. Its contents eflect the interests of the two authors. Their arrange- nent is novel and perhaps to some may be confusing. The first quarter of the book is devoted to the physio- ogical problems, pre- and postoperative care, and the naking of observations on the newborn baby. It is ollowed by a section on tracheostomy, the insertion of annulas into the great veins, and intravenous nutrition. Another chapter is devoted to respiratory emergencies and it is to be hoped that the treatment advocated for he Pierre-Robin syndrome is not too often followed. t is surprising to find tracheo-oesophageal fistula and esophageal atresia included amongst these respiratory mergencies. There is a long section on cardiovascular mergencies which reflects the modern tendency to ndertake more and more curative operations at a much ounger age than has been the custom in the past. Nevertheless, this section is probably too extensive or most surgeons who undertake the emergency treat- nent of the newborn since they are unlikely to do much cardiac surgery. It must be extremely unusual for a baby to be born with an incarcerated hernia, though this is one of the possibilities mentioned in a very short section on hernia, and the use of gallows traction in the conservative treatment of an incarcerated hernia is not mentioned.

This book provides a satisfactory account of the diagnosis and treatment of surgical emergencies in the newborn child, but it is unlikely to compete successfully for the interest of specialists in paediatric surgery with other more extensive books on this subject which have preceded it. For those who require a shorter account of the problems of the first days or weeks of life this book will be satisfactory and its lower price compared with the more extensive volumes is, of course, an advantage.

Practical Procedures in Diagnostic Radiology. Second edition. Edited by H. M. Saxton, M.B., M.R.C.P., F.F.R., D.M.R.D., Guy's Hospital, London, and Basil Strickland, F.R.C.P., F.F.R., F.A.C.R. (Hon.), Westminster Hospital, London. 9¾ × 6¼ in. Pp. 305 + xii. Illustrated. 1972. London: H. K. Lewis. £5.

After a lapse of 8 years the second edition of this popular book should be welcomed by both trainee and radiological registrars, for it covers a number, if not all, of the more common investigations undertaken in most diagnostic

X-ray departments. This book's size and price have naturally increased a little since the original publication, as has the number of contributors. Certain chapters contain a few references though some of these may be a little out of date. In this age of closed-circuit television within X-ray examination rooms, techniques requiring accurate organ and site localization abound and are the radiologists' responsibility. These include biopsy techniques of the lung, kidney, liver, bone, jejunum, etc., gastro-camera, fibrescopy, and duodenal intubation. It might be expected that these should be included in any future edition. It would also be appropriate if some basic advice was given to the radiologist who is expected to perform right-heart catheterization for the investigation and treatment of pulmonary embolus, as most vascular radiologists are *au fait* with catheterization techniques of the left side of the heart and aorta and its branches. Why not the right? Isotopic organ scanning techniques in relation to diagnostic radiology would also be worthy of mention, if only briefly, as some diagnostic X-ray departments may undertake this work independently of nuclear medicine departments and the handling and application of radionuclides are in the syllabus for diagnostic radiological training. The technique of ductography in conjunction with mammography might also have been included. These omissions, in the mind of the reviewer, are not necessarily critical but might be included at the expense of the unnecessary text and space devoted to an almost historical section on vascular radiology! Do we really have to know about catheter preparation in this age of 'disposables', the availability of which has made the preparation of catheters of less value than formerly. Furthermore, surely direct-vision laparoscopy with air and water tubation now makes uterosalpingography almost obsolete except in the case of suspected uterine abnormalities or cervical insufficiency. These criticisms, mainly of omission, in no way detract from the value and worthiness of this book and the editors and publishers must be again congratulated on their effort in producing such a lucid manual of instructional techniques. It is well recommended.

Stoffwechsel. Edited by DR. R. FREY, Mainz, DR. F. KERN, St. Gallen, and PROFESSOR DR. O. MAYRHOFER, Wien. 9 × 6 in. Pp. 142 + x. Illustrated. 1972. Berlin: Springer Verlag. DM.48.

THIS is a report of a symposium held in October, 1970, in Mainz on metabolic changes in relation to intensive care. The papers presented report assorted aspects of metabolic changes in stress, following injury, and after burns. The ensuing discussions are reported in full and this book is likely to be of interest only to research workers in this particular aspect of pathology and physiology in relation to shock.

The Care of Minor Hand Injuries. Third edition. By ADRIAN E. FLATT, M.A., M.D., M.Chir., F.R.C.S., F.A.C.S., Iowa. $9\frac{3}{4} \times 6\frac{3}{4}$ in. Pp. 293 + xi. Illustrated. 1972. London: Henry Kimpton. £9·70.

THIS is the third edition of a book which was first published in 1959. Readers will agree with the author that strictly speaking there is no such entity as a 'minor injury to the hand'. By his definition, however, such an injury implies 'a relatively small amount of tissue damage, out-patient treatment and freedom from postoperative complications'.

There are those who may well feel that some of the surgical techniques described should not be carried out in an out-patients' department, and that all but the most trivial injuries should be admitted for a period of strict elevation of the hand.

The book is divided into two sections: Part 1 deals with general principles of care and Part 2 describes the care of specific injuries. Part 1 is well written and illu trated and emphasizes most of the important requiremen for successful hand surgery.

In Part 2, however, there is a certain imbalance. F example, skin replacement for pulp loss includes description of the use of local flap-grafts whereas t treatment of tendon injuries is only superficially discusse

Nevertheless, this is a reference book that should be every emergency and accident department. It will found most helpful by students and casualty officers alik

Chirurgie. Ein kurzgefasstes Lehrbuch mit 3 Prüfungsfragen. Second edition. By MARTIN REIFFE SCHEID, Aachen. $7\frac{1}{2} \times 4\frac{3}{4}$ in. Pp. 658 + xiv. Illustrate 1972. Stuttgart: Georg Thieme Verlag. DM.19.80.

THE second edition of this paperback has been carefu revised and it will remain a very useful book for medic students who are conversant with the German languag The subject matter is conveniently arranged and the ind is quite complete. The addition of 94 groups of matchi questions, however, is no gain, as matching questions a the most passive form of testing knowledge.

Outline of Fractures. Sixth edition. By JOHN CRAW FORD ADAMS, M.D., M.S., F.R.C.S., St. Mary's Hosp tal, London. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. 312 + vii. Illustrate 1972. Edinburgh: Churchill Livingstone. £2·25.

THIS little classic continues to grow in popularity and now reaches its sixth edition within a short 15-year perio Its price has been maintained at a very reasonable lev which is well within the student's pocket or purse con taining his or her allowance. The success of this boo has resulted from the clarity of its writing and the hig quality of its illustrations and definitions. One sma point which should be mentioned is that although M Crawford Adams has correctly sensed the requirement of the undergraduate as regards fractures and thei management, one would like to see in the next editio more of the basic sciences which are taught in the pre clinical years brought into this field of trauma.

The references and bibliography have been well selecte and provide an excellent and extensive background f anyone interested in fractures.

The textbook is warmly recommended to all students who should enjoy reading it and even learning from it.

Thromboembolism: Diagnosis and Treatmen Edited by V. V. KAKKAR, F.R.C.S.E., F.R.C.S., King' College Hospital Medical School, London, and A. JOUHAR, M.B., M.R.C.S., Kabi Pharmaceuticals Ltd Ealing, London. $8\frac{1}{2} \times 5\frac{1}{4}$ in. Pp. 241 + xii. Illustrate 1972. Edinburgh: Churchill Livingstone. £3·50.

THERE can be few more dismaying complications to th surgeon than deep-vein thrombosis and pulmonary embo lism. It is heartening that our understanding of thrombo embolism has been on the growing edge of medic knowledge over the past decade. During this time man surgical meetings have been enlivened by a series of excel lent original papers on the subject by V. V. Kakkar and is particularly apt that he should have joined with A. Jouhar, Medical Director of Kabi Pharmaceuticals Ltd., i editing the proceedings of a recent symposium on thrombo embolism to produce such an excellent up-to-the-minut account.

The book as a whole presents a careful survey modern techniques of investigation and treatment wit a scrupulously fair appraisal of their merits. The text logically arranged, easily readable, and enlivened with number of excellent illustrations and diagrams. It divided into four parts. The subtle processes of hyper coagulation and associated phenomena are well describe in Part 1; inevitably this involves laboratory studies b these are presented with ease and clarity. Part 2 will appeal especially to the surgeon, for all the techniques that have so brilliantly displayed the thrombotic processes as they occur are described. For those who have not kept abreast with this work it will make compelling reading. Our methods of prevention are now based on clear insight and it is possible to measure in fairly precise terms the success of any form of treatment, be it the use of a drug, a device to encourage emptying of the soleal veins, or, most practical of all, the active postoperative contraction of calf muscles.

The topic of thrombectomy in the deep vein is not referred to, presumably because it was outside the brief of the symposium. However, this book covers a lot of ground and is certainly a 'must' for the younger surgeon who is programming his personal biological computer for a lifetime's use in surgery; there is no better source from which to glean the best of our present understanding. For the established surgeon it is an important book, for he will find that the half-formed ideas of yesterday have taken a sharply defined shape and that the scourge of thrombo-embolism need not be quite so mysterious and terrifying as of old. The reviewer thoroughly recommends this book to all surgeons and, needless to say, physicians.

Spezielle Frakturen und Luxationslehre: Gesichtsschadel. Edited by H. Nigst, Basel. 10 × 7 in. Pp. 213 + xii. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.164.

This is the first of a series of five volumes which are to be published under the general title, 'A Guide to Special Fractures and Joint Injuries'. Volume I, which is reviewed here, is entitled 'The Facial Skeleton'.

The book is divided into two parts. Part 1 is concerned with diagnosis and the general principals of treatment of facial fractures, and is, therefore, directed particularly to the casualty officer and accident surgeon. The outstanding feature of this section is an excellent account of the radiology (and radiography) of the facial bones.

The book is profusely illustrated throughout and the line drawings and radiographs are of excellent quality. However, the radiographs are printed as positives and in some views the overprinted arrows are so numerous that they tend to obscure detail. Nevertheless, this is a minor criticism and Part 1 is to be recommended for its lucidity.

Part 2 is written for the maxillofacial specialist. It gives a good account of the methods of jaw fixation which are favoured in Swiss and German units, the emphasis being on the plating of mandibular fractures. The book will be read with interest by specialists in this field, but at the price of DM.164 it is expensive reading.

Intravenous Hyperalimentation. Edited by George S. M. Cowan, jun., B.A., M.B., Ch.B., Washington, and Walter L. Scheetz, M.D., Washington. 9 × 6 in. Pp. 225 + xxiii. Illustrated. 1972. London: Henry Kimpton. £5·40.

This book contains the proceedings of the conference on intravenous hyperalimentation held in the U.S. Army Institute of Surgical Research, San Antonio, Texas, in November, 1970. The purpose of the conference was to provide a review of current concepts in intravenous hyperalimentation, to answer some of the questions in this area, and to stimulate further research in the nutritional problems of surgical patients.

The book is comprised of 18 chapters by noted authorities of whom all but two are from North America. They cover the effects of starvation, the metabolism of foodstuffs, energy balance, and the general principles, technique, and experience in the use of hyperalimentation in various surgical conditions. Each chapter is carefully balanced and covers physiology as well as practical points with references and discussion at the end.

The reviewer must confess to a dislike of the rather ugly word 'hyperalimentation' which to him has no real meaning, as the subject covered is really that of intravenous feeding. Hyperalimentation is defined as a technique of total parenteral nutrition which provides nutrients adequate in quality and quantity to support normal growth and development in immature animals and man as well as to ensure a positive nitrogen balance in adults for indefinite periods of time. The basic nutrient solutions used consist of 20–25 per cent dextrose and 4–5 per cent protein hydrolysates or crystalline amino-acids. These are supplemented by electrolytes, vitamins, and other micronutrients as required. Since in Europe intravenous fat preparations are used as the main sources of calories more discussion on this would have been preferred.

The book is excellently produced with well-chosen line diagrams and tables to illustrate various points. It is not a simple book to read at bedtime, but study of it will pay dividends in the care of patients with nutritional problems. It can therefore be warmly recommended to all who have an interest in surgical metabolism.

Kopf- und Hals-Chirurgie. Band 1: Hals. Edited by H. H. Naumann, München. 11 × 8 in. Pp. 518 + xii. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.350.

This handbook of operative surgery is the first to appear of a set of three. Judging from this volume the series rightly calls the field of head and neck surgery its own, for this first book seems to cover its subject-matter very completely. As is usual with books of this kind, it appears to be primarily written for the general surgeon specializing in this particular field, or being forced by circumstances to care for an unfamiliar lesion arising in it. The present volume is restricted to the region of the neck and is subdivided into twelve major sections. As would be expected, the contributors come from such disciplines as otolaryngology, anaesthesiology, and general surgery. The sections are further split up according to particular operations, though occasionally subdivision is on diagnostic criteria as, for example, in the excellent chapter on vascular lesions. The operative procedures are lavishly illustrated in the established step-by-step way in very clear black and white drawings with an artistic stroke of red used sparingly. The sober accompanying text has been arranged closely around the illustrations, making the reading of it very convenient. The text is, however, not just a companion to the drawings; it is expanded to give short summaries of 'errors and safeguards' and of postoperative care. As for the operations selected, it is a very pleasing feature that the editor has picked his choice and has presented the readers with the techniques favoured by himself and which he has found effective in actual practice. This is much more helpful than giving a kaleidoscopic review and leaving the less-experienced reader with an awkward 'judgement of Paris'.

The book can be thoroughly recommended, but will probably be mainly found in medical libraries because of its extremely high price.

Ultrasonics in Clinical Diagnosis. Edited by Peter N. T. Wells, Welsh National School of Medicine. 8½ × 5½ in. Pp. 187 + xi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £3.

Eight contributors, each an expert in his field, have produced this book which has been edited by Professor Wells. Three main sections are included in the text: (1) the basic principles and diagnostic methods, (2) diagnostic applications, and (3) biological effects. An appendix is added dealing with the equipment available. The text is illustrated by numerous reproduced scans explained by labelled drawings.

Although ultrasonic techniques have been known for the past 20 years, it is only in recent years that their place in clinical diagnosis has been established. The editor wishes the book to satisfy the needs of candidates for the Fellowship of the Faculty of Radiologists and to serve as a guide for the higher examination of the Society of Radiographers. It certainly does more than this. The main areas where ultrasonics provide a useful addition to our diagnostic methods are in obstetrical and gynaecological practice, in the investigation of the brain, and, to a limited extent, in certain abdominal areas, e.g., liver and kidneys, abdominal aneurysms, etc. Many other areas where developments are continuing are included in the text, e.g., ophthalmology, cardiology, and even dentistry. The value and limitations of this technique are emphasized by each contributor. No claim is made that ultrasonics can always be the sole diagnostic tool; their use and interpretation should be in conjunction with other diagnostic methods, mostly radiological. The authors point out the value of ultrasonic methods as a screening device, e.g., in the examination of head injuries.

Many clinicians may find the earlier chapters on the fundamental physics a little difficult to follow, but the authors have succeeded in outlining the facts necessary to understand the broad principles of the techniques. In these chapters the principles of the A-scope, the two-dimensional B-scope, and Doppler methods are included.

This book gives an understandable account of the place of ultrasonics in medicine today. It should be read by radiologists studying for both the D.M.R.D. and F.F.R. examinations, and it can be used as a reference book for those developing experience in these techniques. Moreover, it is of value to non-radiologists who wish to know when and how to use this diagnostic tool, and wish to understand its values and limitations.

Hemobilia (Biliary Tract Hemorrhage). By PHIL SANDBLOM, M.D., Ph.D., Sweden. 9¾ × 7 in. Pp. 1 +xxi. Illustrated. 1972. Springfield, Ill.: Charles Thomas. $19.75.

THIS monograph on haemobilia will be a most welcor addition to the library of any surgeon with an interest the surgery of the biliary system and in trauma. Phil Sandblom was for years the leading exponent in Swed in the surgery of portal hypertension, and those wl visited him in Lund will have appreciated his spec flair for dealing with the intricate emergency situatio His first experience of encountering blood-loss from t liver via the common bile-duct over 20 years ago prompt him to call this condition 'hemobilia'. In this mon graph he relates the history of the description of t condition as far back as Glisson in 1654, Morgazin and Portal (although Realdus Columbus described probable case in 1559—the post-mortem of St. Ignati Loyola). The history is followed by chapters on patholog diagnosis, and treatment derived from a collection of 5 published cases in the world literature. Trauma leads the list of causes, and careful history-taking in making preoperative diagnosis is emphasized. Arteriograph cholangiography, and scintiscanning are useful confirm tory investigations. A successful outcome depends large upon early recognition and operation. The general cha ters are followed by those which describe the experienc related to specific causes, such as trauma, inflammatio gall-stones, tumour, and vascular disorders.

As Warren Cole says in his appreciative Foreword, t detail in this book represents an enormous amount work presented in a refreshing and easily followed styl Truly a book to be prized.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers].

Les Traumatismes du Thorax. Edited by DE H. LE BRIGAND, Paris. 10½ × 8 in. Pp. 97. Illustrated. 1971. Paris: L'Expansion Scientifique. 38F.

Behaviour of the Human Ureter in Health and Disease. By JAMES A. ROSS, M.B.E., M.D., F.R.C.S., Honorary Consultant in Surgery to the Army in Scotland, PETER EDMOND, F.R.C.S., Edinburgh Royal Infirmary, and IAN S. KIRKLAND, F.R.C.S., Western General Hospital, Edinburgh. 8¾ × 5½ in. Pp. 136 + viii. Illustrated. 1972. Edinburgh: Churchill Livingstone. £3·50.

The Early Diagnosis of the Acute Abdomen. By Sir ZACHARY COPE, B.A., M.D., M.S. (Lond.), F.R.C.S. (Eng.), St. Mary's Hospital, London. 8 × 5½ in. Pp. 210. Illustrated. 1972. London: Oxford University Press. £1·20.

Sauerstoffüberdruckbehandlung. Probleme und Anwendung. By I. PODLESCH, Dusseldorf. 9 × 6 in. Pp. 97. Illustrated. 1972. Berlin: Springer-Verlag. DM.38.

The Biochemistry of Animal Fossils. By RALF W. G. WYCKOFF, Arizona. 8¾ × 5⅝ in. Pp. 164. Illu trated. 1972. Bristol: Scientechnica (Publishers) Lt £5·25.

Crohn's Disease. By JAMES KYLE, M.Ch., F.R.C.S Royal Infirmary, Aberdeen. 8½ × 5½ in. Pp. 210. Illu trated. 1972. London: William Heinemann. £3.

Cardiovascular Surgery 1971. Edited by EARLE MAHONEY, M.D., New York. 10 × 7½ in. Pp. 16 Illustrated. 1972. New York: American Heart Associ tion, Inc. $5.

The Upper Cervical Spine. By DETLEF VON TORKL and WALTER GEHLE, Hamburg. 10½ × 7½ in. Pp. 10 Illustrated. 1972. Stuttgart: Georg Thieme Verla DM.48.

Rheinisch-Westfalische Akademie der Wissenshaf ten. By WERNER TH. O. FORSSMANN and CARL-HEIN FISCHER. 9½ × 6½ in. Pp. 79. Illustrated. 197 Opladen: Westdeutscher Verlag. DM.15.

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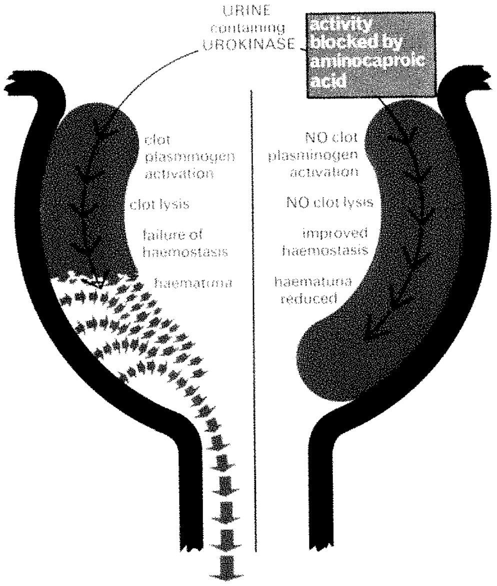
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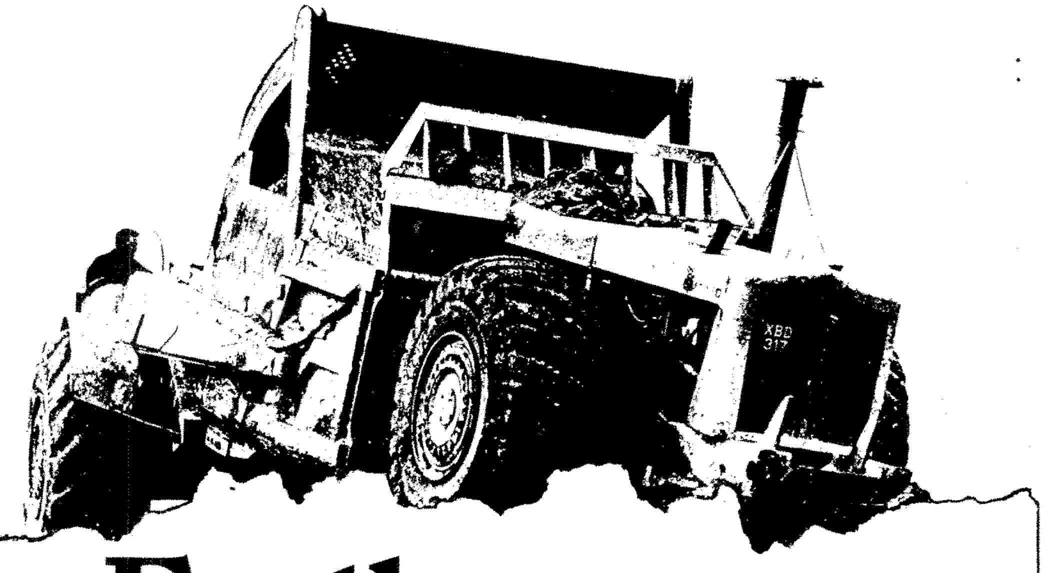

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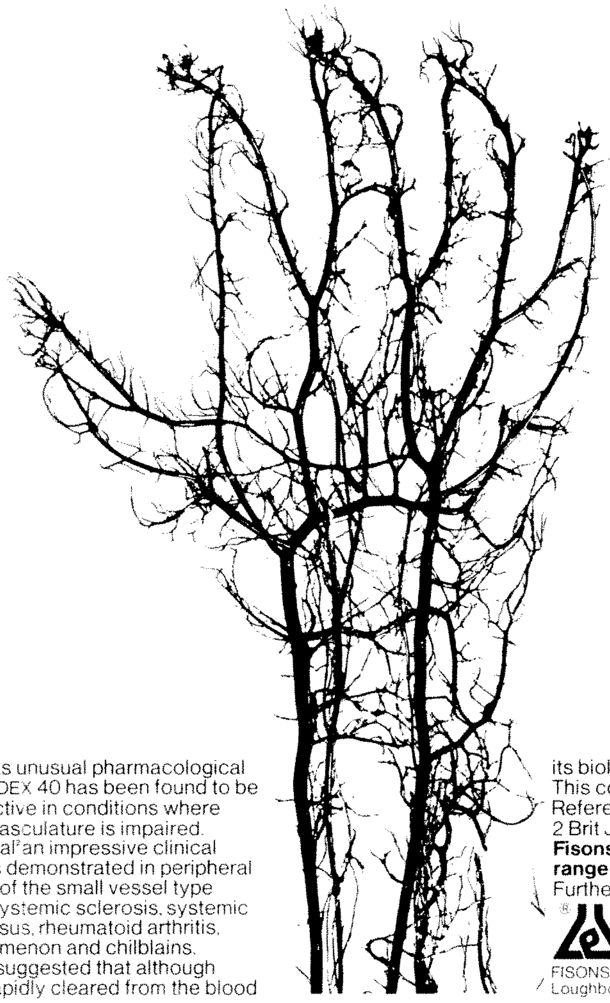

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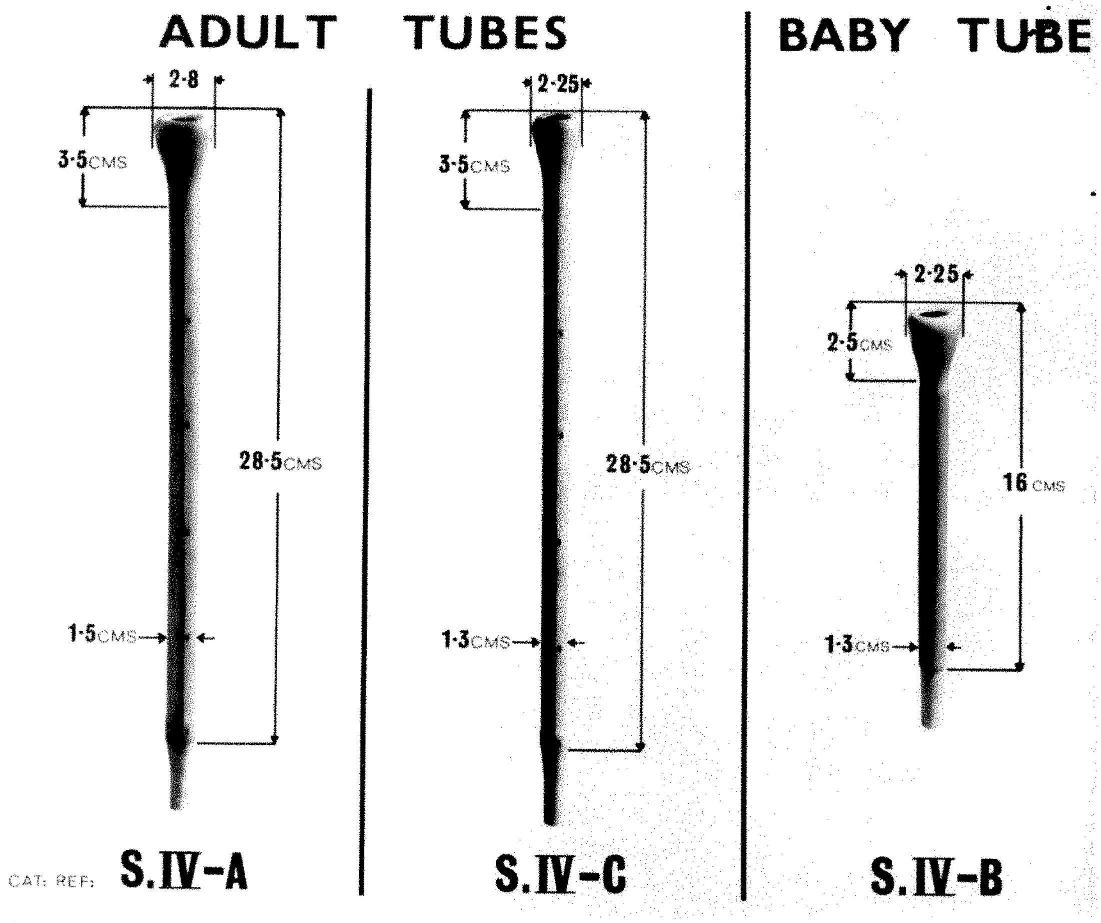

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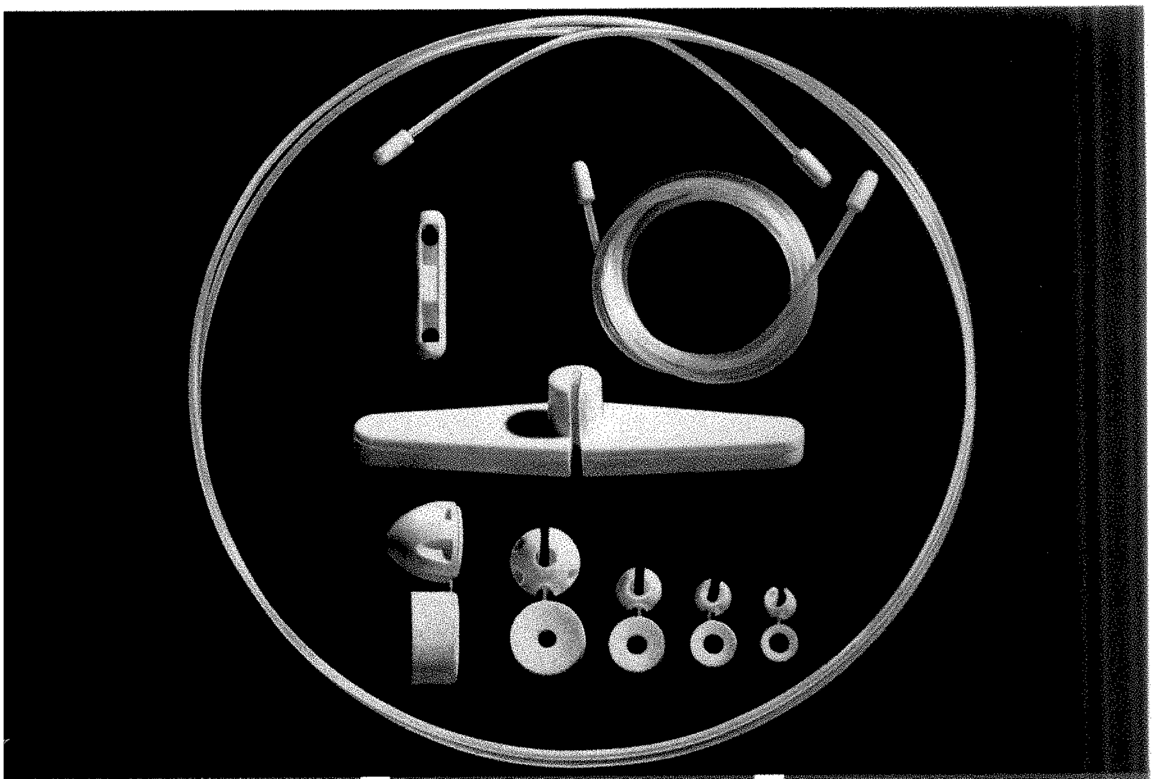

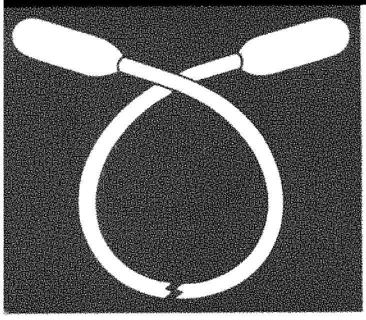

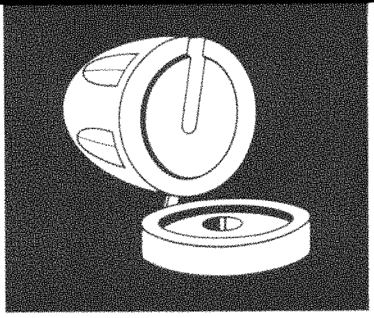

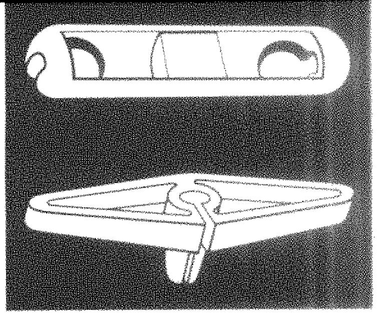

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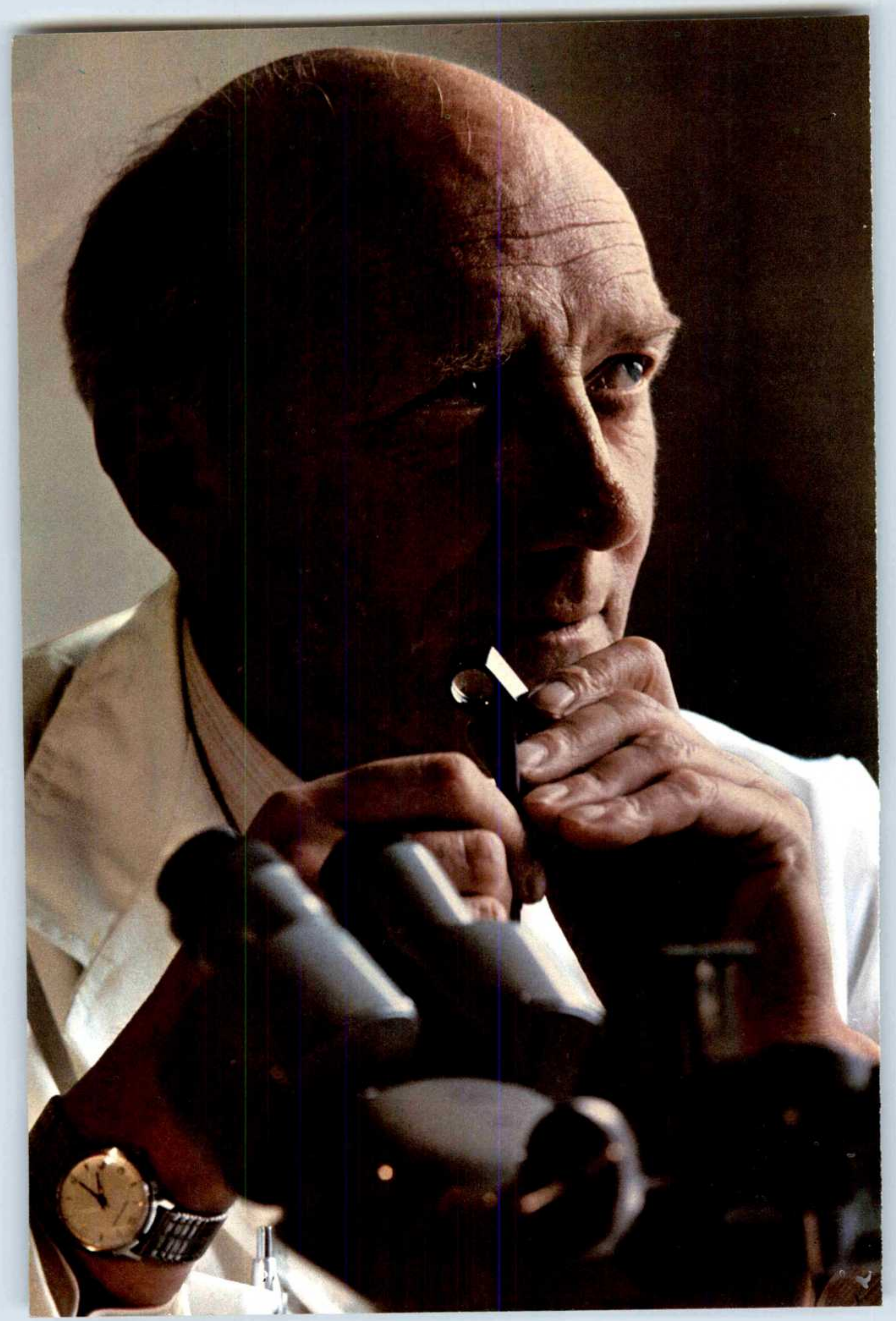

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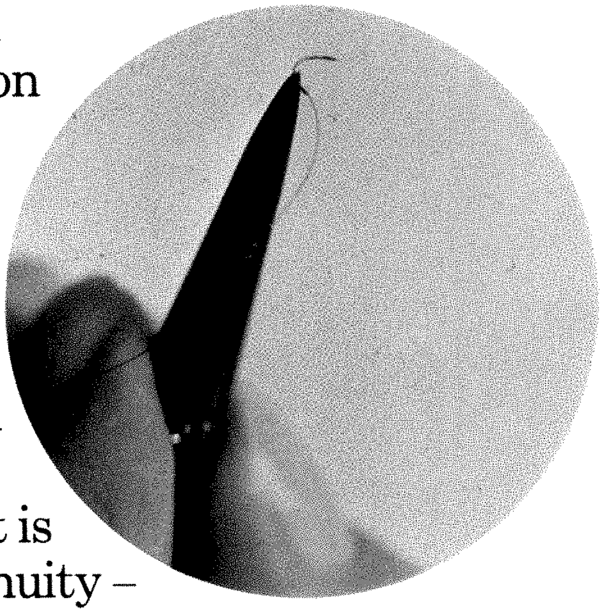

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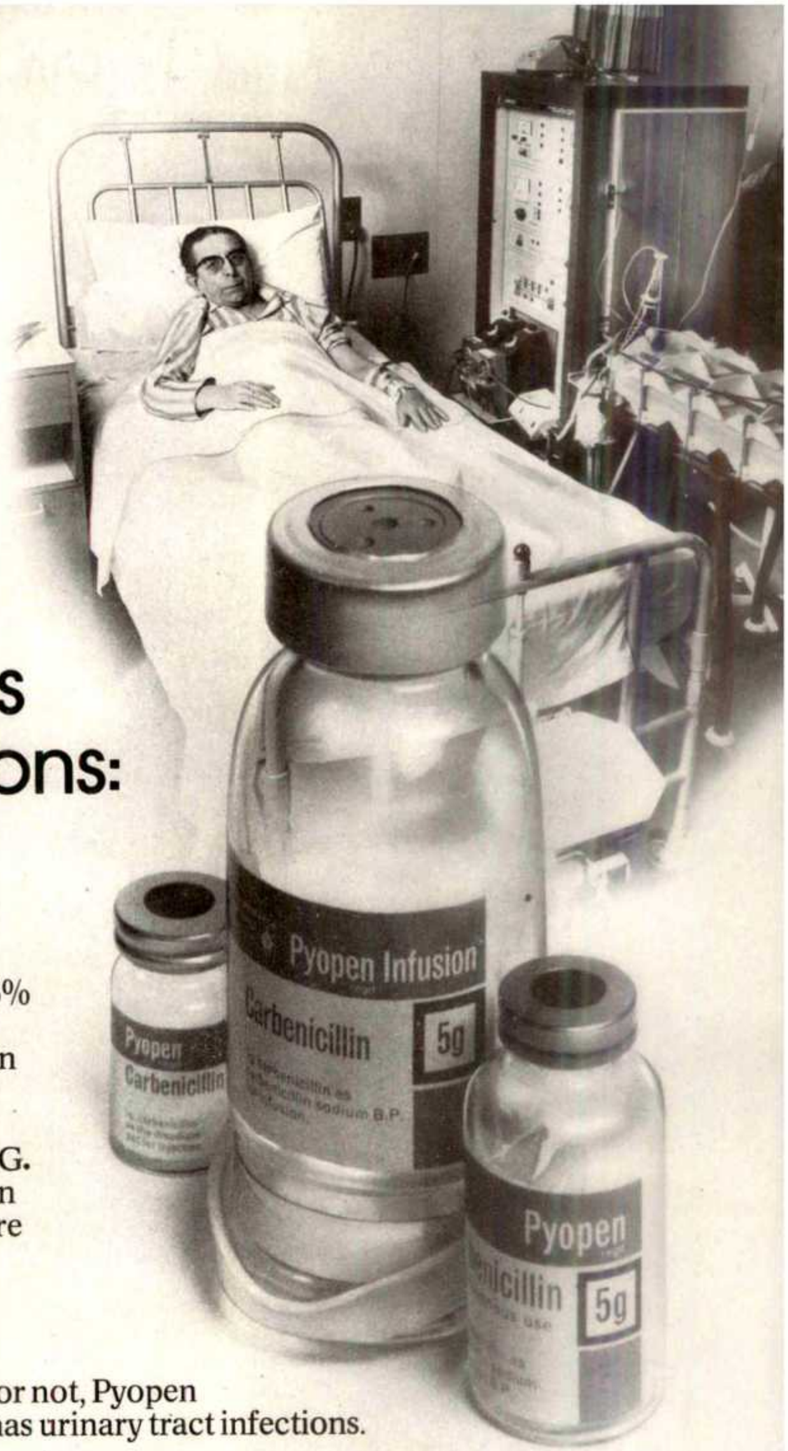

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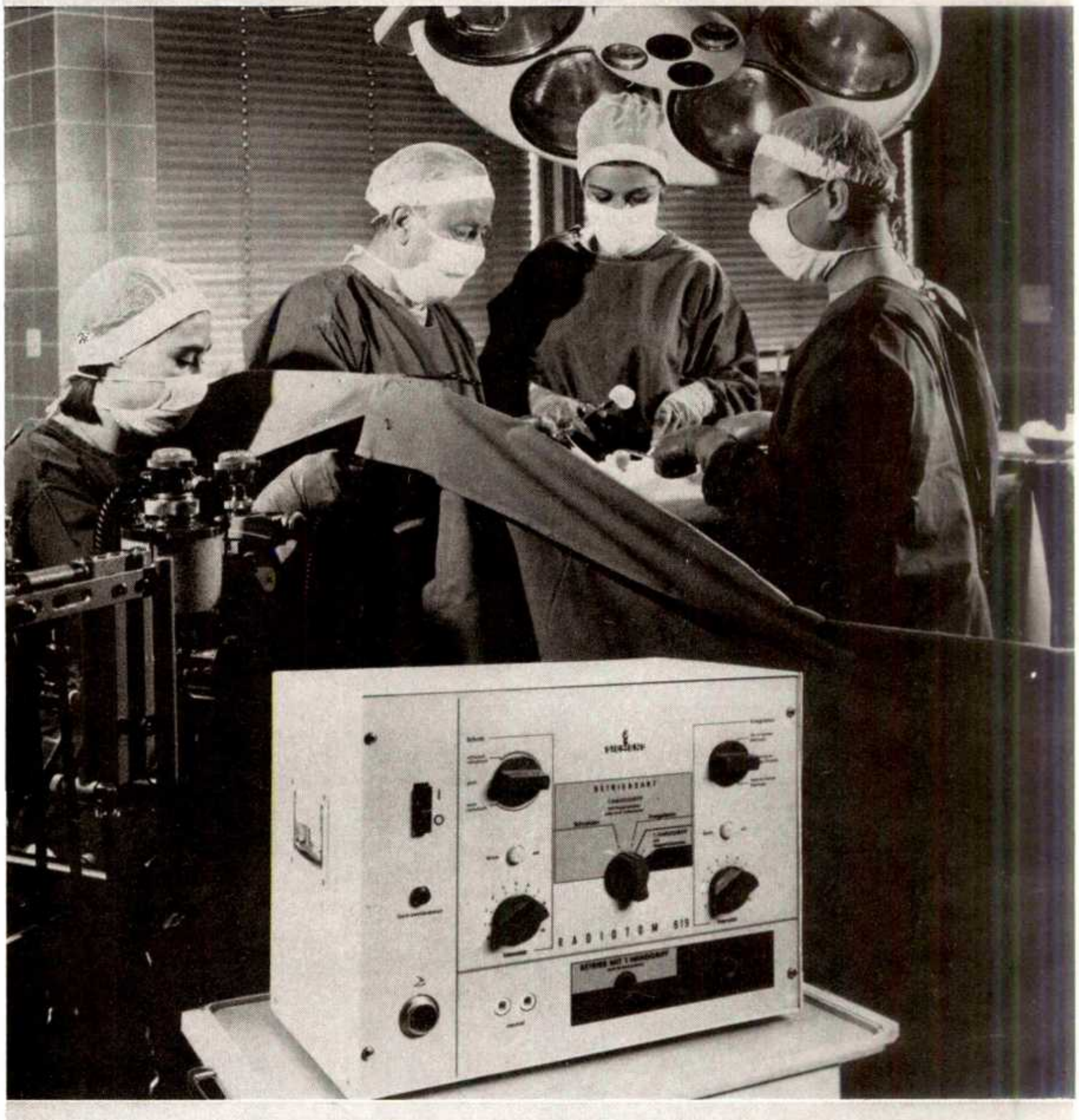

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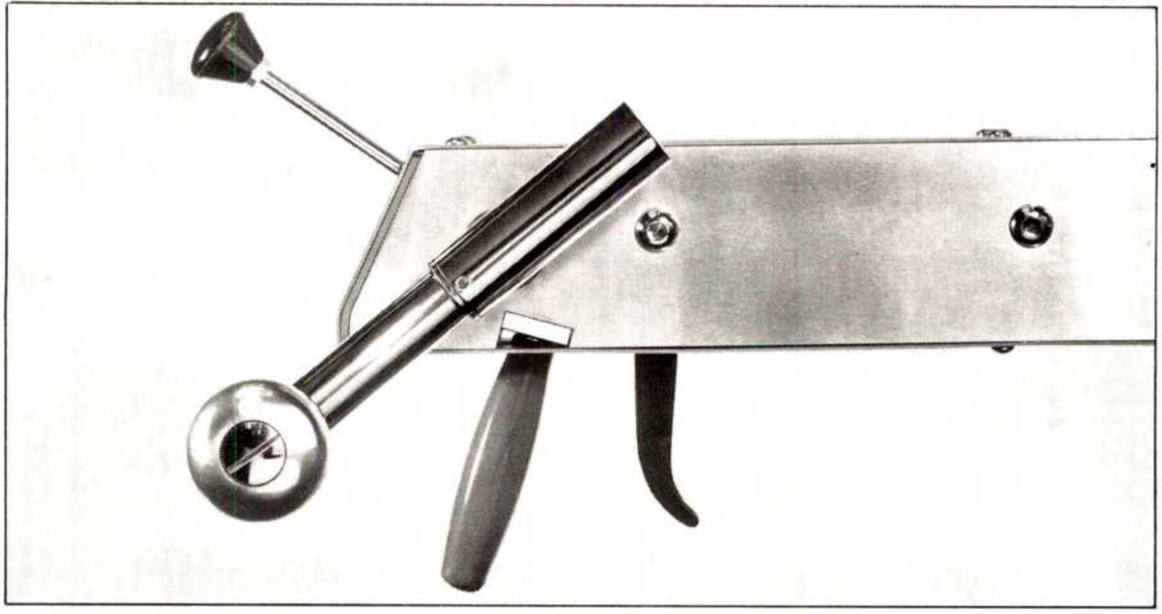

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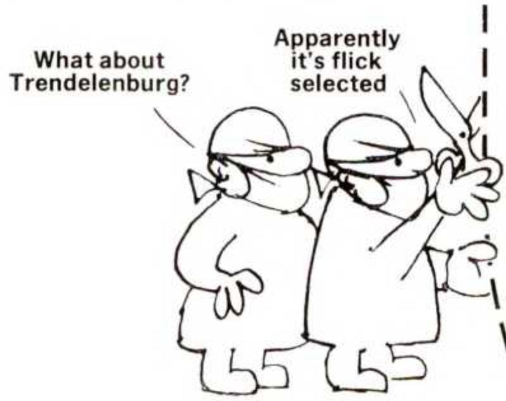

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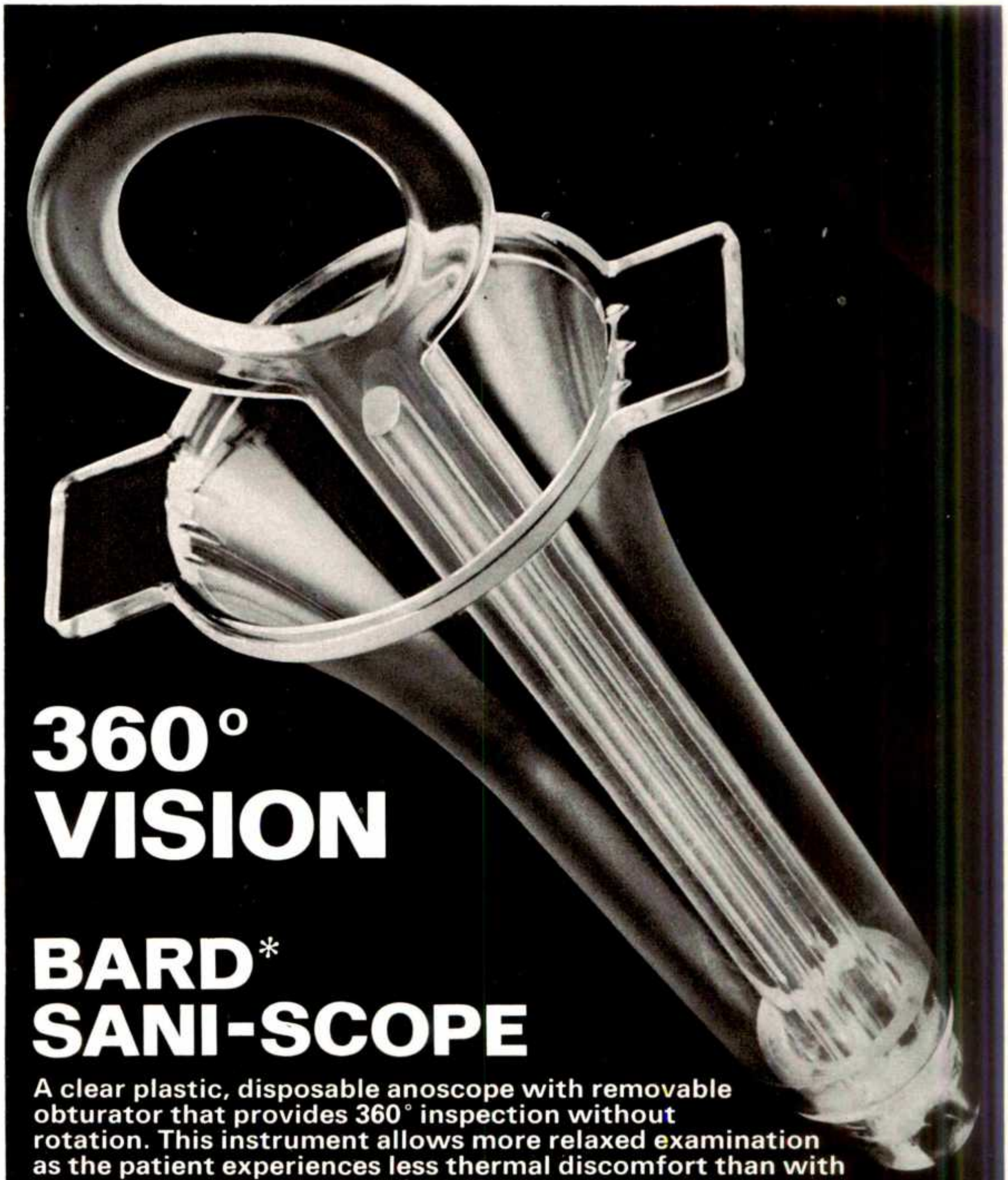

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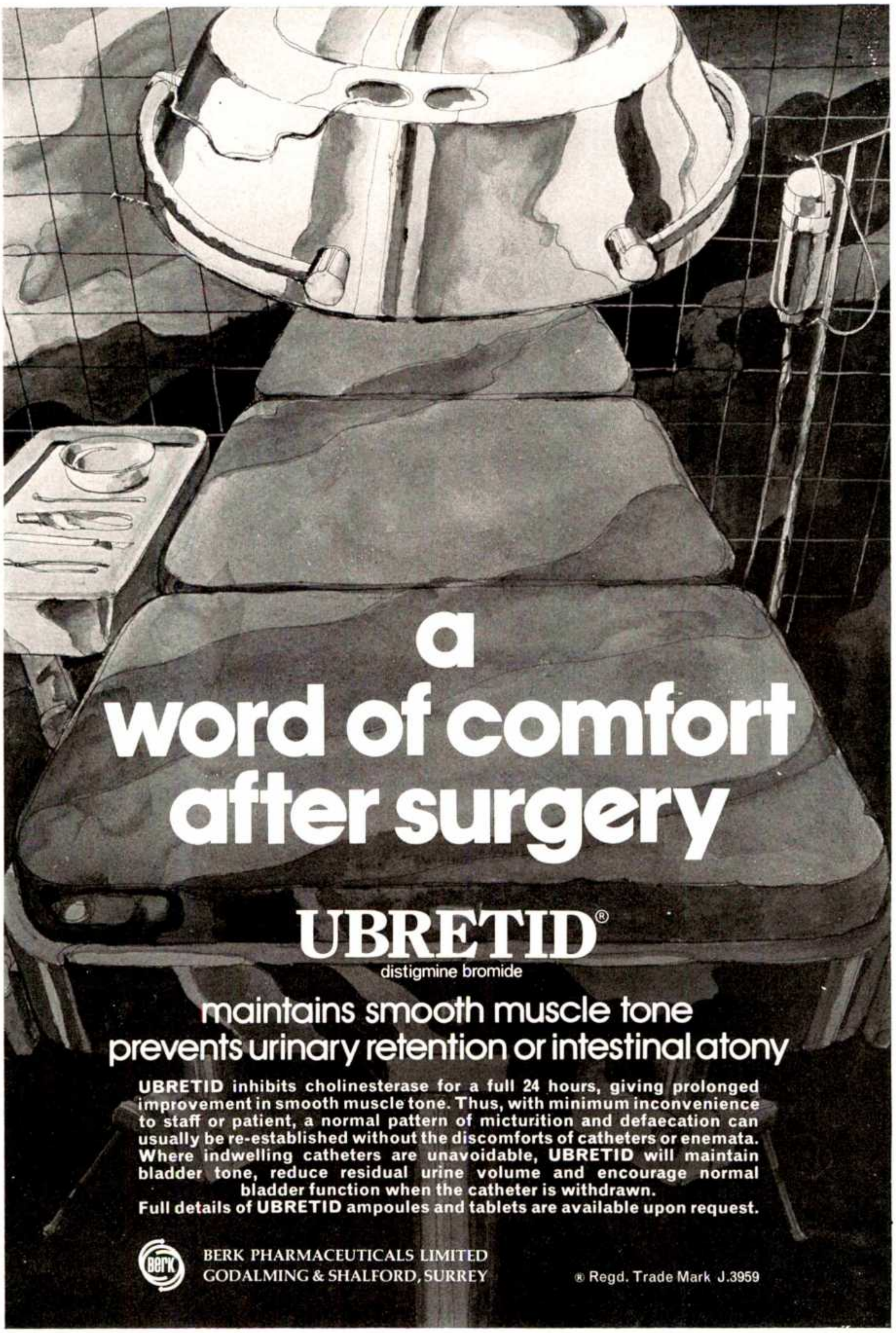

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Vol. 60 MAY, 1973 No. 5

ORIGINAL PAPERS

URETEROCELE

By RICHARD E. SHAW
WALSGRAVE HOSPITAL, COVENTRY

SUMMARY

Ureterocele occurs more frequently in the female than in the male and may present at any age. The ectopic ureterocele must be distinguished from the orthotopic variety. Small ureteroceles are often symptomless, but larger ones may cause loin pain, retention of urine, and external prolapse. There is an increased incidence of duplication in cases of ureterocele. Attention is drawn to the significance of dilatation of the intramural ureter which leads to reflux after incision of a ureterocele.

Small symptomless ureteroceles need no treatment. Although perurethral diathermy incision may be followed by reflux there is a place for this treatment in adults. Large ureteroceles and those presenting in childhood should be treated by open excision employing a reflux-preventing technique.

Papers dealing with the subject of ureterocele have often failed to distinguish the ectopic ureterocele from the more common variety of the condition in which the ureter terminates in the bladder. The main feature of ectopic ureterocele is a cystic dilatation of the lower end of a ureter draining the upper component of a double kidney. The swelling bulges into the bladder or urethra or both, while the ureteric orifice is situated in the urethra. Careful study of the descriptions of cases of ureterocele in papers purporting to deal with the simple type often reveals examples of the ectopic variety, and renders suspect some of the conclusions reached about the features of the disorder. The ectopic ureterocele should be regarded as an entirely separate and distinct entity. Royle and Goodwin (1971) suggested that the non-ectopic variety should be distinguished by the name 'intravesical ureterocele', but this may lead to confusion as the ectopic type is also usually intravesical in part. The term 'orthotopic' has been employed in some recent papers to designate the non-ectopic ureterocele and this is a more acceptable word.

Ureterocele has been defined as 'an intravesical dilatation of the lower end of the ureter' (Aas, 1960). A ureterocele presents a striking appearance on cystoscopy. A typical example is seen as a cystic swelling in the position of a ureteric orifice. It has a thin wall and a translucent appearance. There is considerable variation in size from quite tiny cysts to large swellings occupying an appreciable part of the bladder capacity (*Fig.* 1). The orifice is most frequently situated on the antero-inferior surface and is circular and very small. The orifice of a large ureterocele may not be visible on cystoscopy. Frequently a ureterocele exhibits rhythmical activity, the cyst filling progressively with urine at each peristaltic wave, and then collapsing suddenly as a fine jet escapes from the orifice. The cycle then begins again. In these cases the observer may fail to recognize a ureterocele if the examination takes place during the phase of collapse, and the diagnosis may be missed, especially when cystoscopy is hurried or if the patient's fluid intake has been reduced prior to general anaesthesia. Other ureteroceles do not exhibit rhythmical change and maintain a constant appearance. An unusual event is sometimes observed: as the bladder fills with lotion the ureterocele suddenly becomes inverted, producing an appearance resembling that of a diverticulum. This can only happen when the intramural part of the ureter is considerably dilated. The author has observed this phenomenon following the incision of a ureterocele.

RADIOLOGICAL APPEARANCES

Ureteroceles show up extremely well on intravenous pyelography. The smaller ones have the well-known 'cobra-head' appearance (*Fig.* 2), but the large ones are more spherical in shape (*Fig.* 1). In either case the shape of the cyst is outlined by a thin dark line.

Some accounts describe a narrowing of the ureter as it passes through the bladder wall, but this is only relative to the dilatation of the remainder of the ureter, and in fact the intramural ureter is quite markedly dilated. This dilatation has an important bearing on the possibility of reflux after incision. The degree of obstruction to the upper urinary tract is usually minimal; moderate dilatation of the ureter, sometimes confined to its lower-third region, is the rule (*Fig.* 3). In a few cases a minor degree of hydronephrosis is present and large ureteroceles may be associated with quite marked ureteric dilatation (*Fig.* 1). Occasionally the contrast between gross dilatation of the lower ureter and the normal calibre of the upper ureter is remarkable. Mention should be made of a type of simple ureterocele which has an unusually thick wall. This ureterocele does not collapse on diathermy incision and is associated with severe obstruction to the upper urinary tract.

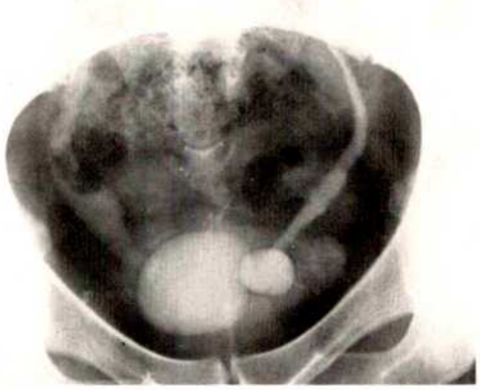

FIG. 1.—*Case* 1. Intravenous pyelogram showing large bilateral ureteroceles. The right-hand one caused retention by prolapsing into the internal meatus.

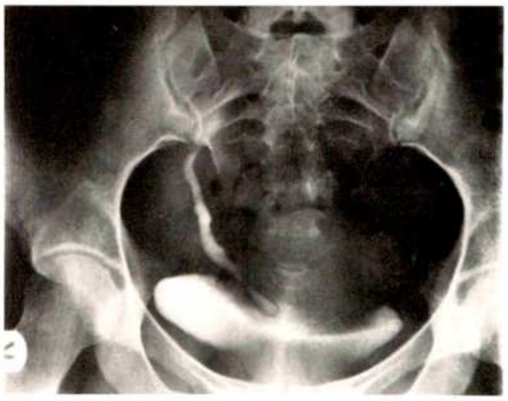

FIG. 2.—Intravenous pyelogram showing the typical 'cobra-head' appearance of a small ureterocele.

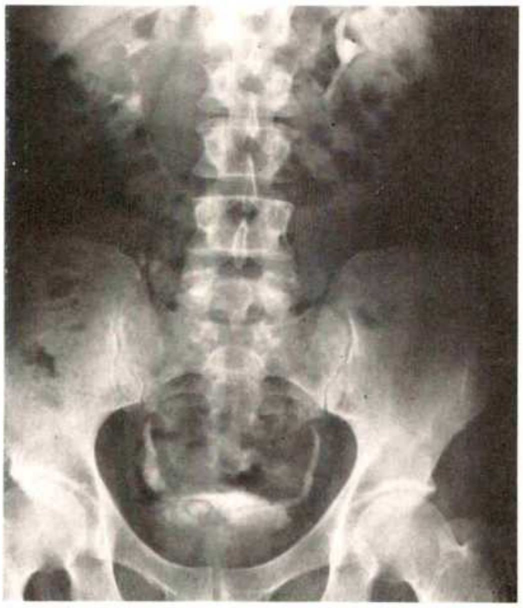

FIG. 3.—Intravenous pyelogram showing bilateral ureteroceles. The left ureterocele has a typical 'cobra-head' shape but the large right one is spherical. Note the minor degree of dilatation of the lower third region of each ureter.

The appearance of a ureterocele on pyelography is so typical that the question of differential diagnosis hardly arises. However, a stone impacted in the intramural part of the ureter can occasionally give rise to the appearance of a stone inside a ureterocele. This condition may, however, be distinguished by observing that the dark halo around the stone has a fuzzy, ill-defined character, which is quite unlike the clearly etched dark line of a ureterocele. Datta, Singh, and Bapna (1971) have recently drawn attention to the 'false ureterocele' associated with stones impacted in the intramural ureter.

MATERIAL AND METHODS

The material comprises 47 ureteroceles in 32 patients who have been seen personally in the past 20 years. Because of the destruction by fire of medical records in Coventry in 1967 the details are incomplete in 3 cases. Examples of ectopic ureterocele have, of course, been excluded.

Sex Incidence (*Table I*).—There is a predominance of females in this series, 60 per cent of the cases being female. This is precisely the sex incidence recorded by Aas (1960), whose series comprised adults only. On the other hand, Thompson and Kelalis (1964) found a female-to-male ratio of 4 : 1. Probably the predominance of females is less than these figures suggest, the relatively more frequent cystoscopy of women for minor urological symptoms yielding a number of cases of symptomless ureterocele.

Table I.—SEX INCIDENCE IN THE PRESENT SERIES

Sex	*No. of Cases*	*Percentage*
Male	12	37
Female	19	60
Not known	1	3
	32	100

Age (*Table II*).—The cases are evenly distributed between the age-groups, except that the oldest age-group is spared and only 2 cases were encountered over the age of 60 years. A similar even distribution of cases was found in the series described by Thompson and Kelalis (1964), and Aas (1960) reported similar findings.

Side affected (*Table III*).—Half the cases were bilateral and half unilateral. Among the unilateral cases the two sides were fairly equally represented. Thompson and Kelalis (1964) commented on the infrequency of bilateral cases among males in their series, only 4 bilateral male cases occurring in 176 patients. However, this has not been found in the present series, as 5 of the 15 bilateral cases were male.

Table II.—AGE DISTRIBUTION IN THE PRESENT SERIES

Age-group (yr.)	*No. of Cases*
0–9	4
10–19	3
20–29	4
30–39	4
40–49	7
50–59	4
60–69	2
70 plus	0
Unknown	4

Table III.—SIDE AFFECTED BY URETEROCELE IN THE PRESENT SERIES

Position	*No. of Cases*
Left	9
Right	6
Bilateral	15
Not known	2
	32

Table IV.—SYMPTOMS ASSOCIATED WITH URETEROCELE IN THE PRESENT SERIES

Symptom	*No. of Cases*
Haematuria	11
Dysuria	8
Frequency	8
Abdominal pain	7
Loin pain	5
Retention of urine	3
Backache	1
Prolapse through external meatus	2
Epididymitis	2

Symptoms (*Table IV*).—The commonest symptoms are those associated with urinary-tract infection, namely frequency, dysuria, and haematuria. Undoubtedly some cases of ureterocele are discovered as incidental findings during investigation of recurrent urinary symptoms, especially in female patients. It is difficult, therefore, to relate these symptoms to ureterocele. Loin pain, however, was significant in 5 patients and 7 others complained of unilateral abdominal pain which may well have been caused by the ureterocele. A similar pattern of symptomatology was reported by Thompson and Kelalis (1964). Large ureteroceles may be associated with more acute symptoms if the cyst prolapses into the urethra, causing retention of urine or even presentation of the ureterocele at the external urinary meatus.

Treatment of Ureterocele (*Table V*).—Eight ureteroceles received no treatment. Twenty-nine ureteroceles were incised by diathermy through a cystoscope. In 2 cases in which there was gross hydronephrosis and hydro-ureter, nephro-ureterectomy was performed, and in another case in which duplication was present, heminephro-ureterectomy was carried out. In 1 case open diathermy incision of bilateral ureteroceles was performed, and in 2 instances where the patients presented with a prolapsing ureterocele a transvesical operation was carried out to excise the ureterocele and to advance the ureter into the bladder through a mucosal tunnel.

Table V.—METHODS OF TREATMENT EMPLOYED FOR 47 URETEROCELES IN THE PRESENT SERIES

Method of Treatment	*No. of Ureteroceles*
Transurethral diathermy incision	29
Transvesical incision	2
Nephro-ureterectomy	2
Heminephro-ureterectomy	1
Open excision of ureterocele and reimplantation of ureter	3
No treatment	8
Not known	2
	47

Table VI.—RESULTS OF TREATMENT OF 16 URETEROCELES ASSESSED BY FOLLOW-UP INTRAVENOUS PYELOGRAPHY

Result	*No. of Cases*
No residual ureteric dilatation	11
Slight dilatation of ureter and/or calices	3
Moderate dilatation of ureter and/or calices	2
	16

Results of Treatment.—It is rather difficult to assess the symptomatic results of treatment since many cases are discovered incidentally and the ureterocele itself is often symptomless. Loin pain is the most frequent significant symptom and this is certainly relieved. Objectively, the pyelographic improvement is usually satisfactory. *Table VI* shows that out of 16 ureteroceles for which follow-up intravenous pyelograms were available, the dilatation of the ureter and calices which had previously been present had disappeared completely in 11 cases and there was only a minor degree of residual dilatation in 3 cases and moderate dilatation in 2. As would be expected, the latter group comprised those in which the initial obstruction had been greatest. No follow-up intravenous pyelogram showed evidence of persistence or recurrence of the ureterocele.

URETERIC REFLUX AND THE TREATMENT OF URETEROCELE

The presence of dilatation of the intramural part of the ureter which is seen so clearly on the intravenous pyelogram indicates the probability of reflux after incision of a ureterocele. Indeed, the cyst in most cases is probably the only protection which exists against the presence of reflux, and one would expect every case to reflux after incision of the cyst. In the present series postoperative micturating cystograms were carried out in respect of 17 ureteroceles and 5 were found to reflux. The examination was, however, made at varying periods after the incision had been carried out but never less than 1 year after treatment. It is possible that the dilated intramural ureter may contract so that reflux ceases spontaneously with the passage of time. Paradoxically it is feasible that some reflux does take place in the untreated ureterocele. Such a case has been described by Amar and Scheer (1964), and Royle and Goodwin (1971) also maintain that reflux does sometimes take place. This point never seems to have been satisfactorily clarified, but the orifice of the ureterocele is so small that it is unlikely that the degree of reflux can be of great significance; on the other hand, it may be quite marked after incision of the cyst.

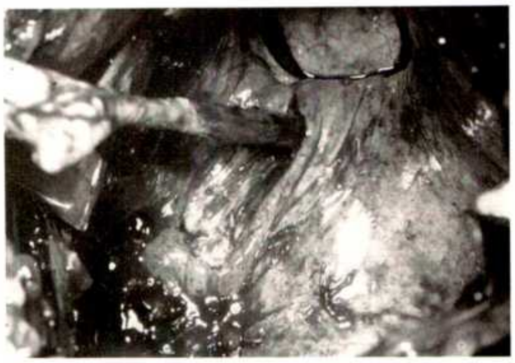

FIG. 4.—Open operation for a large ureterocele. A substantial length of ureter is easily mobilized. Note how the space left by the excised ureterocele leaves room for a long submucosal tunnel.

The likelihood of producing ureteric reflux should induce the surgeon to reconsider the treatment of ureterocele and to question whether any treatment is necessary in many cases. Although the results were satisfactory in 3 out of 4 children who were treated by perurethral diathermy incision in this series, a thoughtful surgeon would be reluctant to employ a procedure which induced reflux in a child. If surgical treatment is considered necessary in a child this should take the form of an open operation employing some reflux-preventing procedure. In adults the dangers associated with reflux are less, and it is questionable whether renal function is at risk in the absence of infection. Certainly, none of the present cases who had reflux after incision appeared to be adversely affected by it, and there was no evidence of any case suffering from declining renal function or recurrent infection. Therefore, in adults with symptoms such as loin pain caused by ureterocele simple perurethral diathermy incision would appear to be a satisfactory form of treatment. A small ureterocele causing minimal obstruction and no symptoms may be left untreated. There is no evidence that the obstruction to the upper urinary tract is progressive and complications such as stone formation are rare. Follow-up of untreated cases is advisable. Large ureteroceles are not suitable for perurethral diathermy and should undergo suprapubic excision, together with a reflux-preventing procedure by one of the techniques described below. Follow-up should include cystoscopy and it is surprising how normal the appearance of the ureteric orifice is after operation. Micturating cystography should also be carried out to determine whether or not reflux is present.

TECHNIQUE OF OPERATIONS FOR URETEROCELE

1. Perurethral Diathermy Incision.—Although the technique of diathermy incision of a ureterocele is simple the operation may miscarry if not performed correctly. A ureteric meatome is passed through the operating cystoscope and the wire is extruded and inserted into the small ureteric orifice. The cystoscope is inclined in order to place tension on the wire, and with the diathermy switched to full cutting current as for transurethral resection the pedal is touched momentarily. The wire cuts through the wall of the ureterocele which collapses at once. If the diathermy power is inadequate the tissue may be coagulated rather than cut, and it is much more difficult to repeat the incision when the cyst has collapsed. When the orifice is not accessible the cyst is punctured at a convenient point on its inferior surface. The cut should be some 3 mm. in length.

Alternative methods of treating the ureterocele include dilatation of the orifice with ureteric bougies, and simple puncture of the cyst with a diathermy needle, but there is a possibility of recurrence of the ureterocele with these forms of therapy.

2. Suprapubic Operation.—Large ureteroceles require a suprapubic approach. Simple incision of the cyst is not satisfactory. Reflux will result and there will also be a large amount of redundant cyst wall which may cause obstruction. Hutch and Chisholm (1966) have described an operation for the suprapubic repair of the condition. They stress the necessity of repairing the dilated hiatus if postoperative reflux is to be prevented. In their operation an incision is made around the base of the ureterocele after suprapubic exposure of the bladder cavity. The cyst is dissected off the bladder wall and the ureter is then mobilized and brought down into the bladder. One is surprised by the ease with which a substantial length of ureter is mobilized (*Fig.* 4). If the ureter is very dilated it may need to be 'tailored'. The ureterocele is excised, the hiatus is repaired, the end of the ureter is sewn to the trigone, and the vesical mucosa is repaired over the mobilized ureter. The author has carried out a similar procedure performed entirely intravesically on 3 ureteroceles in 2 patients and has found it to be a very easy and satisfactory operation. It is questionable whether repair of the hiatus is as important as Hutch and Chisholm (1966) claimed, since a long submucosal tunnel for the ureter is easily contrived and this should be more than adequate to prevent reflux. In the cases in the present series prevention of reflux has been confirmed by subsequent micturating cystography. Boatwright (1971) described an alternative operation in which a part of the wall of the ureterocele is retained for reconstructing the ureter, and a similar procedure was described by Mason (1971). All these techniques promise to be extremely satisfactory ways of carrying out open operation for ureterocele. Hutch and Chisholm (1966) maintained that small ureteroceles may be treated by a linear meatotomy performed on the surface of the cyst below the ureteric orifice, i.e., an inferior meatotomy. This cannot be done transurethrally and requires open operation. They maintain that this procedure guards against reflux, but it is difficult to believe that this operation has wide application.

COMPLICATIONS OF URETEROCELE

Calculus Formation.—Stasis caused by the ureterocele establishes conditions favourable for stone formation especially if infection supervenes. The well-known phenomenon of a stone within a ureterocele was not encountered in this series, but 3 patients had renal calculi and in 1 instance stones were also present in the dilated ureter. Aas (1960) reported an incidence of urinary calculi of 39 per cent in 52 patients with ureterocele. Possibly there was an element of selection in the cases of Aas (1960), for Lowsley and Kirwin (1956) give the frequency of renal calculi as 4 per cent, and this is certainly more in harmony with the present author's experience of the disorder.

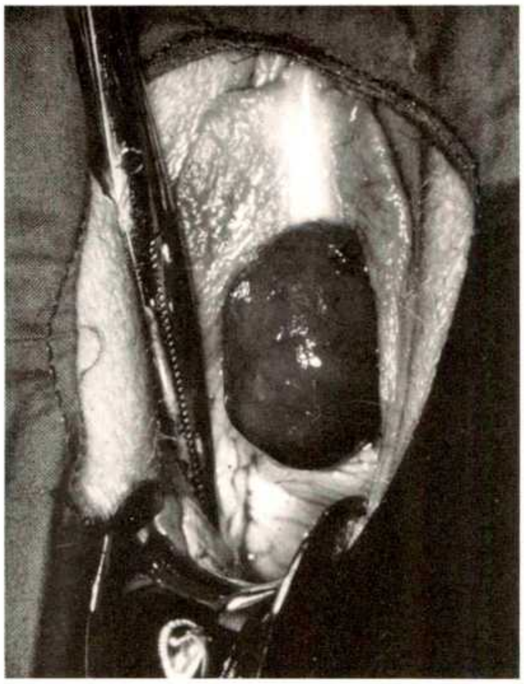

FIG. 5.—*Case* 2. Ureterocele prolapsing through the external urinary meatus. Note the drop of urine escaping from the ureteric orifice at the upper part of the swelling.

Retention of Urine.—A large ureterocele may prolapse into the internal urinary meatus and cause retention of urine, although this is often of a transient nature. Three examples were encountered in this series. Retention takes place in characteristic episodes in which the patient complains of pain in the loin which is immediately relieved on spontaneous termination of the retention.

CASE REPORT.—

Case 1.—A 45-year-old woman was admitted in February, 1964, with a 13-year history of periods of retention of urine which were always associated with pain in the right loin. She had learned by experience that if she walked about the retention would be relieved and followed by immediate disappearance of the loin pain. On the occasion of her admission this had failed and the retention and loin pain had persisted. The intravenous pyelogram (*Fig*. 1) showed large bilateral ureteroceles and it was clear that her symptoms were caused by prolapse of the right ureterocele into the internal urinary meatus. Both cysts were treated by diathermy incision through a cystoscope with permanent relief of symptoms. A second intravenous pyelogram in 1964 showed no evidence of ureterocele on either side and there was considerable reduction in the ureteric dilatation. A micturating cystogram demonstrated reflux on the right side but not on the left, and the patient has remained free of urinary symptoms up to the present time.

Prolapse.—Not only may a ureterocele fall into the internal meatus causing retention, but it may also pass through the urethra to prolapse at the external urinary meatus. Clearly this can only take place in the case of a large ureterocele in a patient of the female sex. This series includes 2 examples of prolapse of a ureterocele.

CASE REPORT.—

Case 2.—A 36-year-old woman was seen in March, 1970, with a 6-week history of cystitis. She had also observed that from time to time a lump presented in the vagina. Two weeks previously there had been considerable blood-loss from the vagina. Forty-eight hours prior to admission the vaginal swelling had returned and its presence had been accompanied by pain, frequency, and urgency. On examination the patient was in considerable distress, and a large red swelling was seen on the anterior vaginal wall with urine spurting from a tiny orifice (*Fig*. 5). The intravenous pyelogram (*Fig*. 6) which was carried out after reduction of the swelling demonstrated a right ureterocele with considerable ureteric dilatation. The patient was very anaemic, the haemoglobin being 8·2 g per cent. The ureterocele was gently pushed back into the bladder under anaesthesia and a balloon catheter was inserted to prevent recurrence of prolapse. Two days later, after correction of the anaemia by transfusion, operation was performed. By a transvesical approach the cyst was excised and the ureter was advanced under a submucosal tunnel, using a technique similar to that described by Hutch and Chisholm (1966). Cystoscopy 6 months later showed a right ureteric orifice of surprisingly normal appearance, and a micturating cystogram confirmed the absence of reflux.

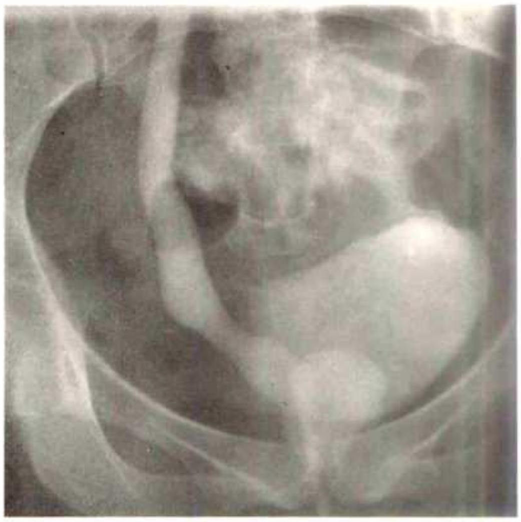

FIG. 6.—*Case* 2. Intravenous pyelogram showing a large ureterocele and a grossly distended ureter (a urethral catheter is in situ).

A striking feature of this case was the severe blood-loss which had taken place from the congested prolapsed cyst, and it is of interest that in a second case of prolapse of a ureterocele in a young woman the haemoglobin estimation on admission was moderately reduced owing to blood-loss from a semi-strangulated ureterocele.

URETEROCELE AND DUPLICATION

There is undoubtedly an increased incidence of renal duplication in cases of ureterocele. In this series of 47 ureteroceles, 4 (9 per cent) were associated with duplication. In 1 instance the two ureters united above the bladder, but the other 3 cases were examples of complete duplication, and in each instance the ureterocele was related to the ureter from the upper segment. This appears to be invariably the case. As in the case of ectopic ureteroceles the orifice of the ureter from the lower segment may be elevated on the surface of the ureterocele associated with the other ureter. Aas (1960), in his study of ureteroceles in adults, reported that of 16 patients with bilateral ureteroceles, none showed signs of renal duplication, but 38 per cent of 36 unilateral cases did so. However, study of his case reports shows that examples of ectopic ureterocele, in which duplication is invariable, are included. The confusion between ectopic and orthotopic ureteroceles is common to most papers, except the most recent, dealing with this subject, and the incidence of duplication has therefore been exaggerated. Indeed, reports of very high incidences of duplication should be examined critically to ensure that cases of ectopic ureterocele have not been included. Cases of orthotopic ureterocele associated with duplication should not be accepted as such unless the orifice has been definitely established as lying in the bladder and not in the urethra.

AETIOLOGY OF URETEROCELE

A number of theories have been advanced to explain the development of ureterocele and they are well summarized by Aas (1960) and will not be detailed here. It is likely that the cause of the condition lies in the minute size of the ureteric orifice; this obstructs the discharge of urine and results in dilatation of the ureter. That portion of the ureteric wall which is adjacent to the vesical mucosa is unsupported and distends to form a cystic swelling. It is equally probable that the small size of the ureteric orifice is a congenital anomaly which develops when the membrane covering the lower end of the ureter in early embryonic life fails to disappear completely. There is very little evidence that ureterocele ever develops as a secondary phenomenon following the passage of a calculus through the ureteric orifice or from other diseases affecting this structure. Although the prime cause of the condition is almost certainly developmental, a ureterocele may take many years to form and may not be fully developed until adult life. In 2 or 3 cases the author has observed at repeated cystoscopy the development of a ureterocele over a period of time. For example, a woman of 42 years had been seen at the age of 27 with urinary trouble, and cystoscopy by another urologist had shown nothing abnormal. The patient had been seen by the author 6 years later with similar troubles and cystoscopy at that time had also shown quite normal appearances. However, in 1970 a further examination revealed that a ureterocele was present on the left side which had certainly been absent on the previous occasions. In cases of unilateral ureterocele the opposite ureteric orifice is often smaller than normal.

Acknowledgements.—My thanks are due to Mr. J. R. Geddes and Mr. F. J. C. Matthews for referring patients with this condition; to Mr. H. D. James for the photographs; and to Mrs. J. Jenson for secretarial help.

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AN EVALUATION OF THE STRENGTH OF THE POSTERIOR WALL OF THE INGUINAL CANAL IN WOMEN

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SUMMARY

In the period 1945–71, 124 women with primary direct inguinal hernia were operated upon. During the same period indirect inguinal hernias in women were noted to be thirteen times more common than the direct type. The commonest site of protrusion of the direct hernia was immediately medial to the inferior epigastric artery. In contrast, in a series of 110 women with recurrent inguinal hernia the majority of the hernias were direct and, of these, most were either situated medially in the posterior wall of the inguinal canal or involved the whole posterior wall.

The significance of these findings in relation to the repair of femoral and inguinal hernias in women is discussed.

During the 26-year period from 1 Jan., 1945, to 1 Jan., 1971, approximately 70,000 hernia repairs were performed in the Shouldice Hospital, Toronto. Some 15,000 of these repairs were performed personally. In this period 1672 primary inguinal hernia repairs and 414 primary femoral hernia repairs were performed in women. Of the inguinal hernias, 1548 were indirect and only 124 were direct, so that in women primary indirect hernia was thirteen times more frequent than the primary direct type. This latter type of hernia, representing only 1 out of every 560 hernia admissions, is so rare that some surgeons may not have encountered a case.

The significance of the rarity of primary direct inguinal hernia in women does not appear to be widely known. It is obviously of importance when considering the most suitable type of operation for repair of a primary inguinal hernia in a woman. Indeed, a primary inguinal hernia in a woman is always best considered to be indirect in type until proved otherwise (Glassow, 1963). Less obviously the knowledge of the rarity of primary direct inguinal hernia is also important in deciding whether it is better to perform a primary *femoral* hernia repair in a woman from above or below the inguinal ligament.

As well as the 1672 primary inguinal hernia repairs 110 repairs in women were performed for recurrent inguinal hernia; 45 for indirect recurrences and 65 for direct recurrences. In every instance the original repair or repairs had been performed elsewhere. The personal experience gained from these recurrent hernia repairs was also important in the development and formulation of the opinions expressed in this article. No detailed discussion of primary direct inguinal hernia in women has been found in the surgical literature. It was therefore considered worth while to report the results of analysis of this series of 124 primary direct inguinal hernias in some detail in order to assess the essential characteristics of this type of hernia. Attention was focused in particular on the exact site in the posterior wall of the inguinal canal through which the direct hernia protruded.

ANALYSIS OF MATERIAL

From a review of the case records of women with primary inguinal hernia the following observations are considered significant.

Primary indirect inguinal hernia is common in women and primary direct inguinal hernia is uncommon. The posterior wall of the inguinal canal in a woman can be considered, therefore, to be typically a strong structure. Detailed examination of the case records of patients with direct inguinal hernia supports this conclusion (*Table I*). In particular, more than two-thirds of all such hernias were situated laterally, immediately medial to the inferior epigastric vessels. In only one-third of these cases, i.e., approximately 2 per cent of all the cases of primary inguinal hernia in women, was any other part of the posterior wall weakened by a direct hernia, and of these, the ones presenting far medially were the smallest and most uncommon. Furthermore, primary bilateral direct inguinal hernia in women is particularly rare (Glassow, 1969), only 9 cases being recorded in the present series. Ipsilateral primary direct inguinal and primary femoral hernia in a woman is also extremely rare, although it is common in men (Glassow, 1971).

DISCUSSION

The accumulated weight of these observations stresses the normal strength of the posterior wall of the inguinal canal in women. It is reasonable, therefore, to suggest that this structure should be left intact by the surgeon wherever possible. However, in all hernia repairs, whether inguinal or femoral, a decision in this respect has to be made.

Because the posterior wall of the inguinal canal is usually strong in women prophylactic repair of a primary indirect inguinal hernia is less important than in men, in whom this structure is often weak. In repair of the rare primary direct inguinal hernia in women it is necessary to divide the posterior wall, either partially or completely, in order to perform an adequate overlapping type of repair, as is used in the Shouldice Hospital, Toronto (Glassow, 1964, 1973).

Table I.—MAIN FEATURES OF 124 CASES OF PRIMARY DIRECT INGUINAL HERNIA IN WOMEN

	No.		PERCENTAGE	
No. of patients older than 50 years (average age 57 years)		79		63·7
Right side		70		56·5
Bilateral direct		9		7·3
Site of hernial protrusion through posterior wall of inguinal canal.—				
Just medial to inferior epigastric vessels (lateral one-half)		88		71·0
Sac excised	43		34·7	
Sac not excised	25		20·2	
Fatty only	20		16·1	
Through medial third of posterior wall of inguinal canal		17		13·7
Sac excised	7		5·5	
Sac not excised	0		0	
Fatty only	10		8·2	
Through centre of posterior wall of inguinal canal		7		5·5
Through all of posterior wall of inguinal canal		12		9·8
Associated with ipsilateral indirect inguinal hernia:—		30		24·5
Indirect sac	19		15·6	
Indirect fatty only	11		8·9	
Associated with ipsilateral femoral hernia		3		2·4
Associated with simultaneous contralateral hernia repair.—		25		20·2
Inguinal hernia on other side		21		17·0
Indirect	12		9·8	
Direct	9		7·2	
Femoral hernia on other side		4		3·2
Known recurrences following repair at Shouldice Hospital, Toronto		2		1·6

It is one of the purposes of this article, however, to stress these considerations with respect to the repair of a primary *femoral* hernia in a woman. The Lothiessen type of repair for a femoral hernia divides the posterior wall, thus necessitating a subsequent inguinal repair. In a subinguinal or low approach for the repair of a femoral hernia the posterior wall is completely avoided. On these grounds the subinguinal operation appears to have much to recommend it and indeed would seem preferable if the associated recurrence rate is low. The treatment and technique of repair of femoral hernia in the female based on the experience gained here are dealt with in detail elsewhere (Glassow, 1965, 1966). A recurrence rate of 1·3 per cent was achieved (Glassow, 1970a).

A brief consideration of the 110 instances of recurrent inguinal hernia repair in women is pertinent to this discussion. It is remarkable that recurrent indirect inguinal hernias in this series were two-thirds *less* common than direct inguinal hernia recurrences, although primary indirect hernias were thirteen times *more* common than the primary direct type. Because the original operations had been performed elsewhere, no records concerning the type of the original hernias and their repair were available. Hence the following arguments regarding the aetiology of the recurrences are only surmise. It is not easy, however, to avoid the conclusion that a number of the direct inguinal recurrences were the result of weakening caused by the previous repair of the posterior wall of the inguinal canal, which could have been either a Lothiessen repair for a femoral hernia or division of the posterior wall during repair of an inguinal hernia. Further weight is lent to this supposition by the fact that in 57 cases (88 per cent of these direct recurrences) the hernia was either situated far medially or protruded through all of the posterior wall, which are both uncommon sites for a *primary* direct inguinal hernia in a woman. In only 5 (8 per cent) of the cases was the direct recurrence found laterally, adjacent to the inferior epigastric vessels, which is the most typical site of the primary direct inguinal hernia (*Table I*).

All these observations support the experience gained here, namely that the low or subinguinal operation for a primary femoral hernia in a woman is a good operation attended by a low recurrence rate. Wakeley (1940), Tanner (1942), Butters (1948), Monro (1950), and Lytle (1957) have all made similar observations but they did not distinguish between the sexes. In women, therefore, the subinguinal approach is recommended as the operation of choice for an elective primary femoral herniorrhaphy. It follows that the main indication for the high or supra-inguinal operation in a woman who has a primary femoral hernia is the presence of a coincidental ipsilateral inguinal hernia. An earlier review has shown this combination to be relatively uncommon in women (Glassow, 1965). When an inguinal element is present it is almost invariably indirect in nature. Indeed, the risk of missing an undiagnosed ipsilateral inguinal hernia during a low repair of a primary femoral hernia in a woman, by not exploring the inguinal region, was estimated to be of the order of 1 per cent (Glassow, 1965, 1970b).

It must be emphasized that these remarks do not apply to the treatment of primary femoral hernia in men. This condition has been separately reviewed (Glassow, 1971) in a series of 687 consecutive repairs performed in the Shouldice Hospital, Toronto, in a 25-year period. Of these, no less than 355 (53 per cent) were associated with an ipsilateral inguinal hernia, this hernia being twice as frequently direct as indirect. This is in marked contrast to the situation in women described in detail in this paper. It is an important differentiating feature in any consideration of the aetiology of primary and recurrent femoral hernias in the two sexes. In some of the cases of combined ipsilateral inguinal and femoral hernias in men the diagnosis of the inguinal element was made clinically, but in many it was only discovered at operation. In men, therefore, in contradistinction to women, it is usually necessary to explore the inguinal region during the repair of a primary femoral hernia, even though the subsequent femoral repair is usually performed from below the inguinal ligament. It is not surprising, therefore, that the recurrence rate for repair of primary femoral hernia in men is higher than that in women, being 2·2 per cent in the series of Glassow (1971).

CONCLUSION

A series of 70,000 herniorrhaphies, including a personal experience of 15,000, in a 26-year period from 1945 to 1970 forms the background for the ideas presented here. During this time operations for 1672 primary inguinal hernias and 414 primary femoral hernias in women were performed. These cases form the basis for this study.

The posterior wall of the inguinal canal in women is demonstrably strong in most instances. Evidence is adduced from an experience of 1548 primary indirect inguinal hernias and 124 primary direct inguinal hernias in women, indicating that this latter condition is relatively rare. The usual site for a direct hernia is immediately medial to the inferior epigastric vessels. Other situations are more rare. Further evidence to support the fact that the posterior wall of the inguinal canal is a typically strong structure is given, including a brief discussion of the aetiology of recurrent inguinal hernia in women. Treatment of primary indirect and direct inguinal hernias in women should recognize this fact.

In women repair of a primary femoral hernia can be very satisfactorily performed from below the inguinal ligament, with a recurrence rate of between 1 and 2 per cent. This route avoids division of the posterior wall of the inguinal canal, as in the 'high' operation.

In men, because a primary femoral hernia is accompanied by an ipsilateral inguinal hernia in more than 50 per cent of cases, these considerations do not apply.

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THE MANAGEMENT OF VARICOSE VEINS

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SUMMARY

A clinical trial was carried out to compare the effectiveness of compressive sclerotherapy with that of the traditional operative procedures in the treatment of varicose veins. One hundred and ten patients were treated by compression sclerotherapy and 91 patients by operation.

The results showed that there was no significant difference in the therapeutic value of the two procedures.

DURING recent years the technique of injection therapy for the treatment of varicose veins and their complications has been revised and extended. A major contributor to this therapy has been Fegan (1967) of Dublin and the term 'compressive sclerotherapy' has been applied to this non-operative form of treatment.

Compressive sclerotherapy is based on the concept that all varices are due to incompetence of the perforating veins connecting the deep and superficial venous systems. As a consequence the venous blood-flow is reversed during muscular contraction, resulting in a greatly increased pressure in the superficial veins with eventual varicosity. If the blood-flow in the incompetent perforating veins can be interrupted, then the progression to varicosity can be halted and reversal to normality hoped for. This can be achieved by ligation and division of the perforating veins, by the traditional Trendelenburg and stripping procedure, and thirdly by obliterating the T-junction of the perforating veins with the superficial veins, using a sclerosant, and subsequently applying continuous pressure to keep the treated veins empty and to produce adhesions of the walls and eventual fibrosis. The concept of valvular incompetence at the saphenofemoral and/or saphenopopliteal junctions is still valid but whether this is primary or secondary in nature is still unknown. It is claimed that using compressive sclerotherapy results in a considerable diminution of saphenofemoral incompetence which tends to support the concept of perforator incompetence.

Several previous studies concerning the value of compressive sclerotherapy have already been published. Fegan (1967) found that 81·8 per cent of patients were satisfied with the treatment and considered themselves cured. De Jode (1970) obtained good results in 83 per cent of 201 legs. However, in that series patients with major saphenous incompetence were treated by operation and thus a degree of selection was evident. A random trial carried out by Hobbs (1968) suggested that incompetence of the saphenous system was effectively treated by either method. In an evaluation of treatment by compressive sclerotherapy Reid and Rothnie (1968) found it to be an effective method but used multiple injections of varicose veins to produce a diffuse sclerosis.

MATERIALS AND METHODS

Like many hospitals there was a large waiting list for patients requiring operative treatment for varicose veins at the Warrington Infirmary, and 4 years ago it was decided that it would be an interesting study to compare the results of the traditional operative procedures with the non-operative method of treatment. Owing to the extremely variable pathology and clinical presentation of varicose veins it was decided to restrict this study to patients in whom operation would usually have been the recommended treatment, i.e., all the patients who had demonstrable incompetence of the saphenous systems and/or venous ulceration due to posterior tibial perforator incompetence.

Table I.—TYPE OF TREATMENT IN 201 PATIENTS WITH VARICOSE VEINS

Treatment	*No. of Legs*	
Compressive therapy		149
Complicated by ulceration	15	
Operation		125
Complicated by ulceration	5	
Total		274

Table II.—AGE DISTRIBUTION OF 201 PATIENTS WITH VARICOSE VEINS

Age-group (yr.)	*Percentage of Patients* *Compressive Sclerotherapy*	*Operation*
10–19	0	1
20–29	12	9
30–39	33	34
40–49	29	32
50–59	13	20
60–69	8	4
70–79	5	0

Accordingly, 201 patients were studied during the years 1967 to 1968 and those offered operative treatment were alternated with those offered compressive sclerotherapy. As a result, 110 patients (149 legs) were treated by compressive sclerotherapy and 91 patients (125 legs) underwent the traditional operative procedure. In 15 of the 110 patients who had compressive sclerotherapy the varicose veins were complicated by ulceration; ulceration was present in 5 of the 91 patients who underwent operation (*Table I*). The age distribution of both groups of patients was also studied and two-thirds of the cases were in the 30–50 age-group (*Table II*).

Operative treatment consisted of the usual Trendelenburg procedure, namely ligation and division of the saphenous vein at the saphenofemoral junction and also ligation and division of the groin tributaries and stripping of the saphenous vein, or multiple ligations if this was not possible. Subfascial ligation and division of the perforator veins were carried out in cases of ulceration, after healing had been achieved, by the use of compressive bandages or admission to hospital if necessary.

With regard to compressive sclerotherapy, the technique was more or less similar to that described by Fegan (1967). The perforator veins were detected by palpation and marked out. They were then injected with the leg elevated so that the vein was completely emptied. A compressive bandage was then applied and an elastic stocking supplied. The injected substance was sodium tetradecyl sulphate and the patients were seen at intervals of 3 weeks until treatment was regarded as complete. The treatment was carried out by consultant surgeons.

RESULTS

The follow-up period extended from 12 to 18 months and all the patients had completed their treatment at least 12 months prior to inclusion in this study. The results were assessed by another consultant surgeon as well as by the author.

Table III.—RESULTS OF COMPRESSIVE SCLEROTHERAPY FOR VARICOSE VEINS

Result	*No. of Cases*
Residual varices	19
Recurrence	7
Failure of technique	3
Recurrent ulceration	2

Compressive Sclerotherapy (*Table III*).—Residual varices were considered to be present in 19 legs (13 per cent). However, 'residual varices' is a term that is difficult to apply to this form of treatment, for it usually means that the treatment has not been completed. However, when wearing of the compression bandages was discontinued, as indicated by the apparent completion of treatment, a trial period of wearing an elastic support only was instituted. If at the end of this time varices were present they were regarded as residual.

Varices which had been treated with apparent success recurred in 7 legs. They were reinjected with a satisfactory result. The technique failed completely in 3 legs as the sclerosant did not appear to have any effect, and all these cases had to be treated by operation. Recurrent ulceration occurred in 2 legs; 1 case was reinjected with satisfactory results, while the second patient had a further recurrence, and subsequent venographic studies showed him to have an obliterated femoral vein. This was probably the result of a deep femoral venous thrombosis which he had had 10 years previously.

Operative Treatment (*Table IV*).—Residual varices were present in 20 legs of those treated by operation and they were all re-treated successfully by local injections. Recurrent varices occurred in 5 legs and again these were re-treated by injection therapy. There was no case of recurrent ulceration.

COMPLICATIONS

Compressive Sclerotherapy (*Table V*).—Thrombophlebitis occurred in 5 patients. It was usually quite localized but in 1 patient it extended in the internal saphenous vein almost to the saphenofemoral junction and she required admission to hospital. The other patients were treated by bandaging only and remained mobile. There was no case of deep venous thrombosis or pulmonary embolism.

One of the recognized complications of compressive sclerotherapy is an injection ulcer and it is usually due either to extravenous injection or more commonly to leakage of the sclerosant fluid outside the vein wall. It is more liable to occur when veins lying close to bone are injected. An injection ulcer occurred in 1 patient in this series.

Table IV.—RESULTS OF OPERATION FOR VARICOSE VEINS

Result	*No. of Cases*
Residual varices	20
Recurrent varices	5
Recurrent ulceration	0

Table V.—COMPLICATIONS OF COMPRESSIVE SCLEROTHERAPY FOR VARICOSE VEINS

Complication		*No. of Cases*
Thrombophlebitis*		5
Injection ulcer		1
Sensitivity to sodium tetradecyl sulphate		3
Eczema—generalized	1	
Eczema—localized	1	
Persistent nausea following injections	1	

* One case required admission to hospital.

Table VI.—COMPLICATIONS OF OPERATION FOR VARICOSE VEINS

Complicated	*No. of Cases*
Wound sepsis	1
Secondary haemorrhage	1
Deep venous thrombosis with pulmonary embolism	1

Sensitivity to sodium tetradecyl sulphate is regarded as rare. It occurred in 3 patients in this series. In the first case there was a generalized eczema. The eczema was localized in the second patient, and in the third patient there was persistent nausea following the injections and these were discontinued and operation was performed.

Operative Treatment (*Table VI*).—Wound sepsis is always a possible complication, particularly when operating in the groin, and this occurred in 1 patient. Secondary haemorrhage is unusual and is usually associated with sepsis; this complication occurred in 1 patient. A third patient developed a deep venous thrombosis in the operated leg with a subsequent pulmonary embolism. Anticoagulant therapy was carried out with a successful outcome.

DISCUSSION

The Advantages and Disadvantages of Each Procedure.—Compressive sclerotherapy has many advantages. All the patients can be treated in an out-patients' department, they are fully mobile, and treatment does not interfere with their daily occupation. The results to date are equal to those obtained by operation but compressive sclerotherapy avoids the necessity for anaesthesia. There is no apparent danger of pulmonary embolism and the cost is very much smaller. One can also treat large numbers of patients and there is no doubt that the waiting list in our particular hospital has been drastically reduced.

There are a number of disadvantages of compression sclerotherapy:—

1. Wearing bandages for several weeks is disliked by some patients. They find the bandages extremely

inconvenient and, of course, unless they are put on carefully they are liable to slip down and redressings are required.

2. Patients have difficulty in washing and bathing, but many patients have found ingenious ways of overcoming this by the use of plastic bags and leg supports.

Table VII.—COMPARISON OF THE RESULTS OF COMPRESSION SCLEROTHERAPY WITH THOSE OF OPERATION FOR VARICOSE VEINS

RESULT	COMPRESSION SCLEROTHERAPY	OPERATION	TOTAL NO. OF CASES
Recurrent varices	7	5	12
Residual varices	19	20	39
Recurrent ulcer	2	0	2
Failure of technique	3	0	3
Satisfactory	118	100	218
Total	149	125	274

$\chi^2 = 2{\cdot}3333$; $P < 0{\cdot}50$. There is thus no significant difference between the two procedures.

3. Owing to the possible slight incidence in venous thrombosis associated with the contraceptive pill, this has to be discontinued during the period of treatment.

The advantages of operation are that treatment is completed in a much shorter time. However, there are the obvious disadvantages of having to be hospitalized for a certain period of time and requiring several weeks off work.

CONCLUSIONS

The statistics presented in this paper (*Table VII*) suggest that the end results of both methods of treatment are largely the same, and that the method of compressive sclerotherapy probably achieves a success rate equal to that of surgery. Complications of compressive sclerotherapy are few and no less acceptable than those of surgery. However, failures do occur for several reasons and surgery may well be required for cure. Thus, surgery continues to have an essential part in the management of varicose veins, although there is no doubt that compressive sclerotherapy is a very valuable adjunct.

Acknowledgements.—I am indebted to Professor Fegan who accorded me the privilege of visiting his clinic and observing the technique, and to the United Liverpool Hospitals for financial support for this study. I wish to express my appreciation to Mr. Donald Young, Consultant Surgeon, Warrington Infirmary, who assisted me in this study and also to the nursing staff of the Infirmary and Dispensary, Warrington.

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THE VALUE OF PLASMA GAMMA-GLUTAMYL TRANSPEPTIDASE IN THE DETECTION OF HEPATIC METASTASES

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SUMMARY

It has been suggested that measurement of the plasma enzyme gamma-glutamyl transpeptidase (GGTP) may be useful in the detection of hepatic metastases.

To assess the value of GGTP as a screening test for hepatic metastases, 40 cases of gastro-intestinal carcinoma were studied prior to surgery.

Ten patients had hepatic metastases, and in 5 of these the plasma GGTP was within normal limits. Abnormal GGTP results were always associated with elevation of the plasma alkaline phosphatase, and preoperative clinical examination of the liver proved to be the most accurate method for the detection of hepatic metastases.

A SMALL proportion of patients who develop recurrent or metastatic disease after surgery for gastro-intestinal cancer may be salvaged by further surgery (Gilbertsen and Wangensteen, 1962; Friesen, Hardin, and Kittle, 1967). It appears that a cure may be possible even in patients who present with hepatic metastases when these are suitable for surgical extirpation (Foster, 1970).

Early detection of recurrent disease is clearly important if further surgery is to be curative but detection of hepatic metastases may be difficult. Radio-isotope scans of the liver and angiography are useful diagnostic aids but are quite impracticable for all the patients routinely attending the follow-up clinic. Aronsen, Nosslin, and Pihl (1970), however, have reported a high degree of accuracy in the detection of hepatic metastases by measurement of the enzyme gamma-glutamyl transpeptidase (GGTP) in serum.

The present study was designed to determine the value of GGTP as a screening test for the detection of hepatic metastases in cases of gastro-intestinal cancer.

MATERIAL AND METHODS

All the cases of carcinoma of the stomach, colon, or rectum who were admitted to the Professorial Surgical Unit, Leeds General Infirmary, over a period of 5 months were studied. There were 31 cases of colonic or rectal carcinoma (17 male and 14 female) and 9 cases of gastric carcinoma (5 male and 4 female). Sixteen control patients (14 male and 2 female) were also studied. These were patients who had been referred to the Out-patients' Department with a diagnosis of groin hernia or varicose veins.

No patient had a history of liver disease, jaundice, or alcoholism and in each case it was ascertained that the patient was not receiving barbiturates or anticonvulsant drugs which might result in elevation of the plasma GGTP (Rosalki, Tarlow, and Rau, 1971).

Table I.—Results of Liver-function Tests (Mean ± S.D.) in Control Patients and in Patients with Gastro-intestinal Carcinoma with or without Hepatic Metastases

	Control Group (16 Cases)	Patients with Gastro-intestinal Carcinoma	
		No Hepatic Metastases (30 Cases)	Hepatic Metastases (10 Cases)
Age (yr.)	50±16	64±6	63±11
SGOT (I.U per litre)	15±5	12±4	27±20
SGPT (I.U. per litre)	11±5	8±3	20±16
Alkaline phosphatase (K.A. units per 100 ml)	8±1	8±2	22±18
Total protein (g. per 100 ml.)	7·5±0 6	7 1±0 6	7 3±0 5
Albumin (g. per 100 ml.)	4 3±0 3	3 8±0 4	3 8±0 4
Globulin (g. per 100 ml.)	3 2±0 6	3 3±0 5	3 5±0 5
Bilirubin (mg. per 100 ml.)	0·5±0·2	0 4±0 2	0 6±0·3
GGTP (I.U. per litre)	20±11	15±10	95±114

Plasma GGTP was measured by the method of Naftalin, Sexton, Whitaker, and Tracey (1969) and compared with the results of routine liver-function tests in all the cases. Glutamic oxalo-acetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT) were estimated on an LKB reaction rate analyser using Boehringer Corporation (UV) test combinations. Plasma alkaline phosphatase was determined by the method of Axelsson, Ekman, and Knutsson (1965), and bilirubin by the method of Simmons (1968). Total plasma proteins were determined by the biuret method (Technicon method sheet AA 11, No. 14), and plasma albumin by the method of Northam and Widdowson (1967).

The findings on preoperative clinical examination of the liver by one or other of two house-surgeons were recorded in all the cases of gastro-intestinal carcinoma and correlated with the subsequent laboratory results and information obtained at laparotomy. At operation the liver was systematically and thoroughly examined for evidence of metastases.

RESULTS

Control Cases.—The results of the liver-function tests in the control cases are shown in *Table I*. The mean age of the 16 patients in this group was 50 years (S.D. ± 16). The routine

Table II.—Correlation between GGTP Results, the Results of Routine Liver-function Tests, and Findings on Preoperative Clinical Examination in Patients with Hepatic Metastases

Case No	Age and Sex	SGOT (I.U per litre)	SGPT (I U. per litre)	Alkaline Phosphatase (K.A units per 100 ml.)	Total Protein (g. per 100 ml)	Albumin (g per 100 ml)	Globulin (g. per 100 ml.)	Bilirubin (mg. per 100 ml)	GGTP (I.U. per litre)	Primary	Hepatomegaly on Preoperative Examination	Findings at Laparotomy
1	54 F.	7	5	9	6 7	2 9	3 8	0 2	23	Colon	Yes	Metastases right lobe of liver
2	59 F	60	41	44	7 3	3 6	3 7	0 8	321	Colon	Yes	Metastases both lobes of liver
3	75 M.	60	50	63	6 8	3 9	2 9	0 6	311	Colon	Yes	Metastases both lobes of liver
4	67 M.	22	14	24	7 5	4·4	3 1	0 6	98	Rectum	Yes	Metastases both lobes of liver
5	62 F.	37	41	11	7 6	4 0	3 6	0 3	28	Rectum	Yes	Metastases both lobes of liver
6	59 F.	36	16	31	8 3	3 9	4 4	0 7	75	Colon	Yes	Metastases both lobes of liver
7	67 M	13	10	6	6 9	4·0	2 9	0·7	10	Colon	Yes	Metastases both lobes of liver
8	65 F.	13	8	11	6 9	4 0	2 9	0 2	33	Rectum	Yes	Metastases both lobes of liver
9	58 M.	7	8	6	6 8	3 6	3 2	1 0	5	Stomach	No	Metastases left lobe of liver
10	69 M.	12	7	16	7 9	3 7	4 2	0 9	48	Stomach	Yes	Metastases right lobe of liver

liver-function tests were within normal limits in each case and the mean value for plasma GGTP was 20 I.U. per litre (S.D. ± 11) with a range of 5–34 I.U. per litre. No correlation was found between the age of the patient and GGTP results.

Cancer Cases without Hepatic Metastases.—Thirty of the 40 patients with gastro-intestinal carcinoma had no evidence of hepatic metastases at laparotomy. The mean age of these 30 patients was 64 years (S.D. ± 6) and the results of the liver-function tests are shown in *Table I*. Plasma GGTP was within the control range in all the cases, as were the other liver-function tests with the exception of the plasma proteins. The mean plasma albumin in this group was significantly lower than the value obtained in the control group ($t = 4{\cdot}779$; $P < 0{\cdot}001$), and in 3 patients with carcinoma the albumin : globulin ratio was reversed. In 3 cases, all with normal liver-function tests, hepatic enlargement was recorded on preoperative clinical examination but no abnormality was found on examination of the liver at laparotomy.

Cancer Cases with Hepatic Metastases.—Ten of the 40 patients with gastro-intestinal carcinoma had hepatic metastases at operation. The mean age of the patients in this group was 63 years (S.D. ± 11) and the mean values for the liver-function tests are shown in *Table I*. In *Table II* the individual liver-function tests are correlated with the findings on preoperative clinical examination and at laparotomy. Plasma GGTP was significantly elevated in 5 patients (*Cases* 2, 3, 4, 6, and 10), all of whom had hepatic enlargement on preoperative examination and abnormal plasma alkaline phosphatase results. In 3 of these cases (*Cases* 2, 6, and 10) there was reversal of the albumin : globulin ratio, and the transaminases were significantly raised in 3 cases (*Cases* 2, 3, and 6).

In 5 patients the plasma GGTP was within the control range despite the presence of hepatic metastases and preoperative evidence of hepatic enlargement in 4 of the 5 cases. The plasma alkaline phosphatase was also normal in all 5 cases, but in 1 patient (*Case* 5) the SGOT was abnormal and in another case (*Case* 1) the albumin : globulin ratio was reversed.

DISCUSSION

Szczeklik, Orlowski, and Szewczuk (1961) reported very high serum GGTP levels in 7 patients with metastatic liver disease, and in some of these cases abnormal GGTP results were obtained before there was any disturbance in the routine liver-function tests. Rutenburg, Goldbarg, and Pineda (1963) obtained abnormal values for GGTP in 59 of 65 patients with hepatic metastases, and 35 per cent of the patients with abnormal GGTP results had a normal serum alkaline phosphatase. Again, Kokot, Kuska, Grzybek, and Cekanski (1965) found that the serum GGTP was significantly elevated in 89 per cent of anicteric patients with metastatic liver disease, and Aronsen and others (1970) obtained the same degree of accuracy for this test in the diagnosis of liver metastases in 51 anicteric patients. It was also noted in the latter study that the serum alkaline phosphatase was a less reliable test than GGTP for the detection of liver tumour and it was concluded that GGTP would be a useful test for the screening of patients for hepatic metastases.

In the present study plasma GGTP results were abnormal in only 50 per cent of the patients with hepatic metastases, and in each of these cases the plasma alkaline phosphatase was also abnormal. In the remaining cases with liver metastases both enzymes were within the normal range. It is difficult to account for the difference between these results and the results of previous studies, but it cannot be explained by the fact that plasma GGTP was measured in the present study whereas serum GGTP was measured in the previous studies. We have found no difference between the results of GGTP measured in plasma and serum in control subjects (Edwards, 1971), and our results are in agreement with those of Rosalki, Rau, Lehmann, and Prentice (1970).

Preoperative clinical examination detected 90 per cent of the cases with hepatic metastases and a false-positive clinical diagnosis was made in 10 per cent of cases. However, we have not produced evidence that clinical examination alone is of practical value as a screening test for hepatic metastases as only 1 of the cases in the present study was suitable for liver resection and this was the only case which was not detected on preoperative clinical examination.

It appears that determination of the plasma GGTP is unlikely to surpass any of the conventional liver-function tests in the detection of hepatic metastases. Our results are in accord with those recently described by Baden, Andersen, Augustenborg, and Hanel (1971). In the latter study more than 50 per cent of the patients with hepatic metastases from gastro-intestinal carcinoma had normal serum GGTP results and GGTP was not more accurate than alkaline phosphatase in the detection of liver tumour.

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INTRAPERITONEAL NOXYTIOLIN AS AN EXPERIMENTAL CHEMOTHERAPEUTIC AGENT

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SUMMARY

The effect of intraperitoneal noxytiolin on the growth of Ehrlich's ascites tumour in mice has been studied. A dose of 1 g. per kg. body-weight produced a significant slowing of the growth of ascites tumours. However, systemic administration (subcutaneous) had no significant chemotherapeutic effect in this tumour model.

NOXYTIOLIN (Noxyflex) is a simple compound of low toxicity on systemic administration and has been found to have a wide bacteriostatic effect *in vitro* and some antifungal and antiprotozoal activity (Block, 1967; Horsfield, 1967; Ross, 1967). It has been thought to be of value in reducing the mortality of faecal peritonitis when instilled into the peritoneum (Browne and Stoller, 1970), and its use as a local adjuvant in the treatment of patients with vesical carcinoma by supervoltage has been claimed to improve the prognosis (Garrett, 1969). The fate of noxytiolin *in vivo* and its exact mode of action is not known, but it is possible that it acts simply by release of formaldehyde. In a previous communication (Jamieson, 1972) the effect of noxytiolin on the viability of human tumour cells (HeLa) in monolayer culture was studied and it was shown that concentrations of more than 0·0025 per cent caused significant inhibition of the growth of tumour cells in culture.

MATERIALS AND METHODS

Mice.—Male mice of strain BALB/c, weighing between 13 and 20 g., were obtained from the breeding colonies of Animal Suppliers (London) Ltd.

Tumour Cells.—Ehrlich's ascites (E.A.) tumour-cell line was obtained from Dr. T. A. Connors of the Chester Beatty Research Institute, London, and maintained by serial transplantation. The tumour cells were harvested under full aseptic conditions and suspended in TC 199 medium (Wellcome Reagents Ltd.; Morgan, Morton, and Parker, 1950). Cell counts were made using a Model B Coulter Counter. The viability of cells was determined by the ability of live cells to exclude trypan blue; 1 ml. of cell suspension was mixed with 0·5 ml. of 1 per cent trypan blue and incubated for 20 minutes at 37° C. Cells excluding trypan blue and those taking up the dye were counted in a haemocytometer chamber, and the results were expressed as a percentage of cells excluding dye. The average viability during each set of experiments was 85–90 per cent.

The tumour cells were inoculated intraperitoneally in each experiment. The growth rate of the tumour was measured by daily weighings of the animals, and the duration of the survival of the animals after the inoculation of E.A. cells was noted.

In a preliminary experiment (experiment I) groups of 12 mice were inoculated with 1×10^4, 1×10^5, 1×10^6, and 5×10^6 E.A. cells suspended in 0·25 ml. of TC 199 medium to determine the effect of varying cell dosage on the rate of tumour growth and survival (*Fig.* 1). Doses of 5×10^6 and 1×10^6 produced rapid growth of tumours, making it necessary to sacrifice the mice at 18 days. Mice receiving 1×10^4 cells continued to live for more than 30 days but exhibited inconsistent takes of tumours, whereas 1×10^5 cells produced consistent takes and satisfactory growths of tumours, and therefore in all subsequent experiments the dosage of 1×10^5 E.A. cells was used.

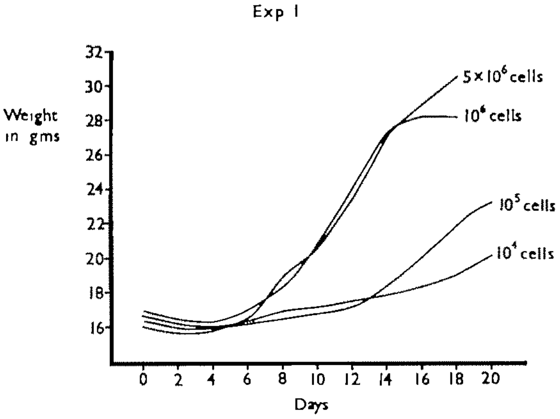

FIG. 1.—The effect of varying cell dosage on the rate of growth of Ehrlich's ascites tumour in BALB/c mice.

Noxytiolin Preparation.—This drug was obtained in its pure form and was stored at 5° C. Fresh solutions of the required concentration were made up for each experiment in TC 199 medium and were sterilized by filtration.

The L.D.$_{50}$ dose of noxytiolin for intraperitoneal administration has been shown to be 1650 mg. per kg. body-weight for mice (Consultox Laboratories Ltd., London, 1965). In the present study to test the toxicity of noxytiolin a group of 10 BALB/c mice was given 15 mg. of noxytiolin (1 g. per kg. average body-weight) intraperitoneally and the dose was repeated 7 days later; a control group was given sham injections of the TC 199 medium on the same days. This amount of noxytiolin had no apparent deleterious effects and experimental animals showed no difference in weight-gain or vitality from the control group up to 30 days of the experiment.

Experimental Protocol to study the Chemotherapeutic Effect of Noxytiolin.—In experiments II and III two groups of 10 BALB/c mice, having received intraperitoneal inoculations of

1×10^5 E.A. cells, were given intraperitoneal injections of 15 mg. of noxytiolin on the first and seventh days after the inoculation of 1×10^5 E.A. cells. For each experimental group there was a control group of 10 mice which received an intraperitoneal inoculation of 1×10^5 E.A. cells and sham injections of TC 199 medium on the first and seventh days after inoculation.

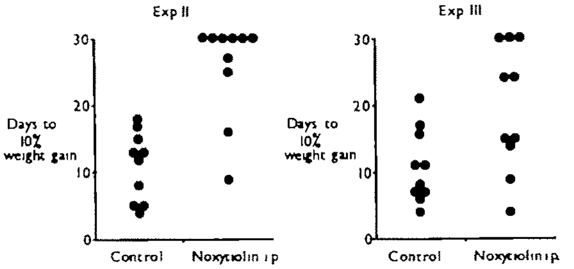

FIG. 2.—The effect of intraperitoneal noxytiolin (1 g. per kg.) on the rate of growth of Ehrlich's ascites tumour (1×10^5 cells) in BALB/c mice.

In experiments IV and V the same doses of noxytiolin were administered subcutaneously on the first and seventh days after the intraperitoneal inoculation with 1×10^5 E.A. cells. A control group of mice received tumour cells intraperitoneally and TC 199 medium subcutaneously on the same days.

Finally, the experiments were repeated using a lower dose of 5 mg. (0·33 g. per kg. average body-weight) of noxytiolin on the first and seventh days after the inoculation of 1×10^5 E.A. cells.

Assessment of the Rate of Tumour Growth.—In our laboratory normal 6–8-week-old BALB/c mice show an average weight-gain of 4 per cent (0·5 g. in a 15-g. mouse). Therefore mice exhibiting a 10 per cent weight-gain and abdominal distension were considered to show evidence of definite tumour take. Some mice in the intraperitoneally instilled noxytiolin groups (experiments II and III) reached 30 days without developing ascites but all of these developed skin metastases. As the mice that had reached a 10 per cent weight-gain due to ascites tumour had invariably died by day 30 (11 out of 20 without reaching a 15 per cent weight-gain), those remaining were sacrificed and given a nominal value of 30 days to enable a statistical analysis to be made.

Statistical Analysis.—The data of experiments II and III were analysed collectively, using the Mann-Whitney test (Snedecor and Cochran, 1967). The same analysis was applied to experiments IV and V.

RESULTS

The results were as follows:—

1. In experiments II and III (*Fig.* 2), in which 15 mg. of noxytiolin were administered intraperitoneally, there was a significant inhibition of ascites tumours when compared with the control animals. The number of days in which the mice increased in weight by 10 per cent owing to development of ascites tumours was significantly higher compared with that for the control mice ($P = 0{\cdot}0001$).

2. In experiments IV and V (*Fig.* 3), in which 15 mg. of noxytiolin were given subcutaneously, no significant protective effect was observed.

3. In experimental groups of mice in which 5 mg. of noxytiolin were given either intraperitoneally or subcutaneously, no protective effect was obtained.

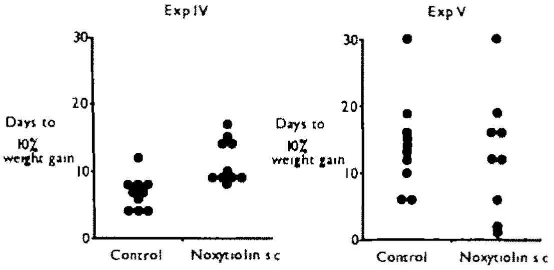

FIG. 3—The effect of subcutaneous noxytiolin on the rate of growth of Ehrlich's ascites tumour (1×10^5 cells) in BALB/c mice.

DISCUSSION

In an earlier report (Jamieson, 1972) the concentration of noxytiolin producing inhibition of tumour cells (HeLa) in culture was much lower (0·0025 per cent) than the reported bacteriostatic concentration of the drug.

The mode of action and fate of noxytiolin *in vivo* remain unknown. However, in one series it appeared to offer increased survival when used as a local instillate in cases of advanced bladder tumours, and it is remarkably free from toxic effects (Garrett, 1969, 1970). The present study tends to support this view, but in this tumour model the concentration of the drug required for inhibition of ascites tumour is very high (1·5 per cent) and its protective effect is only seen when used as a local instillate, suggesting that its action is short-lived and perhaps only local.

Acknowledgements.—The authors wish to thank Mrs. Margaret Ryder and Mrs. Sheila Siggins for technical assistance, and Geistlich Ltd. for supplies of noxytiolin and financial assistance in this investigation. We also wish to thank Dr. T. A. Connors of the Chester Beatty Research Institute for providing the Ehrlich's ascites tumour, and Mrs. Doreen Irving for statistical advice.

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DEPRESSION OF IMMUNE RESPONSIVENESS IN BREAST AND LARGE-BOWEL TUMOURS AS MEASURED BY HETEROPHILE ANTIBODY ACTIVITY

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SUMMARY

Decrease in heterophile antibody activity to cow, pig, and sheep red blood-cells was found in groups of patients with large-bowel and breast tumours irrespective of the extent and spread of the tumour or the length of known history. The significance of these observations is discussed in the light of known cancer-surveillance mechanisms. The findings may reflect decreased host immunological resistance to these tumours even in the early stage of their development, and the measurement of heterophile antibody activity may provide a useful and uncomplicated screening test.

IT has been shown that a balance may well be present between immunological defence mechanisms and the growth of certain tumours, and there is evidence that in some cases at least an immunologically mediated host resistance is involved (Fairley, 1969; Mathé, 1969). It has also been demonstrated that in some patients with tumours there is reduced reactivity on the part of the host. Whether this is a primary or secondary event, the behaviour of the disease and final prognosis will be influenced by the defence that the host is able to offer (Burnet, 1970; Klein, 1970; Whittaker and Clark, 1971).

A rise in heterophile antibodies has been found in some recipients of human transplants in the presence of immunological rejection (Iwasaki, Talmange, and Starzl, 1967; Rapaport, Kano, and Milgrom, 1968). These observations have prompted the present experiments to investigate whether alterations in heterophile antibody titres could reflect the presence, rate of growth, and invasive characteristics of mammary and large-bowel tumours.

MATERIALS AND METHODS

The study comprised 51 patients with carcinoma of the breast and 46 with carcinoma of the large bowel. All the patients were admitted to hospital for primary surgical treatment of their tumours and a blood sample was taken prior to surgery. Fifty patients admitted for non-malignant 'cold' surgery (herniorrhaphy, varicose veins, etc.) were used as controls.

Twenty ml. of blood were collected in a dry sterile tube, the clot was allowed to retract, and the serum was further separated by centrifuging. The serum was decomplemented by heating to 56° C. for 30 minutes and stored at −20° C. until a convenient time for the agglutination studies.

Agglutination activity of each serum sample was then tested in serial dilutions against cow, pig, rabbit, rat, and sheep red blood-cells. Results were read after 24 hours' incubation at 37° C. and the value taken as the last dilution at which agglutination occurred.

RESULTS

In a pilot study agglutinations of sera from 12 patients with carcinoma of the large bowel and 12 with carcinoma of the breast were compared with those of 13 control subjects. The titres for cow, pig, and sheep were significantly lower in patients with tumours compared with those of the control subjects, but virtually equal when tested against rabbit and rat red blood-cells. Agglutination studies with rabbit and rat red blood-cells were therefore not pursued further.

Table I.—SIGNIFICANCE (*P*) OF HETEROPHILE HAEMAGGLUTININ TITRES TESTED AGAINST DIFFERENT ANIMAL RED BLOOD-CELLS IN PATIENTS WITH TUMOURS COMPARED WITH THOSE IN CONTROL SUBJECTS OF THE SAME AGE-GROUP

AGE-GROUP	PIG RED BLOOD-CELLS		COW RED BLOOD-CELLS		SHEEP RED BLOOD-CELLS	
	Large-bowel Cancer	Breast Cancer	Large-bowel Cancer	Breast Cancer	Large-bowel Cancer	Breast Cancer
30–39	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$
40–49	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$	$>0{\cdot}10$
50–59	$>0{\cdot}10$	$<0{\cdot}05$	$<0{\cdot}05$	$<0{\cdot}005$	$>0{\cdot}10$	$>0{\cdot}10$
60–69	$<0{\cdot}025$	$>0{\cdot}10$	$<0{\cdot}025$	$>0{\cdot}10$	$<0{\cdot}05$	$>0{\cdot}10$
70+	$>0{\cdot}10$	$<0{\cdot}025$	$>0{\cdot}25$	$>0{\cdot}10$	$<0{\cdot}01$	$<0{\cdot}005$

Fig. 1 shows the distribution of haemagglutinin titres (means) to pig, cow, and sheep red blood-cells, comparing results according to age in the control subjects with those in patients with large-bowel or mammary tumour. A small reduction of agglutinin titres was demonstrated for pig and cow red blood-cells in control subjects with advancing age, but there was no statistical difference between the youngest and the oldest subjects ($P < 0{\cdot}10$). This trend was also seen in the tumour cases, but in patients with either mammary or large-bowel tumour the readings were lower than in the control subjects. *Table I* gives the statistical breakdown of the differences according to age. Significant differences were seen in patients who were 50 years of age or older, particularly with cow red blood-cell agglutination in large-bowel tumour cases.

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Figs. 2, 3, and 4 are scatterograms of the haemagglutination titres to cow, pig, and sheep red blood-cells for patients with tumours compared with those of the control subjects, with separation according to sex. Mean results are also given. There was some difference between the heterophile agglutination activity of female and male control subjects but this

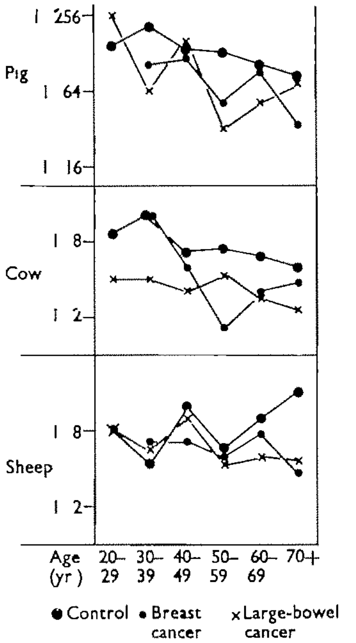

FIG. 1.—Relationship of haemagglutinin titres tested against pig, cow, and sheep red blood-cells to age in patients with breast or large-bowel malignant tumours and in control subjects

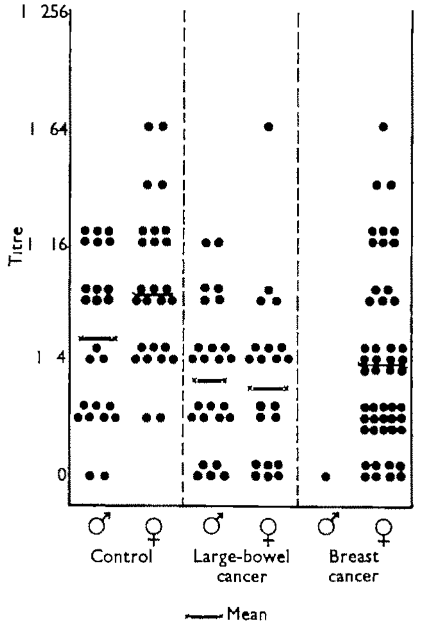

FIG. 2.—Haemagglutinin titres tested against cow red blood-cells in patients with large-bowel or breast cancer and in control subjects.

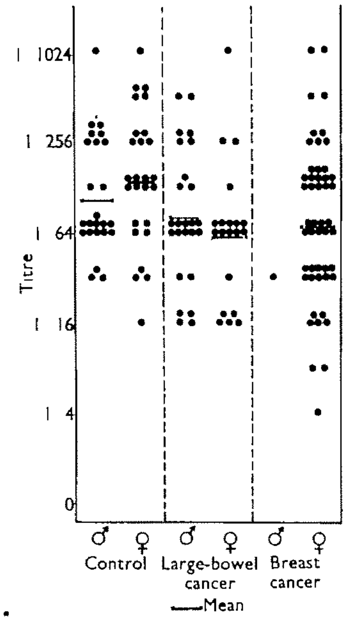

FIG. 3.—Haemagglutinin titres tested against pig red blood-cells in patients with large-bowel or breast cancer and in control subjects.

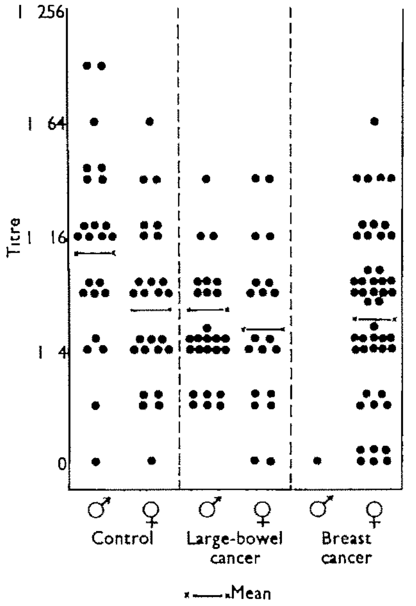

FIG. 4.—Haemagglutinin titres tested against sheep red blood-cells in patients with large-bowel or breast cancer and in control subjects.

was without statistical significance. Results in the tumour cases were compared with those of the control subjects according to sex (*Table II*). Titres from patients with tumours were significantly lower than those of control subjects when tested against cow red blood-cells for all the values examined, against pig red blood-cells in female large-bowel and breast tumour cases, and against sheep red blood-cells in large-bowel tumours.

Table II.—SIGNIFICANCE (*P*) OF COMPARISONS BETWEEN HETEROPHILE HAEMAGGLUTININ TITRES TESTED AGAINST DIFFERENT ANIMAL RED BLOOD-CELLS IN PATIENTS WITH AND WITHOUT CANCER

COMPARISON	COW RED BLOOD-CELLS	PIG RED BLOOD-CELLS	SHEEP RED BLOOD-CELLS
Male patients with carcinoma of the large bowel versus male control subjects	<0·05	>0·10	<0·005
Female patients with carcinoma of the large bowel versus female control subjects	<0·005	<0·01	>0·10
Female patients with carcinoma of the breast versus female control subjects	<0·005	<0·01	>0·10

Table III.—SIGNIFICANCE (*P*) OF COMPARISONS BETWEEN HETEROPHILE HAEMAGLUTININ TITRES TESTED AGAINST DIFFERENT ANIMAL RED BLOOD-CELLS IN PATIENTS WITH TUMOURS DEMONSTRATING VARIOUS FEATURES

FEATURE	COW RED BLOOD-CELLS	PIG RED BLOOD-CELLS	SHEEP RED BLOOD-CELLS
Carcinoma of the breast			
Spread	>0·10	>0·10	>0·10
Lymphocytic infiltration	>0·10	<0·10	>0·10
Fibrosis	>0·10	>0·10	>0·10
Differentiation	>0·10	<0·25	<0·005
Length of history	<0·10	>0·10	>0·10
Carcinoma of the large bowel			
Spread	>0·10	>0·10	>0·10
Lymphocytic infiltration	<0·10	<0·10	>0·10
Differentiation	>0·10	>0·10	<0·10
Length of history	>0·10	>0·10	>0·10

Agglutination titres were also reviewed in relation to the degree of histological differentiation. The tumours were graded into three categories according to differentiation (poor, moderate, and good). Mean titres were generally lower in the well-differentiated tumours than in the poorly differentiated ones, but the difference in readings between neoplasms which were poorly differentiated and those showing differentiation was statistically significant in only the sheep red blood-cell titrations (*Table III*).

A further breakdown of the agglutinin results was carried out according to the spread of the tumour and the degree of lymphocytic infiltration, fibrosis, and length of history. Two categories were made in each. The tumour was either localized or had spread into lymph-nodes and/or further; lymphocytic infiltration and fibrosis were either absent or minimal, or marked; the tumour had presented for under or over 3 months. No significant differences of agglutinin values were found among any of these groups (*Table III*).

DISCUSSION

There is evidence that the immune response against tumours resembles an allograft reaction with cell-mediated immunity playing the major part (Klein, 1970). The concept of immunological surveillance by the body against tumours advocated by Burnet (1970) has been summarized and placed into four groups by Keast (1970): (1) cancer occurs characteristically at the extremes of life when the immune system is either maturing or is weakened; (2) the incidence of tumours is increased by immunosuppressive drugs and (3) experimentally by thymectomy; (4) the rare diseases that involve a deficiency of cell-mediated immunity are characterized by a high incidence of tumours in those subjects who survive long enough to allow their development.

Increased heterophile activity in the presence of immunological rejection of allografts is known (Iwasaki and others, 1967; Rapaport and others, 1968). In view of similarly mediated mechanisms in some cases of host–tumour resistance, it seemed reasonable to investigate the heterophile response in cancer patients and to compare the results with those in control subjects. These observations have shown a very significant diminution of agglutinin titres to cow, pig, and sheep red blood-cells in groups of subjects with breast or large-bowel tumour.

Previous results using other methods have indicated a reduced immune competence in recurrent or advanced breast cancer (McKay and Baum, 1968; Williams and Roberts, 1968; Whittaker and Clark, 1971). There was some increase when host lymphoid infiltration in and around the tumour was present (Black, Opler, and Speer, 1954; Bloom, Richardson, and Field, 1970). In a series of patients cured by surgery and/or chemotherapy (Lee, Rowley, and Mackay, 1970) the antibody-producing capacity was greater than that in patients with active cancer, but yet was *significantly less* than that of healthy subjects. The present observations using heterophile antibody activity have shown no correlation with the size or extent of the tumour, lymphoid infiltration, length of known history, or amount of interstitial fibrous-tissue formation. Some of the lowest titres were found in patients with small and very early tumours. It is probable, therefore, that in some cases at least the reduced heterophile agglutination activity was present at the very start of the tumour formation and may thus reflect a diminished immunological resistance capability of the host against the neoplasm which facilitates its formation and growth. Low readings were recorded in some normal control subjects. If reduction of heterophile haemagglutinin activity does reflect a decrease of immune surveillance mechanisms it is interesting that a gradual diminution of the titres was observed with advancing age in control patients. Whether the younger subjects, in particular, who were found to have low titres are more at risk to cancer than their average-titre fellows is a subject for a further report.

Acknowledgements.—We are grateful to the United Sheffield Hospitals' Endowment Fund and the

Medical Research Council for supporting this work and also to Mr. R. A. Dixon for statistical assistance. We wish to thank Mr. D. J. Robertson and Mr. J. Thompson Rowling whose patients were used in this study.

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THE EFFECT OF TOPICAL AMPICILLIN ON WOUND-INFECTION RATE AFTER CHOLECYSTECTOMY

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SUMMARY

No carefully controlled trial of the use of topical ampicillin in cholecystectomy wounds has been described. A series of 100 consecutive cholecystectomies performed by one surgeon using this drug in a double-blind manner is reported. The efficacy of topical ampicillin in lowering the wound-infection rate as shown by other authors is not confirmed.

THE commonest complication following cholecystectomy which delays the patient's discharge from hospital is wound infection. Any technique or aid which would reduce the rate of this complication would be of considerable economic benefit to both the patient and to the hospital service. With this in mind a controlled double-blind trial to evaluate the effect of topical ampicillin in cholecystectomy wounds was carried out.

MATERIAL AND METHODS

One hundred patients were operated upon by the author using the same incision (right upper paramedian muscle splitting) and suture materials. Routine cholangiography was performed in each case. A corrugated drain was inserted through a stab incision. This was removed on the fourth postoperative day and the sutures were removed on the ninth and tenth postoperative days. The patients were not selected before operation and were consecutive, only those having added procedures being excluded. The sex distribution and average age of the patients are shown in *Table I*. At the time of operation the patients were arbitrarily placed in one of the categories 'thin', 'medium', and 'fat'. The distribution of these is shown in *Table II*.

Randomly numbered opaque glass phials were prepared by Beechams Research Laboratories and were either empty or contained 250 mg. of ampicillin powder. During cholecystectomy 5 ml. of normal saline were added to each phial by a nurse outside the operating theatre and the solution was then put in the wound after closure of the peritoneum. The wound was not dried until closure was complete.

Table I.—THE SEX DISTRIBUTION AND AVERAGE AGE OF PATIENTS HAVING EITHER AMPICILLIN OR SALINE (CONTROL) IN THEIR WOUNDS FOLLOWING CHOLECYSTECTOMY

	AMPICILLIN	SALINE
Males	12 (23·1 per cent)	9 (18·8 per cent)
Females	40 (76·9 per cent)	39 (81·2 per cent)
Average age (yr)	52·4	53·9

Table II.—THE BUILD OF PATIENTS HAVING EITHER AMPICILLIN OR SALINE (CONTROL) IN THEIR WOUNDS FOLLOWING CHOLECYSTECTOMY

TYPE	AMPICILLIN		SALINE	
	No. of cases	Percentage	No. of cases	Percentage
Thin	5	9·6	8	16·7
Medium	18	34·6	20	41·7
Fat	29	55·8	20	41·7

On the tenth postoperative day the wound was inspected and its state recorded in one of five grades. These were: 0, normal; 1, slight redness; 2, oedema; 3, pus; and 4, disrupted. The code for the phials was broken at the end of the trial.

RESULTS

Twelve patients showed abnormalities of their wounds at 10 days (*Table III*). Eight of these had had ampicillin added to their wounds and in 4 saline only had been added. The majority of the infections were minor and clinically insignificant in both series, being in grades 1 and 2. There were

2 patients in grade 3 who had had ampicillin added to their wounds but there were no control patients in this grade. Of the 2 wounds in grade 4, one was in each group. Grades 1 and 2 are of minor significance and did not prolong the patients' stay in hospital. Grades 3 and 4 are significant infections and it can be seen that the control group fared better than those having ampicillin in their wounds. This infection rate is low but there were 7 patients whose wounds discharged after they left hospital. Three of these were in the control group and 4 were in the ampicillin group. Even taking this into account it can be seen that ampicillin did not reduce the wound-infection rate.

Table III.—THE GRADING OF THE WOUNDS IN WHICH AMPICILLIN OR SALINE (CONTROL) WAS ADDED

GRADE	AMPICILLIN	SALINE
0	44	44
1	3	1
2	2	2
3	2	0
4	1	1
Total	52	48

DISCUSSION

Postoperative systematic antibiotics have not been shown to affect appreciably the rate of wound infections (Johnstone, 1963; Committee on Wound Infections, 1964). It has been suggested that infection in clean wounds takes place at the time of operation and is probably contamination from the noses of the theatre personnel (Browne, Glassow, Martin, and Shouldice, 1959). The inoculum is assumed to be small and therefore the topical application of an antibiotic should overcome the infection.

To institute a trial to test this hypothesis requires care especially in the choice of a control substance. Lactose has been used for this purpose when ampicillin was added to wounds in powdered form (Rickett and Jackson, 1969) but this in itself may not be inert and may encourage bacterial growth. To overcome this normal saline was used as the control solution in the present series and also as the solvent for the ampicillin, and thus the only difference in the two groups was the presence or absence of ampicillin. Although limiting the size of the experiment all the cases were operated upon by one surgeon using an identical technique. This and the fact that all the patients had cholecystectomies make the series more uniform than those of some of the other authors.

Stoker and Ellis (1971) used ampicillin powder (1 g.) in a comparison with noxytiolin and found that the former reduced the incidence of wound infections. The same authors (Stoker and Ellis, 1972) also compared ampicillin powder (1 g.) with penicillin and Sulphadiazine and again showed the efficacy of ampicillin. The number of biliary cases in their second series was small, there being 18 and 19 cases in each group with a control group of 4 cases. Nash and Hugh (1967) reported a dramatic decrease in wound infections using 1 g. of powdered ampicillin in wounds following colonic surgery, and Rickett and Jackson (1969), using 500 mg. of powdered ampicillin, also showed a significant fall in wound infections following appendicectomy. Ryan (1967) showed the efficacy of topical penicillin in reducing infection in a large number of herniorrhaphies where surgery was performed by the author. However, the figures presented in this trial, where ampicillin was used in a smaller dose dissolved in saline, show no significant reduction in wound infection. There are three possible explanations for the difference between these results and those of the other series. First, the dose used was smaller and may have been insufficient to eradicate the inoculum of bacteria. Secondly, the ampicillin was used in a fluid form and therefore it was removed too quickly from the wound while the powdered ampicillin remained for a considerably longer period. Finally, the powdered ampicillin would give a higher local concentration of the antibiotic and this may well be the most important factor in explaining the discrepancy.

Acknowledgements.—I wish to thank Messrs. Beecham Ltd. for supplying the ampicillin and for preparing the phials and Mrs. F. McCartney for her help with the manuscript.

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A CONTROLLED TRIAL OF CLOSED WOUND SUCTION

DRAINAGE IN RADICAL MASTECTOMY

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SUMMARY

A controlled clinical trial has been performed to compare the effectiveness of suction drainage with that of static drainage. The trial has shown that in 53 radical mastectomy wounds the rate of wound healing was faster in those cases in which suction drainage was used, with a reduction in incidence of wound infection, breakdown, and necrosis.

THE healing of a radical mastectomy wound presents several difficulties. The incision is long, the flaps are thin, and the volume of blood, lymph, and serous drainage is large. To collect this fluid a traditional method of wound drainage uses one or more lengths of soft rubber or plastic. The fluid drains into pads bandaged to the patient and the volume may be so considerable that during the evening of the operation new pads have to be applied because the fluid soaks through to bed linen or clothing.

Suction drainage for mastectomy wounds was first introduced in 1947 by Murphey, and its use was also described by Raffi (1952). Since then portable units for the evacuation of wounds have been devised (Redon, 1955) and found to have several advantages. In particular they give added comfort to the patient and eliminate the need for bulky compression bandages and frequent changes of dressings (Thoren, 1964); also the wound can be kept dry and cool. Drainage gives rise to an increased incidence of wound infection (Public Health Laboratory Service, 1960; National Research Council, 1964) but it has not been established with certainty whether suction drainage reduces this risk (Medical Research Council Subcommittee, 1968).

Suction drainage has been used in the Guy's Breast Clinic in the past but the small-bore tube then in use tended to become blocked. It could not maintain suction for long so that pockets of fluid accumulated under the flaps and the method was not adopted. A new wide-bore tube (6·4-mm. bore Zimmer) is now available and has been found to be effective in wounds where a large volume of fluid drainage is likely to occur. A controlled clinical trial was carried out to compare the effects of static and suction drainage on the healing of radical mastectomy wounds.

METHODS

The trial was carried out in the first 8 months of 1970. All patients undergoing treatment for early breast carcinoma by radical mastectomy were admitted to the trial. The start of the trial coincided with the opening of the new Guy's Breast Unit at New Cross Hospital and the majority of the patients were treated there and nursed in single rooms. The operations were performed by the consultant and registrar staff of the Breast Clinic. An identical operative technique of radical mastectomy was carried out in all the cases. Proof that the lesion was a carcinoma of the breast was determined either by a biopsy taken up to 6 days before operation or by a frozen-section biopsy immediately before the mastectomy. After marking out the skin incision the upper and lower flaps were infiltrated with a solution of 1 : 400,000 adrenaline in normal saline to separate the tissue planes and to assist haemostasis. A radical mastectomy was then performed leaving the clavicular head of the pectoralis major in place. A full axillary lymph-node clearance was carried out. Haemostasis was achieved by diathermy coagulation of all except the major vessels which were ligatured with chromic 00 cat gut. In the final stage of the operation lavage of the wound was carried out using warm sterile distilled water. Before closure the type of drainage to be used was selected by a third party drawing a labelled ticket from a box. Two lengths of Paul's tube in which side holes were cut were used as static drainage, one for the upper flap emerging at the lower end of the wound, the second via a stab incision in the lower flap to drain it and the axilla. In the suction-drainage series two 6·4-mm. bore tubes were inserted using a trocar, one to drain the upper flap, the other to drain the lower flap and axilla. Both drains were placed to emerge from the lower flap at least 5 cm. apart to minimize any interference with the blood-supply of the lower flap. The wound was closed using interrupted silk sutures, and sealed with a layer of plastic skin (Nobecutane) to make it airtight. In both groups of patients a pressure dressing of wool and two 15-cm. crêpe bandages was applied in order to keep the postoperative conditions as nearly comparable as possible. In the suction-drainage group the suction bottles were connected to the drains and as soon as this dressing was in place the clamps were released and, by firm manual pressure over the flaps, the initial aspiration of any haematoma was encouraged.

Postoperative Treatment.—In both groups of patients the dressings were left undisturbed for 48 hours with additional packs applied when necessary. Subsequently, in the static-drainage group change of dressings with reapplication of wool and crêpe was performed daily until healing took place. The drains were usually retained until the thirteenth day, but if the volume of drainage was slight the drains were removed earlier. On a few occasions when large volumes of fluid were still being obtained the drains were left longer than 13 days. In the suction-drainage group the drains were left until the volume of drainage dropped below 25 ml. in any 24-hour period but were always retained for at least 5 days if the drainage was slight. In both groups the sutures were left in place until the tenth postoperative day, when one-third was removed if the wound healing was proceeding satisfactorily. Half the remaining sutures were removed on the next day and all were removed by the twelfth day.

RESULTS

The following six factors were used in the assessment of the results:—

1. Volume of fluid drainage (*Table I*). For suction-drainage cases the volume of fluid in the bottles was measured and recorded every 24 hours. Accurate measurement of fluid loss in the static-drainage group was not possible, but by weighing the dressings daily a measure of the variation in loss could be made.

Table I.—Measured Drainage

Type of Drainage	Average Time Drain left in Wound (d.)	Average Time of Drainage (d)	Volume of Drainage (ml)
Suction	8·1	7·8	780 total 100 daily
Paul's tube	13·2	10·6	578 total 54·56 daily

Table II.—Delay in Wound Healing

Type of Drainage	Infection		Necrosis				Wound Breakdown			
			Total		*Area greater than 2·5 cm. in diameter*		*Total*		*Length greater than 2 5 cm long*	
	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No of Cases	Percentage	No. of Cases	Percentage
Suction	1	4	5	18	3	11	2	7	0	0
Paul's tube	8 $\chi^2=5\cdot68$ $P<0\cdot02$	32	10	40	8 $\chi^2=2\cdot46$ $P<0\cdot20$	32	7	28	5 $\chi^2=4\cdot07$ $P<0\cdot05$	20
Paul's tube (excluding patients over 70 years old)	6 $\chi^2=4\cdot25$ $P<0\cdot05$	29	7	33	5 $\chi^2=0\cdot70$ $P<0\cdot50$	25	5	24	4 $\chi^2=3\cdot54$ $P<0\cdot10$	19

Table III.—Postoperative Care

Type of Drainage	Aspiration of Fluid as an In-patient		Post-discharge Aspiration		Post-discharge Dressings	
	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Suction	8	29	7	25	4	15
Paul's tube	3	12	3	12	13	52
Paul's tube*	2	10	2	10	10	48

* Excluding patients over 70 years old.

2. Haematoma or fluid accumulation. The wound was inspected at least once every 3 days for signs of loculated fluid and the volume of fluid aspirated was recorded.

3. Delay in healing defined as an area of breakdown of the wound or necrosis of the skin flaps (*Table II*).

4. Infection, defined as severe sepsis with purulent discharge from the wound or accumulation of pus requiring drainage with frequent dressings and prolonged hospital stay. Routine wound swabs were taken on removal of the drain.

5. Any dressings or aspiration of fluid required after discharge from hospital, or any delay in commencing radiotherapy (*Table III*).

6. Length of postoperative stay in hospital (*Table IV*).

DISCUSSION

Radical mastectomy is still the orthodox treatment for early breast cancer. Technically it is not a difficult operation but there are many details to be observed in obtaining good results. This trial shows that the type of wound drainage is a major factor in determining wound healing. Closed-suction drainage is shown to have several important advantages over open drainage.

The average length of postoperative stay in hospital was 1 week less for the suction-drainage group. This gave a saving over the 9 months of the trial of 28 weeks' hospital stay for the cases in which suction drainage was employed.

Table IV.—Length of Postoperative Stay in Hospital

Type of Drainage	No. of Cases	Age (yr)	Length of Stay (d.)
Suction	28	36–66 (46·9 average)	12–20 (13·6 average)
Paul's tube	25	33–79 (54·2 average)	13–75 (20 6 average)
Paul's tube*	21	33–67 (49·5 average)	13–45 (19 0 average)

* Excluding patients over 70 years old.

The random selection of the patients in this trial by chance included 4 patients over 70 years of age in the static-drainage group. As this might bias the results a comparison has also been made between the suction-drainage and the Paul's-tube groups omitting the patients who were over 70 years old. Suction drainage gave a shorter stay in hospital postoperatively and a significantly decreased incidence of postoperative infection whether the patients over 70 years old were included or not. The incidence of necrosis was also reduced in the group having suction though, as would be expected, the incidence of wound necrosis was greater in the older patients.

The lower incidence of wound breakdown in the suction-drainage group is statistically significant although when the patients over 70 years old are excluded the difference is less significant.

In the trial the only patient in the suction-drainage group whose wound became infected had the suction tubes accidentally clamped off for 24 hours on the fifth postoperative day. The infection developed 48 hours later. In this case the suction method was incompletely applied and this may have contributed to the infection.

With suction drainage the need for a bulky dressing is eliminated. This gives greater comfort to the patient, and the absence of a tight, constricting dressing allows easier movement of the chest postoperatively. The wound can be exposed early, keeping it dry and cool. Frequent changes of dressings are not required with a subsequent considerable saving of nursing time and expense.

The incidence of accumulation of pockets of fluid in the wound is greater when suction drainage is employed, but the fluid can easily be removed by aspiration using a technique similar to that used for aspirating cysts (Tong, 1969) and gives rise to no permanent trouble. The volume of drainage cannot be accurately compared in this series as the method of collection in the Paul's tube series allowed considerable evaporation. However, the amounts of fluid lost were probably comparable for the two series of cases, and it seems unlikely that suction drainage is associated with a significantly increased production of fluid. As there is considerable evaporation from the dressings in the open-drainage method, it may be that the volume of drainage is less when suction drainage is employed. It is interesting that in the cases where the lymph-nodes were found to be involved at mastectomy the fluid loss was greatest.

Acknowledgements.—I am grateful to Professor Sir Hedley Atkins and Mr. J. L. Hayward for their help and advice in performing this trial, and also to Mr. M. Feldstein for preparing the statistical report. I would like to thank Sister N. Sansom and the nursing staff of the Breast Unit for their invaluable help.

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TORSION OF THE GALL-BLADDER IN THE AGED

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SUMMARY

Torsion of the gall-bladder in 2 women in the tenth decade of life is described. The aetiology of the condition is discussed and the importance of keeping the diagnosis in mind in this age-group is stressed.

TORSION of the gall-bladder is an unusual surgical emergency, fewer than 300 cases having been reported. Perhaps because of its rarity the diagnosis is seldom made clinically, the condition generally being recognized only at laparotomy. Although its occurrence has been reported in children—the youngest was aged 5 (Cuervo and Cuervo, 1939)—its highest incidence is in patients between the ages of 65 and 75. Hitherto the oldest reported case was aged 93 (Case, 1951).

The present paper reports 2 cases of torsion of the gall-bladder in the aged. The first of these was aged 96 years, and this appears to be the oldest case so far recorded. The second was also a nonagenarian, aged 92 years, in whom the diagnosis was made pre-operatively.

CASE REPORTS

Case 1.—Mrs. C. H., aged 96 years, was admitted as an emergency on 18 April, 1970, from a cottage hospital where she had been treated for congestive cardiac failure for 3 weeks. The previous day she had suddenly developed abdominal pain and vomiting. On admission she had a temperature of 37·4° C. and a pulse-rate of 100 per minute. The abdomen was distended, with some generalized tenderness. A plain radiograph of the abdomen showed gaseous distension of the gut with some small-bowel fluid levels. A provisional diagnosis of small-bowel obstruction was made.

The abdomen was explored through a right paramedian incision (Dr. P. W. Griffin). Free fluid was present in the peritoneal cavity but no obvious mechanical obstruction was found. A black, pear-shaped tumour was discovered suspended from the inferior surface of the right lobe of the liver on a pedicle which had undergone torsion through one and a half turns. It became clear that this was a case of torsion of the gall-bladder. The pedicle was ligated and the gall-bladder removed. The abdomen was closed without a drain. The patient made a good recovery and was transferred back to the cottage hospital on 4 May, from where she was discharged home on 23 May. She is still alive, now aged 98, and enjoys reasonable health.

PATHOLOGY.—The gall-bladder was grossly congested with early gangrenous changes. It contained several small stones.

Case 2.—Mrs. A. J., aged 92 years, was admitted as an emergency on the evening of 12 Jan., 1972. She had been seen that afternoon in domiciliary consultation, when a provisional diagnosis of torsion of the gall-bladder had been made. There was a history that on the previous afternoon she had been seized with upper abdominal pain accompanied by repeated vomiting. The vomiting had soon stopped, but the pain had persisted and had become localized in the right upper abdomen. Before this episode she had enjoyed good health for her age, was mentally alert, and ambulant. On examination she was thin and had a dorsal kyphosis. She was in considerable pain. Her temperature was normal, pulse-rate was 80 per minute, and blood-pressure was 130/60. There was marked guarding over the right hypochondrium although the rest of the abdomen was soft and not distended. Bowel-sounds were infrequent but of normal character.

At operation (Mr. T. Duncan) shortly after admission the clinical diagnosis was confirmed. Through a short, upper right, paramedian incision a gangrenous gall-bladder that had undergone torsion on a narrow pedicle was easily delivered into the wound. The pedicle was ligated and divided to remove the gall-bladder. The wound was closed without drainage, the operation being completed in 15 minutes. Although an intravenous infusion was used during the procedure, this was discontinued immediately postoperatively and the patient was started on oral feeding next morning. Her recovery was uneventful and she was discharged home a week after operation, her sutures being removed by her own doctor on the tenth postoperative day. The wound healed by first intention and the patient has remained well.

PATHOLOGY.—The gall-bladder was necrotic and contained several stones.

DISCUSSION

Among the possible aetiological factors in torsion of the gall-bladder in the older age-groups, loss of fat and visceroptosis have been cited (Gross, 1936), as these tend to produce a gall-bladder mesentery. Kyphosis may also be a factor by making the gall-bladder more dependent (Rais and Thulin, 1957). Both patients reported here were very thin and kyphotic. Although Ashby (1965) has postulated that a syndrome of recurrent gall-bladder torsion occurs, there was nothing in the history of the present cases to suggest previous attacks.

What initiates the torsion is debatable. It has been suggested that vigorous peristalsis in the neighbouring viscera or sudden violent body movement may be responsible (Short and Paul, 1934; Shah, 1966). The presence of gall-stones may be a contributory factor in some cases. Both the patients described in this paper had stones in the gall-bladder, and Levene (1958) noted that stones were present in 50 per cent of the reported female cases of gall-bladder torsion compared with a post-mortem incidence of 5 per cent in women of the same age-group. It is thought that stones might precipitate torsion by giving the colon more purchase on the gall-bladder (Short and Paul, 1934) or by increasing peristalsis in the gall-bladder (Levene, 1958). It is also possible that a small stone obstructing the cystic duct and causing a sudden increase in tension in the gall-bladder might lead to torsion if the gall-bladder has acquired a mesentery, by a mechanism similar to that which is sometimes seen when an acutely obstructed appendix curls upon its mesentery owing to the sudden increase in tension in the organ.

Torsion of the gall-bladder occurs primarily in elderly women and as these are increasing in number the condition will no doubt increase in frequency. It is important that it should be distinguished from acute cholecystitis, as conservative treatment in torsion of the gall-bladder would be fatal. The clinical presentation does vary, however, and Flannery and Caster (1956), in a review of 27 reported cases, found that none had been diagnosed preoperatively. The present *Case* 2 was diagnosed as torsion on the basis of the patient's age and body configuration, and the fact that the degree of guarding over the gall-bladder was out of proportion to the systemic upset to be expected in acute cholecystitis.

Since gall-bladder torsion is readily amenable to surgical treatment even in the very elderly, as is shown in this paper, a plea is made that the condition is borne in mind in the differential diagnosis of the acute abdomen in this age-group.

ADDENDUM

Just before this paper was submitted for publication the author had occasion to respond to the plea made in the last paragraph.

Case 3.—Late in the evening of 19 March, 1972, a woman aged 83 years was admitted as an emergency with a diagnosis of acute cholecystitis. She had a 24-hour history of upper abdominal pain and vomiting, the pain localizing in the right upper abdomen. Her temperature was 37·6° C. and pulse-rate 96 per minute. She had marked tenderness in the right hypochondrium with some guarding. Although the clinical picture was consistent with acute cholecystitis it was noted that she was thin and kyphotic, and, with the previous cases in mind, the possibility of torsion of the gall-bladder was considered. Because of this, laparotomy was carried out that night. A torsion of the gall-bladder was indeed present. The gall-bladder was tense and congested and had undergone torsion through one complete turn in a clockwise direction. A small gall-stone was found impacted in the cystic duct. (This finding supports the theory of aetiology postulated above.) An easy cholecystectomy was performed and the patient made an uneventful recovery.

Acknowledgements.—I wish to express my thanks to Mr. F. C. Walker for permission to report *Case* 1, and to Mr. T. Duncan for permission to report the other 2 cases.

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PROBLEMS IN ACUTE HYPERPARATHYROIDISM

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SUMMARY

The diagnostic and therapeutic problems of acute hyperparathyroidism are discussed on the basis of 4 selected cases. A highly raised serum-calcium level was demonstrated in all 4 cases. Serum-calcium determinations should be undertaken in every case which presents a vague clinical picture. Primary hyperparathyroidism should be treated by operation as soon as the diagnosis has been made, before any other surgical therapy of accompanying disorders is carried out, such therapy being liable to provoke a crisis requiring immediate operation.

PRIMARY hyperparathyroidism is most commonly featured in its chronic form, which in rare cases may be complicated by a hypercalcaemic crisis. Hypercalcaemic crises have been described with increasing frequency in recent years, but the total number of cases reported remains just over 100 (Burcharth and Vibe-Hansen, 1969; Boquist, Bergdahl, and Andersson, 1971).

Recognition of this condition is very important, as failure to operate is nearly always fatal (Lemann and Donatelli, 1964; Anglem, 1966). As only a few patients with primary hyperparathyroidism develop a hypercalcaemic crisis, certain releasing factors must be required. It is recognized that mental and physical stress, e.g., surgical operation, can produce a crisis (Carlsson, Bates, and Boyce, 1960; Burcharth and Vibe-Hansen, 1969; Heimann and Nilsson, 1970; Boquist and others, 1971).

Acute hyperparathyroidism is characterized by an intensification of the symptoms of hypercalcaemia. The disease begins with vague and non-specific general symptoms, such as fatigue, anorexia, weight-loss, vomiting, and abdominal pain, and in some cases paralytic ileus. Mental symptoms, particularly depression, and in some cases psychoses, may be noticed from the outset. If the crisis is allowed to continue, progressive clouding of the consciousness is seen proceeding to stupor and coma. Left untreated the crisis will culminate in cardiovascular shock.

Four case histories are reported here, and the problems concerning diagnosis and treatment of acute hyperparathyroidism are discussed. The cases have been selected from a series of patients with primary hyperparathyroidism treated within the period 1965–71.

CASE REPORTS

Case 1.—A woman aged 56 years, over a period of 3 years had repeatedly had symptoms of renal calculi and hypertension, and intermittent attacks of fatigue, abdominal pain, pancreatitis, and mental disorders. Primary hyperparathyroidism was suspected. In confirmation the serum-calcium level was 15·5 mg. per 100 ml. Exploration of the neck disclosed two adenomas in the lower parathyroid glands, which were removed. Postoperatively the serum-calcium level fell to 10·4 mg. per 100 ml. and remained normal.

Three years later symptoms recurred, and the serum calcium had risen to 12–13 mg. per 100 ml. Exploration of the neck revealed no further adenomas. The patient then improved, and after 2 years she failed to appear for 'follow-up' examination.

Eleven years later (17 years after the first symptoms) the patient returned with pronounced hyperparathyroidism and the serum calcium was 19·6 mg. per 100 ml. Peritoneal dialysis was performed, but despite this the serum calcium rose to 24·5 mg. per 100 ml. in 48 hours. Haemodialysis in the next 24 hours reduced the serum calcium to 14·0 mg. per 100 ml. Exploration of the neck revealed an adenoma in the upper left pole of the thyroid gland which was removed. Postoperatively the serum calcium fell to 11·7–12·6 mg. per 100 ml. One month later it had risen to 20·7 mg. per 100 ml. and the patient was again undergoing a hypercalcaemic crisis.

On reoperation a fourth adenoma was found at the upper right pole of the thyroid. Histological examination showed water-clear hyperplasia. Postoperatively hypoparathyroidism developed which required prolonged treatment with vitamin D and calcium.

The serum calcium has remained normal since. The patient still has her symptoms of impaired renal function, renal calculi, and grave hypertension.

Case 2.—A woman aged 57 years was admitted with a few months' history of fatigue, nervousness, mental depression, and a weight-loss of 14 kg. The serum-thyroxin level was found to be raised to 342 nmol. per litre, which was compatible with hyperthyroidism, and the patient was treated with propyl-thio-uracil. During the patient's stay in hospital her mental symptoms became aggravated, and she became confused. The serum-calcium level (not measured before) was 18·3 mg. per 100 ml. The level fell to 14 mg. per 100 ml. after intravenous therapy with phosphate, and her condition became relatively stabilized. As other causes of the hypercalcaemia were absent exploration of the neck was performed with removal of one parathyroid adenoma and resection of the thyroid gland. The serum calcium and serum thyroxin have remained normal since, and the patient is symptom-free except for mild nervous symptoms.

Case 3.—A woman aged 65 years, with mild diabetes mellitus but otherwise previously in good health, was subjected to left thoracotomy with excision of a tuberculous process. The patient was given anti-tuberculous chemotherapy pre- and postoperatively.

The first 3 postoperative days were uneventful, but on the fourth day the patient became depressed and increasingly drowsy. The blood-sugar level had risen to 470 mg. per 100 ml., but returned to normal after the injection of insulin. The patient grew even more distant, became highly febrile, and complained of diffuse abdominal pain. On the sixth postoperative day, when all other possible causes of the patient's condition had been investigated, the serum-calcium level was measured and found to be elevated (17·8 mg. per 100 ml.).

Initially treatment was attempted with large doses of a cortisone compound intravenously, and the serum-calcium level dropped to 16·1 mg. per 100 ml. and there was some improvement in the patient's condition. On the eighth postoperative day the serum calcium rose again to 17·8 mg. per 100 ml. and the patient became comatose.

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Acute primary hyperparathyroidism was suspected and an infusion of sodium phosphate was commenced in an attempt to prepare the patient for operation, but she died after 1 hour's treatment.

Post-mortem examination disclosed a parathyroid adenoma, 1 cm. in diameter, in the superior mediastinum. There were no adenomas in the neck. Nephrocalcinosis was also present.

Case 4.—A man aged 27 years presented with polyuria of 4 years' duration, a weight-loss of 10 kg. within the past 6 months, intermittent abdominal pain, and vomiting. Following a traffic accident he was admitted to an orthopaedic surgical unit with a fractured patella. Five days after admission the patient became nauseated and vomited several times. The serum creatinin rose from 1·9 to 5·2 mg. per 100 ml. On the tenth day anuria set in. The serum calcium, which had not been measured before, was 18·7 mg. per 100 ml. A 1·5 × 1-cm. soft tumour was palpable inferiorly on the left side of the neck. The patient was subjected to haemodialysis, and consequently his condition improved. The serum calcium fell to 13·7 mg. per 100 ml. and the serum creatinin to 4·2 mg. per 100 ml. within 12 hours.

Eleven days after his admission and 24 hours after acute hyperparathyroidism had been diagnosed an operation was performed to remove three parathyroid adenomas, two of which weighed 5 g. and one 40 g.

Postoperatively the patient developed severe pulmonary oedema, which was treated by positive-pressure ventilation. The postoperative serum calcium was 11·9 mg. per 100 ml. A few hours after the operation the patient had a cardiac arrest. Artificial respiration and external cardiac massage were administered without effect.

Post-mortem examination disclosed bilateral pneumonia and pronounced bilateral nephrocalcinosis.

DISCUSSION

A diagnosis of acute hyperparathyroidism can often be made from the clinical picture. The disease is particularly suspected if the serum calcium is about 16–17 mg. per 100 ml. or higher. In the majority of cases values above 17 mg. per 100 ml. are found (Pyrah, Hodgkinson, and Anderson, 1966; Burcharth and Vibe-Hansen, 1969). The patients described here had serum-calcium values ranging from 17·8 to 24·5 mg. per 100 ml. On the other hand, in some reported cases a crisis occurred although the values were only slightly raised (Smith, Bradshaw, and Holleman, 1963). This may be due to an increase of the ionized serum-calcium fraction owing to concomitant acidosis and hypoproteinaemia.

The present *Case* 1 had had her hyperparathyroidism controlled for some years, since the first operation, with a persistent, slightly raised serum calcium. She presented again with acute symptoms of hypercalcaemia and a high serum-calcium level. The other 3 patients had never before been suspected of having hyperparathyroidism, and the diagnosis was made at such an advanced stage that the symptoms of crisis were pronounced.

In *Case* 2 the symptoms were for a long time interpreted as due to hyperthyroidism. Aggravation of the condition and impairment of the consciousness despite treatment with propyl-thio-uracil raised a suspicion of acute hyperparathyroidism, a diagnosis which was confirmed by a serum-calcium level of 18·3 mg. per 100 ml.

A high incidence of thyroid disorders in relation to primary hyperparathyroidism has been demonstrated by several investigators (Hellstrøm and Ivemark, 1962; Burcharth, Castberg, and Vibe-Hansen, 1972). A significantly raised serum-calcium value has been measured in patients with thyrotoxicosis (Lim, Jacob, and Khoo, 1969). This is probably due to a stimulating effect of thyroxin on the parathyroid glands (Heydenreich and Bock, 1970). Furthermore, the thyroid gland is the main site of production of calcitonin.

Case 3 had not previously displayed any signs or symptoms of hyperparathyroidism. Her condition was at first interpreted as the beginning of diabetic coma. Her condition deteriorated despite control of the diabetes, and after excluding other possibilities, acute hyperparathyroidism was suspected and confirmed by a serum-calcium level of 17·8 mg. per 100 ml.

Case 4 had for some length of time had symptoms compatible with a diagnosis of primary hyperparathyroidism. The symptoms progressed excessively in a few days, and a diagnosis of acute hyperparathyroidism was again confirmed by a serum-calcium level of 18·7 mg. per 100 ml.

In *Cases* 3 and 4 the crisis was provoked by surgical intervention and injury respectively. In *Cases* 1 and 2 there were no obvious provoking factors.

Several other diseases accompanied by non-specific general symptoms may raise problems in the differential diagnosis of acute hyperparathyroidism, particularly in the earlier phases of the crisis. Hypercalcaemia may also be present in association with various other conditions, but in these the serum-calcium level rarely exceeds 16 mg. per 100 ml. (Henley, 1964). In the fulminant crisis, however, the symptoms are so pronounced and characteristic that these, together with the high serum-calcium level, exclude any other diagnosis. The fully developed crisis is a life-threatening condition and therefore an early diagnosis is of great importance. Patients with urolithiasis, thyroid disorders, non-characteristic general symptoms, non-characteristic abdominal complaints, mental disorders, hypertension, peptic ulcer, pancreatitis, and osseous changes with decalcification should always be examined for the presence of hyperparathyroidism.

Medical treatment of primary hyperparathyroidism has been attempted. The following methods are those most frequently employed: phytate by mouth to reduce the calcium absorption from the intestine, kelate- and complex-forming substances, sodium phosphate, mithramycin, calcitonin, and dialysis. None of the stated methods is capable of reducing a high serum calcium, as seen in the hypercalcaemic crisis, to normal.

Phosphate treatment was given with a limited response in *Cases* 2 and 3. Preoperative dialysis, employed in *Cases* 1 and 4, effected a transitory lowering of the serum-calcium level.

Calcitonin, whose chemical data and production in pure form have been clarified within recent years, has been considered with great expectations in the treatment of both chronic and acute hyperparathyroidism. Calcitonin depresses the bone resorption by a negative 'feed-back' mechanism. Possibly it also enhances the phosphate excretion in urine. Copp (1970) recently showed that calcitonin has strong sodiuretic and diuretic effects. Calcitonin only has a hypocalcaemic effect in osteolytic bone diseases. Copp (1970) also showed that possibly it is useful in the treatment of Paget's disease and the hypercalcaemia attending osteolytic bone metastases. However, Sørensen and Hindberg (1970) demonstrated in animal experiments that prolonged calcitonin administration causes secondary hyperparathyroidism with compensatory hypercalcaemia. Therefore, we cannot yet say with certainty whether or not calcitonin can replace the surgical treatment of primary hyperparathyroidism. It may, however, when available for clinical use, be employable for preoperative treatment in cases of acute hyperparathyroidism.

The only rational treatment of primary hyperparathyroidism consists of surgical removal of abnormally acting parathyroid tissue. Surgery must be carried out as soon as the diagnosis has been made and ought to precede the treatment of other accompanying diseases if such are present, e.g., urolithiasis, owing to the risk of provoking a hyperparathyroid crisis.

Acute hyperparathyroidism should be treated by immediate operation, even though such patients often are in a very poor state with grave fluid and electrolyte disorders. This is because conservative methods are incapable of controlling the crisis. In the presence of a crisis the patient's condition will deteriorate rapidly, and the mortality-rate will rise considerably, despite operation, with the increasing length of the crisis. Anglem (1966) found a mortality-rate of 57 per cent. The present *Cases* 3 and 4 had a fatal course which ended in cardiovascular shock.

Acute hyperparathyroidism is most commonly due to an adenoma of the 'chief-cell' type, and less frequently is due to multiple adenomas, diffuse hyperplasia, or cancer (Boquist and others, 1971). In *Cases* 2 and 3 solitary adenomas were found, in *Case* 4 multiple adenomas, and in *Case* 1 diffuse hyperplasia.

It is important to identify all four parathyroid glands during the operation. In the presence of hyperplasia the treatment consists of removal of three and a half glands. This is illustrated by *Case* 1, in which the patient had hyperplastic parathyroid tissue removed by three operations within a period of 14 years, the later two being performed with the patient in a crisis.

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POSTOPERATIVE WOUND INFECTION IN COLONIC AND RECTAL SURGERY

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Summary

There was a statistically significant association between the species of bacteria isolated from the bowel at operation, and the species subsequently isolated from a postoperative wound infection in 100 patients who underwent colonic or rectal surgery. There was also a statistically significant increase in the incidence of Gram-negative bacteriaemia in patients who developed a wound infection following such surgery. This bacteriaemia was most commonly detected before and during the operation. Its role in the aetiology of postoperative wound infection has not yet been established.

In 1969 a prospective investigation of 100 patients submitted to elective colonic and rectal surgery was carried out in the Royal Melbourne Hospital (Burton, 1972). The purpose of this paper is to report on the aetiology, incidence, and type of postoperative wound infections which occurred in these patients.

METHODS

All the patients were examined daily from the morning before the operation until the day of discharge or death. Systemic venous blood cultures were obtained from each patient on the day before operation, on the day of the operation, before, during, and after the procedure, and then once a day for 5 days, unless the date of admission, discharge, or death occurred within this period. Nineteen patients also had a single peroperative portal venous blood culture. In addition to the blood cultures peroperative swabs of the bowel lumen at the site of the operation were obtained in 92 patients.

When a postoperative infection was suspected bacteriological cultures were taken from the site in question. A postoperative wound infection was recorded when inflammation of the wound, a serosanguineous or purulent discharge, and culture of a pathogen from the discharge were all present. The infections were graded as follows:—

Grade 1: Localized minor inflammation with a serosanguineous discharge only.

Grade 2: Purulent infection with less than half of the wound involved.

Grade 3: Purulent infection with more than half of the wound involved.

RESULTS

Fifteen different operations were performed on the 56 male and 44 female patients included in the study (*Table I*).

Table I.—CORRELATION OF THE OPERATIONS PERFORMED WITH THE DEVELOPMENT OF A POSTOPERATIVE WOUND INFECTION

OPERATION	NO OF PATIENTS	NO. OF PATIENTS WITH WOUND INFECTION
Abdominoperineal resection of the rectum	16	15
Sigmoid colectomy*	16	9
Anterior resection of the rectum	14	8
Closure of colostomy	10	7
Pull-through resection of the rectum	7	2
Right hemicolectomy	6	3
Sigmoid colostomy	6	3
Transverse colostomy	6	3
Total colectomy†	5	3
Left hemicolectomy	4	1
Segmental colonic resection	3	3
Sigmoid colotomy	2	2
Hartmann's resection of the rectum	2	1
Ileotransverse anastomosis	2	0
Caecostomy	1	1
	100	61

* One patient also had a transverse colostomy performed.
† One patient had an ileorectal anastomosis, and 2 an ileostomy.

Table II.—SUMMARY OF 68 CASES OF WOUND INFECTION (61 PATIENTS)

	GRADE I	GRADE II	GRADE III	TOTAL
Abdominal	15	30	9	54
Perineal	5	6	3	14

Sixty-one patients developed a postoperative wound infection, and a total of 68 such infections, of various grades, was recorded (*Table II*). Eight patients developed an intraperitoneal abscess and 3 patients had generalized peritonitis, and in each case an abdominal wound infection was present.

Prophylactic antibiotics were administered to 48 patients, 31 of whom developed a postoperative wound infection. There is no statistically significant difference between the incidence of wound infection in this group and in the group of 52 patients who did not receive prophylaxis. The antibiotics were either given orally preoperatively in a non-absorbable form, or were administered systemically during and/or following the operation. The numbers were too small to make a valid comparison of the régimes employed; however, the lowest incidence of wound infection (5 of 13 patients) was in the patients who received penicillin G intravenously during the operation.

Thirty-one of the 42 patients who had an abdominal intestinal stoma formed or closed during their operation developed an abdominal wound infection. This incidence of wound infection is significantly greater than that in the remaining 58 patients ($P<0·05$, $\chi^2 = 4·9$). The pathogens isolated from the wound, blood, and bowel were, with the exception of 17 *Staphylococcus aureas* wound isolates, all enteric flora (*Table III*). Of the patients with wound infection, 54 had pathogens isolated from their bowel swabs and in 35 cases the species was the same as that isolated from the postoperative wound infection. This association is statistically significant ($P<0·05$, $\chi^2 = 4·7$).

Table III.—ENTERIC PATHOGENS ISOLATED FROM THE BLOOD, WOUND, AND BOWEL CULTURES

SPECIES	NO. OF ISOLATES			
	Blood	Bowel	Wound	Total
Escherichia coli	23	77	46	146
Proteus sp.	8	28	38	74
Klebsiella sp.	28	10	16	54
Enterobacter sp.	28	3	7	38
Paracolon sp	2	2	3	7
Total Enterobacteriaceae sp.	89	120	110	319
Streptococcus faecalis	14	16	13	43
Anaerobes	8	16	10	34
Pseudomonas pyocyanea	3	8	5	16
Total isolates	114	160	138	412

Table IV.—GRAM-NEGATIVE BACTERIAEMIA AND WOUND INFECTION IN 100 PATIENTS

BLOOD CULTURES	WOUND INFECTION	NO INFECTION
Positive	27	8
Negative	34	31

$\chi^2 = 5·8$, $P<0·05$.

Gram-negative bacteriaemia was significantly more common in the patients who developed a postoperative wound infection (*Table IV*). However, only 9 of the 27 patients who had positive blood cultures and a postoperative wound infection had the same species of bacteria isolated from the two sites. This association is not statistically significant.

DISCUSSION

The wound-infection rate following colonic and rectal surgery reported here is high (61 per cent). However, it is comparable to the rates reported by other authors who employed a similar definition of wound infection and kept a careful prospective surveillance for its occurrence. Everett, Brogan, and Nettleton (1969) reported an overall incidence of 58 per cent, and Jepsom, Larsen, and Thomsen (1969) an incidence of 53 per cent in their bowel-surgery cases. Many authors exclude the grade 1 wound infections from their figures, which would reduce the incidence of wound infection in this investigation to 50 per cent. This is comparable to the incidence of 46·2 per cent reported by Kippax and Thomas (1966) in the first year of their survey, and to the figure of 50 per cent reported by Hughes (1967) for the group of patients in his survey who did not receive prophylactic antibiotics.

The very high wound-infection rate in abdomino-perineal resection has been noted by other authors. If the grade 1 infections in this investigation are excluded, this incidence becomes 63 per cent, which is comparable to the figure of 53 per cent reported by Jepsom and others (1969) and also to the 58 per cent of Hughes, Hardy, Cuthbertson, and Rubbo (1970) in the group of patients in their survey who did not receive prophylactic antibiotics. These patients comprise almost one-third of those whose operations involved formation or closure of an intestinal stoma. These procedures are often associated with extensive contamination of the operative field, and therefore, as Cowling (1962) reported from the Royal Melbourne Hospital, the wound-infection rate for these operations is significantly higher.

The predominance of Gram-negative bacilli of the family Enterobacteriaceae is typical of wound infections occurring after colonic and rectal surgery (Rubbo, Hughes, Blainey, and Russell, 1965; Kippax and Thomas, 1966; Azar and Drapanas, 1968). These wound infections are assumed to be endogenous (Everett and others, 1969). The results of this investigation show a statistically significant association between the identity of the bacteria isolated from the colon or rectum at the operative site, and that of the bacteria subsequently recovered from the post-operative wound infection. This provides good evidence that these infections are caused by bacteria spilled into the wound from the bowel during the operation.

The high incidence of systemic and portal Gram-negative bacteriaemia in patients with large-bowel pathology submitted to operation has been previously reported (Eade and Brooke, 1969; Burton, 1971, 1972). Positive blood cultures are most often obtained before or during the operation, and are rarely found after the third postoperative day unless the patient develops severe sepsis (Burton, 1972). The role of Gram-negative bacteriaemia in the causation of post-operative wound infections is uncertain. Although patients who have positive blood cultures do have a statistically significantly increased incidence of postoperative wound infection, there is no statistically significant association between the identities of the bacteria isolated from the blood and the wound infection. There is, however, good experimental evidence that circulating bacteria can lodge in surgical wounds and cause a wound infection (Howe, 1969).

Since a major factor in the aetiology of postoperative wound infections following colonic or rectal surgery is contamination of the wound by enteric bacteria at the time of surgery, then, to be effective, prophylactic antibiotics should be in the tissues at this time. This principle has been proved experimentally (Burke, 1961), and the only double-blind prophylactic antibiotic trials to demonstrate a statistically significant advantage for these agents in human colonic and rectal surgery have employed peroperative systemic antibiotics (Bernard and Cole, 1964—penicillin G + methicillin + chloramphenicol; Polk and Lopez-Mayor, 1969—Cephaloridine; Hughes and others, 1970—penicillin G). Similar investigations have shown that preoperative non-absorbable antibiotics are not effective in the prophylaxis of wound infection (Gaylor, Clarke, Kudinoff, and Finegold, 1960; Everett and others, 1969). Uncontrolled, or non-double-blind trials, are not a worth-while source of evidence in this field, and as there is not yet a published double-blind trial of the use of topical antibiotics prophylactically in colonic and rectal surgery their worth is unknown. In terms of the principle outlined above they should be effective, and one double-blind trial has demonstrated a statistically significant reduction in postoperative wound infection following appendicectomy (Rickett and Jackson, 1969—ampicillin).

Acknowledgements.—I am indebted to Professor M. R. Ewing and all the honorary surgeons, and their registrars and residents, who co-operated with me and encouraged this study in the Royal Melbourne Hospital. This work was supported in part by the Victor Hurley Medical Research Fund of the Royal Melbourne Hospital.

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AN EPIDEMIOLOGICAL STUDY OF REGIONAL ENTERITIS IN THE GLOUCESTER AREA

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GLOUCESTERSHIRE ROYAL HOSPITAL

SUMMARY

An epidemiological study has been made of regional enteritis in the Gloucester area during the period from 1 Jan., 1966, to 31 Dec., 1970. There were 19 cases in an average population of 253,000, giving an average incidence of new cases of 1·5 per 100,000 per year. There was a significant peak of cases in the 15–24 age-group. The incidence in men was slightly higher than in women. There was a family history of ulcerative colitis in 2 cases. There were 3 cases of regional enteritis of the large bowel only, all occurring in women. Extensive large- and small-bowel involvement occurred predominantly in the younger patients.

ONLY two studies of regional enteritis in the United Kingdom have provided an incidence rate for a defined geographical area (Evans and Acheson, 1965; Kyle and Blair, 1965). In addition, Davis (1961) derived an approximate incidence rate based on the records of three London hospitals. In a review of regional enteritis Law (1969) stated: 'To make such data [incidence rates] even more useful, we should have incidence and prevalence rates from different parts of the country and the world.' We hope that this study will enhance the usefulness of those mentioned above.

STUDY METHODS

The design of this survey is based on that of Evans and Acheson (1965) with modifications. A 5-year period was reviewed from 1 Jan., 1966, to 31 Dec., 1970. The geographical area under review was that covered by the Gloucester, Stroud, and Forest Hospitals Group which serves eleven urban and rural districts. Population figures were determined from the *Municipal Year Book* for each year. The distribution by age and sex was obtained from the Office of Population Censuses and Surveys. The total population per year was almost static, rising from 248,000 in 1966 to 258,000 in 1970, an increase of about 4 per cent. An earlier independent study for the Hospital Management Committee had shown that of the people in the catchment area who required admittance to hospital for any reason, less than 2 per cent were referred to hospitals outside the study area.

Retrieval of Cases.—The primary source of information was the in-patient diagnostic index of the Gloucestershire Royal Hospital covering the period stated. To allow for delay either in admitting a case or in establishing the correct diagnosis the records for 1971 were also reviewed. Dyer and Dawson (1970) indicated an initial misdiagnosis rate of up to 27 per cent of cases of regional enteritis as some form of colonic disorder; accordingly, notes of all the patients who were admitted with a diagnosis of ulcerative colitis, chronic colitis, sigmoiditis, diverticulitis, proctitis, and miscellaneous bowel disorders were reviewed. From all of these sources 38 possible cases were retrieved. Inquiry of the hospital's consultant physicians and surgeons concerning their private practice produced 2 more cases.

This study was restricted to patients who were admitted to hospital at some time during their illness. This approach was dictated by the fact that there is no out-patient diagnostic index, and it would be quite impractical to review the notes of every hospital out-patient. Of all the patients with regional enteritis who were traced 80 per cent were admitted within 3 months of first presenting at an out-patients' clinic and 90 per cent within 12 months. The search of in-patients' records for 1971 also ensured as complete a retrieval of cases as possible. Discussions with the consultant staff indicated that no patient with regional enteritis was being treated or followed as an out-patient who had not already been admitted for investigation or operation.

ASSESSMENT OF CASES

Initially a total of 40 case histories was scrutinized for acceptance, the criteria for which are listed below.

Presentation.—Cases were only accepted for this series if they had presented for consultant opinion during the period studied. Ideally the date of onset of symptoms should be the point of acceptance to the series, but this date is difficult to establish. In some patients the first symptoms complained of were so vague that it was difficult to be sure that they were due to regional enteritis, even in retrospect. Other patients, particularly those with long histories, could not give an accurate date of the onset of symptoms. In contrast, the date of first presentation to a consultant is accurately known for all the patients. In fact, about 75 per cent of our series presented within 6 months of their first symptoms. A total of 15 cases was rejected from the series because they were first seen before the study period.

Residence.—Cases were rejected if the patient had not been resident in the study area for at least a year prior to presentation. Only 1 case was rejected on these grounds. All the patients in the final series had been resident in the area for at least 10 years and 75 per cent were born in the area.

Diagnostic Criteria.—The diagnostic methods used were radiology, laparotomy, and histology. According to the findings, cases were either put into one of two categories: 'definite regional enteritis' and 'probable regional enteritis', or rejected. Cases had to meet at least one of the following criteria to be included in the series:—

1. A characteristic radiological appearance seen on barium follow-through and/or barium-enema examinations.

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* Present address: Radcliffe Infirmary, Oxford.

2. A characteristic macroscopic appearance at laparotomy.

3. Characteristic microscopic appearances in biopsies taken at laparotomy or sigmoidoscopy.

Cases were only designated as 'definite regional enteritis' when a histological diagnosis was available. If the histology report was inconclusive (usually reported as 'compatible with regional enteritis') the case was designated 'probable regional enteritis', provided that the other criteria were satisfied. All the histological material was reviewed by one of us (A. N.) with no prior knowledge of the clinical histories. One case was rejected because the clinical and laparotomy findings were not sufficiently characteristic of regional enteritis and no biopsy had been taken. Four other cases were rejected because no evidence of regional enteritis was seen on review of the histological material.

ACCEPTED CASES

The final series comprised 19 cases; 6 of these were designated 'definite regional enteritis' with typical appearances at laparotomy and on microscopy. The other 13 were classified as 'probable regional enteritis'. Of the latter category, 2 were diagnosed without laparotomy; both were severe and clinically typical with unequivocal radiological evidence of the disease. A further 2 cases in this 'probable' category were diagnosed on laparotomy appearances only, no biopsy being taken. These patients, presenting initially as suspected acute appendicitis, were probably cases of so-called 'acute' regional enteritis and have been asymptomatic since discharge from hospital. A further 'acute' case was diagnosed on the basis of radiology and laparotomy, the histology of a mesenteric node being inconclusive.

Follow-up.—Nine of the patients in the series are currently being followed up in the out-patients' clinic. Two others have only recently defaulted from follow-up. Postal questionnaires were sent to all the patients, inquiring about their present medical condition, residential history, family history, associated disorders, etc.

RESULTS

Incidence.—The average annual population for the 5-year study period was 253,000. There was a total of 19 new cases, giving an average incidence of 1·5 cases per year per 100,000 of population.

Age and Sex.—The distribution of the sexes in the general population in the study area is 49 per cent males and 51 per cent females. In our series there were 10 males and 9 females. The average incidence in each sex, therefore, was 1·61 males and 1·39 females per 100,000. The difference is not significant.

The age-group and sex distribution of the cases are shown in *Table I*. Separate incidence rates are calculated for each age-group, but not for each sex in any one age-group. The youngest patient was 12 at presentation and the oldest, 77.

As shown in *Table I* there is a peak incidence of 5·05 per 100,000 in the age-group 15–24. Compared with the adjacent age-groups this difference is statistically significant. Differences between other age-groups are not statistically significant. There is no bias in the distribution of sexes within each age-group.

Geographical Distribution.—The patients' addresses were plotted on a 3-miles-to-the-inch map of the study area. There was no grouping of the cases other than that expected on the basis of population differences. In addition, the cases occurring in the city of Gloucester were plotted on a large-scale street map of the city. Again there was no obvious grouping.

Table I.—AGE AND SEX DISTRIBUTION OF 19 CASES OF REGIONAL ENTERITIS

AGE-GROUP (yr.)	ESTIMATED POPULATION	NO. OF CASES OBSERVED			INCIDENCE PER 100,000	95 PER CENT CONFIDENCE LIMITS
		Male	Female	Total		
0–14	62,700	0	1	1	0·32	*–1·78
15–24	35,600	5	4	9	5·05	2 31–9 60
25–34	33,400	1	0	1	0 60	*–3·33
35–54	65,600	3	1	4	1 22	0·33–3·12
55–74	45,800	1	2	3	1·31	0·27–3·83
75+	9900	0	1	1	2·10	*–11·25

* The value of the lower confidence limit was so small that a detailed calculation was not recorded.

Table II.—SITES OF INVOLVEMENT IN 19 CASES OF REGIONAL ENTERITIS

SITE	SEX			PERCENTAGE OF TOTAL	NO. OF CASES	
	Male	Female	Total		Under 25 Years	Over 25 Years
Small bowel only	6	4	10	52·4	4	6
Large and small bowel	3	3	6	31·8	5	1
Large bowel only	0	3	3	15·8	1	2

Family History.— A number of surveys have shown that up to 11 per cent of patients with regional enteritis have blood relatives with either regional enteritis or ulcerative colitis (Kirsner and Spencer, 1963). Two of our 19 patients (11·5 per cent) have relatives with ulcerative colitis.

Associated Disorders.—Inquiry was made for disorders which have previously been reported to be associated with regional enteritis. Skin disorders are a common association (Dyer, Verbov, Dawson, Borrie, and Stansfeld, 1970); 1 of our patients had psoriasis of many years' standing, a second case had erythema and hyperkeratosis of the hands for some months, and a third had intermittent diffuse skin rashes for many years. An association with hepatobiliary disease has also been reported (Palmer, Kirsner, Goldgraber, and Fuentes, 1963; Dordal, Glagov, and Kirsner, 1967; Perrett, Higgins, Johnston, Massarella, Truelove, and Wright, 1971). One of our patients admitted to having had a 'liver disorder' in the past, the precise nature of which could not be ascertained.

Sites of Involvement.—The sites of involvement are shown in *Table II*. The age and sex distributions are also shown. All the patients with disease confined to the large bowel were females. Of the 6 patients with large- and small-bowel involvement, 5 were aged under 25. One aged 16 was a particularly severe case with lesions in the ileum, caecum, colon, and rectum, and a probable lesion in the jejunum. Another patient aged 12 had extensive involvement of the colon and jejunum.

Race and Mortality.—All the patients were white United Kingdom citizens. There were no deaths in this series.

Chronological Distribution.—The number of new cases occurring in each of the 5 years studied was determined. There was no distinct pattern in the distribution and so separate incidence rates for each year were not calculated. We would not expect to see any pattern in such a short study period.

DISCUSSION

The average annual incidence of regional enteritis in this series was 1·5 new cases per 100,000 population. This compares with previous reports of 0·8 in Oxford (Evans and Acheson, 1965), 1·3 in North-east Scotland (Kyle and Blair, 1965), and 1·0 (approx.) in London (Davis, 1961). Comparison may also be made with thyroid carcinoma (1·4 per 100,000) and Hodgkin's disease (2·37 per 100,000). At first sight there appears to be a regional variation in incidence, particularly between Gloucester and Oxford, which are geographically closely related. However, with a condition as uncommon as regional enteritis these differences are not significant and could represent the sampling errors inherent in such small series (34 cases in the Oxford study).

The sex distribution showed a slight male preponderance, though this was not significant.

With regard to age-specific incidence, regional enteritis is traditionally considered to affect mainly young adults (Crohn, Ginzburg, and Oppenheimer, 1932; Thayer, 1970). Monk, Mendeloff, Siegel, and Lilienfeld (1967) determined age-specific incidence rates for the disease in Baltimore, U.S.A., and concluded that there is 'no age pattern evident in regional enteritis', but the condition was studied only in persons aged 20 years or over. The present study is the first in the United Kingdom to produce age-specific incidence rates, and we found a definite and statistically significant peak in the 15–24 age-group. This appears to be superimposed on a general trend of increasing incidence with increasing age. Although this latter trend is not statistically significant, we believe it may represent the generally increasing susceptibility to disease that occurs with ageing.

Regional enteritis of the large bowel only has been found to be more common in females than in males, and it also tends to occur in an older age-group than small-bowel disease (Cornes and Stetcher, 1961). In the present series all cases of primary large-bowel disease occurred in females. Five of our 6 patients with both the large and small bowel involved were aged under 25. Two patients with jejunal involvement were aged 12 and 16 respectively. It seems, therefore, that extensive severe disease is more likely to occur in the younger patient. The relative frequency of large- and small-bowel lesions matches closely that reported by Atwell, Duthie, and Goligher (1965).

Acknowledgements.—We would like to express our thanks to all who helped in the carrying out of this survey, especially the staff of the Medical Records Department of the Gloucestershire Royal Hospital. We are indebted to Dr. Martin Vessey, of the Department of the Regius Professor of Medicine at Oxford, for his helpful advice and encouragement. We would also like to thank those consultants and general practitioners who supplied us with information.

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CYTOTOXIC PERFUSION OF THE LIVER VIA THE UMBILICAL VEIN FOR LIVER METASTASES IN CARCINOMA OF THE COLON

By P. G. BEVAN
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SUMMARY

Four patients with carcinoma of the large bowel and liver metastases have been treated by primary resection and perfusion of the liver with 5-fluoro-uracil via an umbilical vein cannula.

Two patients survived for 14 and 17 months respectively, 1 is still alive after 17 months, and 1 was relieved of deep obstructive jaundice but died 4 months after treatment. The patients were studied clinically, by serial haematological and liver-function tests, and by hepatography and liver scanning. The only severe toxic effect was diarrhoea in 1 patient. The rationale of this method of treatment is discussed along with other applications. It is considered justifiable to use this technique in this group of patients in an attempt to improve the poor prognosis.

A TECHNIQUE for cannulating the umbilical vein in the adult to gain direct access to the portal vein was first described by Carbalhaes in Mexico in 1959 (*Fig.* 1). The method can be used for diagnostic purposes to measure portal pressure, for biochemical estimations of the portal blood, and to record radiological appearances; to investigate the liver metabolism; and therapeutically for portal venesection or porta-systemic shunts in portal hypertension, or to introduce antibiotics or cytotoxic drugs into the portal circulation.

This paper reports 4 cases of carcinoma of the large bowel in which portal cannulation of the umbilical vein has been utilized to perfuse liver metastases with a cytotoxic agent after resecting the primary growth. It is important for the primary carcinoma to be operable in the conventional sense, apart from the liver metastases, without local infiltration beyond the bowel wall and widespread lymph-node involvement.

METHODS

The technique of cannulating the 'obliterated' umbilical vein in the adult has been described in detail by Watts and Douglas (1971). An improved success rate is obtained if the vein is dilated with gum-elastic filiform bougies, avoiding metal probes which may perforate the vein wall. A No. 9 plastic umbilical catheter has been used for the perfusions. Trickle hepatograms have shown that complete perfusion of the whole liver can normally be achieved by drip infusion at ordinary pressure.

5-Fluoro-uracil has been used as the perfusing agent in a dosage of 15 mg. per kg. body-weight per 24 hours. The total dose given in each case is stated below. Response to treatment has been monitored in five ways: clinically, by serial haematological studies, serial liver-function tests, portal hepatograms, and liver scanning. The serial haematological estimations and liver-function tests for each patient are shown in the form of graphs in *Figs.* 2–5.

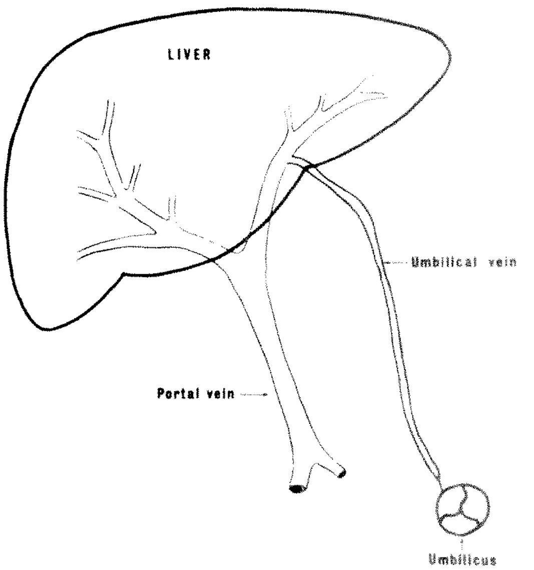

FIG. 1.—Cannulation of the obliterated umbilical vein in the adult gives direct access to the left branch of the portal vein.

CASE REPORTS

Case 1.—A male, aged 65 years, gave a 2-year history of diarrhoea which had become worse over the previous 3 months. On rectal examination there was a palpable carcinoma in the upper third of the rectum. At laparotomy a second carcinoma was found in the sigmoid colon, and the liver contained multiple, moderate-sized metastases (*Fig.* 6). Both carninomas were mobile and limited to the bowel wall, and the local lymph-nodes were not involved. The remainder of the colon appeared normal. Abdominoperineal resection of the rectosigmoid was performed, removing both growths, with a terminal left iliac colostomy. Ten days later the umbilical vein was cannulated through a short supra-umbilical midline incision and an operative hepatogram confirmed complete perfusion of the liver. 5-Fluoro-uracil was given in a dosage of 840 mg. per day for 4 days, followed by a 7-day pause, and then 420 mg. per day for 4 days (a total of 5 g.). There were no toxic effects. The umbilical perfusion ran for 25 days with no trouble, and the catheter was then removed.

The preinfusion hepatogram (*Fig.* 7) demonstrated the larger metastases, but the postinfusion hepatogram was a failure due to spasm of the portal venous radicles. The haematological studies showed that the white-cell and

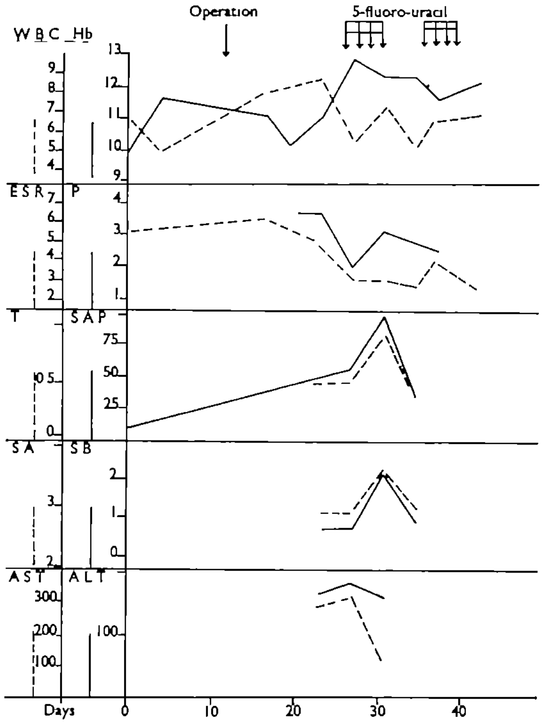

FIG 2.—*Case* 1. Serial haematological investigations and liver-function tests. The figures for the white blood-count (W.B C.) are $\times 10^3$ per mm.^{3}, the haemoglobin (Hb) in g. per cent, the platelet (P) count $\times 10^5$ per mm.^{3}, and the erythrocyte-sedimentation rate (E.S.R.) × 10 mm. per hour (Westergren). Serum bilirubin (S B.) is in mg. per cent, alkaline phosphatase (S A P.) × 10 units per cent, thymol turbidity (T) in units per cent, albumin (S.A) in g. per cent, and alanine (A.L T) and aspartate transaminase (A.S.T.) × 10 international units per litre. The date of the operation is marked. The 5-fluoro-uracil doses are represented by a large arrow for 1 g. and a small arrow for 0·5 g.

platelet counts remained within normal limits. The serum alkaline phosphatase and bilirubin rose during the early part of the perfusion but fell towards normal by the end. The serum transaminases, which were initially high, became higher during the perfusion but then fell to their original level. The serum albumin showed no significant change (*Fig.* 2). The patient remained well and symptom-free for 15 months after the operation, and then developed anorexia, loss of weight, upper abdominal pain, and rapidly increasing hepatomegaly, and died 2 months later.

Case 2.—A male, aged 60 years, was admitted as an emergency with gross intestinal obstruction. The previous history was of only 3 weeks' duration: anorexia, central abdominal colic, and constipation. Operation was performed on the morning after admission and revealed an operable carcinoma of the splenic flexure of the colon with diffuse small liver metastases, and two larger ones just above the hilum (*Fig.* 8). A one-third colectomy was performed with end-to-end anastomosis after decompressing the proximal colon; a safety-valve caecostomy was added and umbilical vein cannulation was carried out. 5-Fluoro-uracil was then infused at a dose of 960 mg. per day for 4 days, followed by a few days' pause, and then 480 mg. per day for 4 days. The patient then developed mild diarrhoea but this settled in a few days. Two further divided doses each of 2 g. of 5-fluoro-uracil were given, and the patient received 10 g. in all. The caecostomy was closed 16 days after the first operation, and the umbilical catheter was removed after the infusion had been running without trouble for 29 days. The preinfusion hepatogram

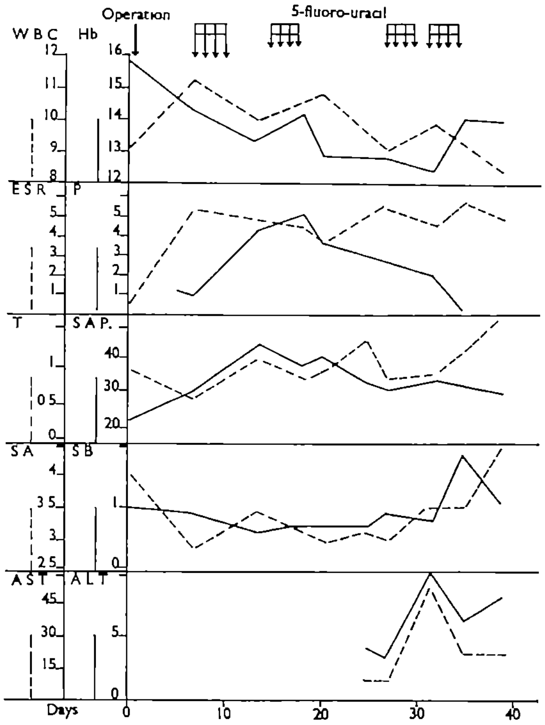

FIG. 3.—*Case* 2. Serial haematological investigations and liver-function tests. The units and abbreviations are as in *Fig.* 2.

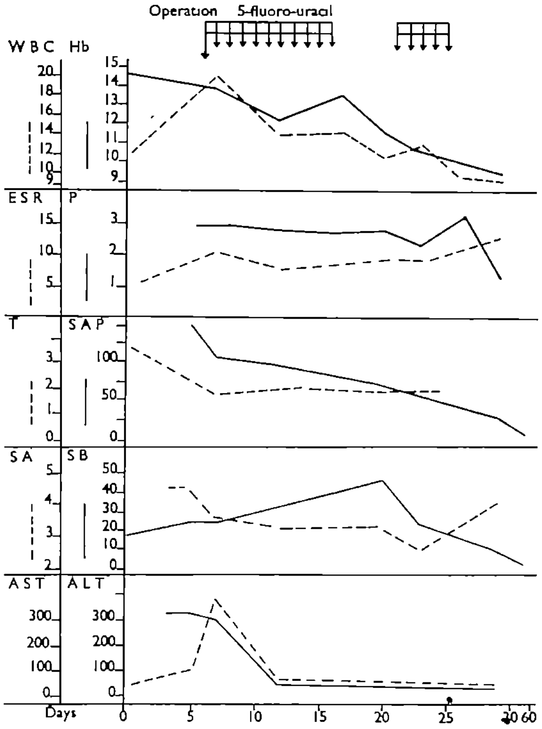

FIG 4.—*Case* 3. Serial haematological investigations and liver-function tests. The units and abbreviations are as in *Fig.* 2.

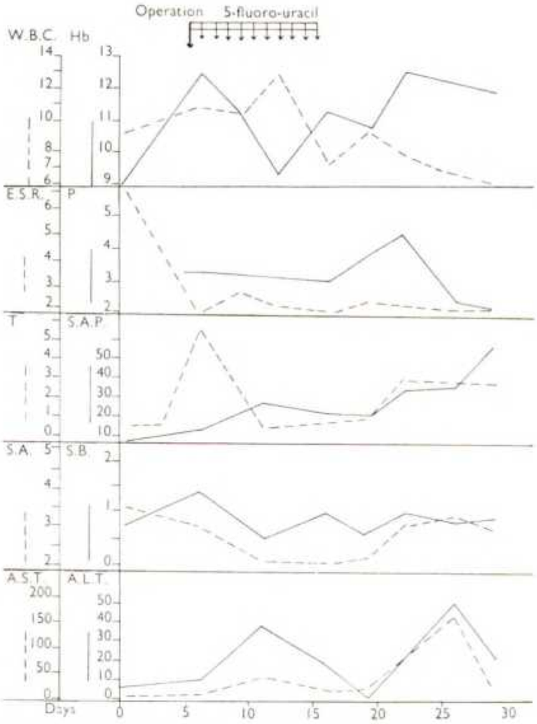

FIG. 5.—*Case* 4. Serial haematological investigations and liver-function tests. The units and abbreviations are as in *Fig*. 2.

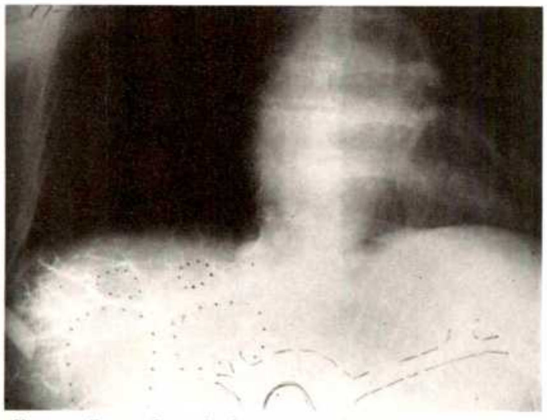

FIG. 7.—*Case* 1. Operative hepatogram, showing large metastases, and complete perfusion of the liver.

(*Fig*. 9) showed the large central metastases clearly and there was diminution in their size on the postinfusion films (*Fig*. 10). The preinfusion liver scan also showed these metastases (*Fig*. 11), but on the scan performed 4 weeks later they had disappeared (*Fig*. 12). There was a slight fall in the white-cell and platelet count towards the end of the perfusion, but not below normal limits. The serum alkaline phosphatase was initially high, rose during the perfusion, and then fell to the previous high level. The serum bilirubin showed a slight rise towards the end of the perfusion, and the transaminases were still rising at this stage. The serum albumin remained unchanged (*Fig*. 3).

The patient remains well and free of symptoms 17 months later.

Case 3.—A male, aged 60 years, was admitted with upper abdominal pain and deep obstructive jaundice of 3 weeks' duration. Fifteen months previously he had undergone abdominoperineal resection for carcinoma of the rectum and there had been no apparent secondaries in the liver. A limited upper midline laparotomy was now performed, revealing multiple, large liver metastases, with one large deposit in the hilum (*Fig*. 13). Umbilical vein cannulation was carried out, and during the next 3 weeks 15 g. of 5-fluoro-uracil were given in divided doses (1 g. per day) with no untoward effects. There was a dramatic response in that the jaundice disappeared clinically by the end of the perfusion. The cannula was removed after the drip had been running for 29 days.

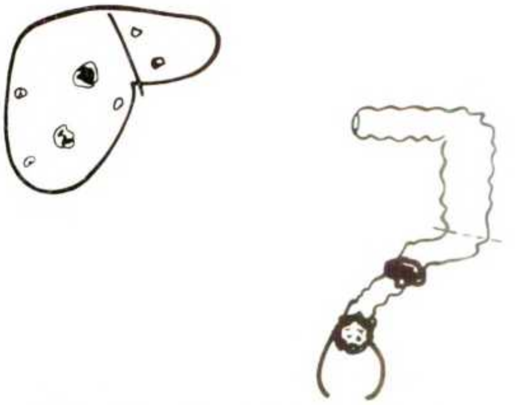

FIG. 6.—*Case* 1. Diagram of the operative findings.

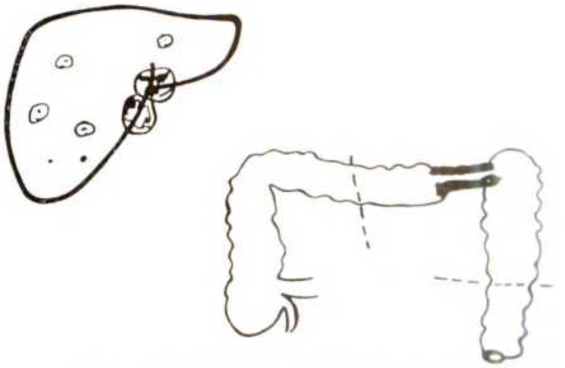

FIG. 8.—*Case* 2. Diagram of the operative findings.

The initial hepatogram showed some of the deposits (*Fig*. 14) which were seen to be diminished on a later examination. The white-cell and platelet count fell slightly at the end of the perfusion but not below normal. The initial serum alkaline phosphatase of 151 mg. per cent fell sharply during the perfusion and was normal at 8·1 mg. per cent 2 months later. The initial serum bilirubin was 17·8 mg. per cent rising to 45 mg. at mid-perfusion and then falling sharply; it was 2·2 mg. per cent 2 months later. The serum transaminases were very elevated before the perfusion, falling to just above normal by the end of the perfusion. The serum albumin showed a slight fall towards the end of the perfusion (*Fig*. 4).

The patient remained well and free of icterus for 3 months after leaving hospital but then developed rapid and severe recurrence of the jaundice and died a few weeks later.

Case 4.—A male, aged 68 years, gave a 6-week history of diarrhoea and rectal bleeding. Rectal examination revealed a carcinoma in the upper rectum that could just be reached with the finger. At operation a carcinoma of the rectosigmoid junction was found, and anterior resection was performed with end-to-end anastomosis (*Fig*. 15). There were multiple, small, diffuse liver metastases present and the umbilical vein was cannulated. Subsequently, 10 g. of 5-fluoro-uracil were given in divided doses, but severe diarrhoea developed and took 3 weeks to settle, so that the infusion was terminated after running for 32 days without giving any more 5-fluoro-uracil. The patient's general condition was poor, and therefore no hepatogram or scan was done for the sake of the patient's comfort. Again, the white-cell and platelet count fell a little during the perfusion, but remained within normal limits. The serum alkaline phosphatase and transaminases rose considerably towards the end of the perfusion, but the serum bilirubin remained normal. The serum albumin showed an early fall at the start of the perfusion but then returned to normal (*Fig*. 5). The patient remained in good health for 12 months after leaving hospital but then deteriorated rapidly and died 1 month later.

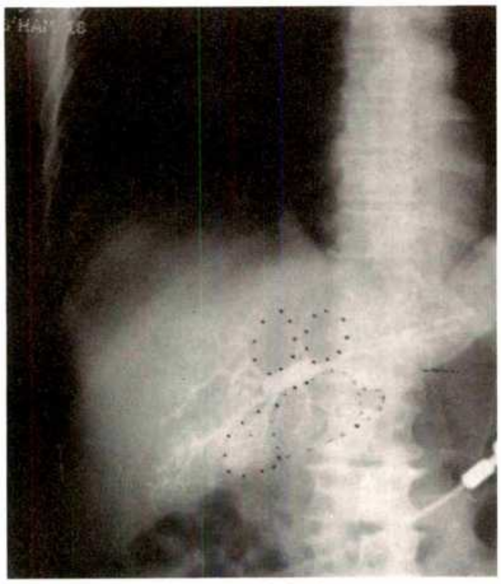
FIG. 9.—*Case* 2. Preinfusion hepatogram.

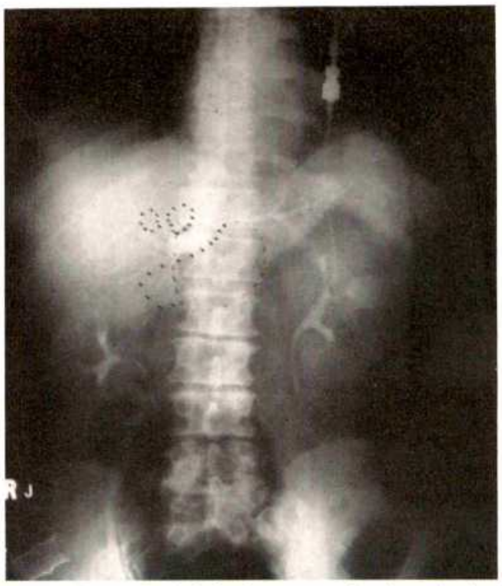

FIG. 10.—*Case* 2. Postinfusion hepatogram showing reduction in size of the metastases.

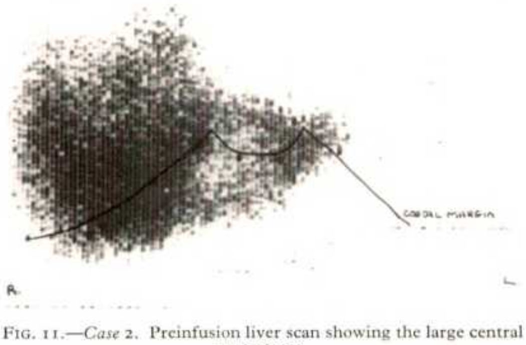

FIG. 11.—*Case* 2. Preinfusion liver scan showing the large central metastases.

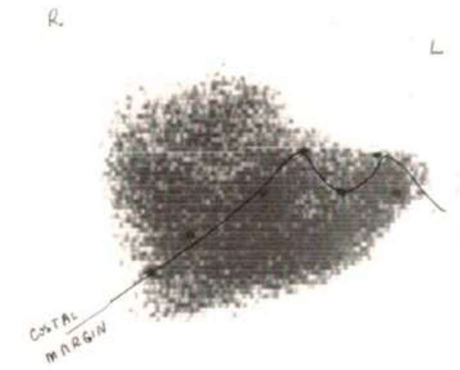

FIG. 12.—*Case* 2. Postinfusion liver scan showing disappearance of these large metastases.

Biopsies of the liver metastases were taken in each case and confirmed secondary carcinoma.

RESPONSE TO TREATMENT

In each of the 4 cases there was evidence of clinical response to the cytotoxic perfusion. The disappearance of the jaundice was striking in *Case* 3, where there was palpable regression of the liver masses; regression of the metastases also occurred in the other 3 cases. *Case* 3 died 4 months after treatment, *Cases* 4 and 1 died 14 and 17 months after treatment respectively, and *Case* 2 is still alive and well after 17 months. Each of the 3 deaths was characterized by sudden and severe deterioration associated with rapid enlargement of the liver metastases, anorexia, loss of weight, and increasing cachexia, leading to a fatal outcome within a few weeks. In 1 patient (*Case* 4) widespread subcutaneous and lymph-node deposits appeared. Until the fairly acute terminal phase each patient had been in good health.

The only side-effect of the cytotoxic perfusion encountered in this series was diarrhoea in 2 cases: mild in *Case* 2 and not leading to curtailment of the drip, but fairly severe in *Case* 4, taking 3 weeks to settle and limiting the amount of 5-fluoro-uracil given to 10 g. Diarrhoea is an indication that the drug has passed through the liver into the systemic circulation and has affected the intestinal mucosa which is particularly sensitive to the drug. In *Fig.* 10 the radio-opaque dye has produced a pyelogram confirming this systemic effect.

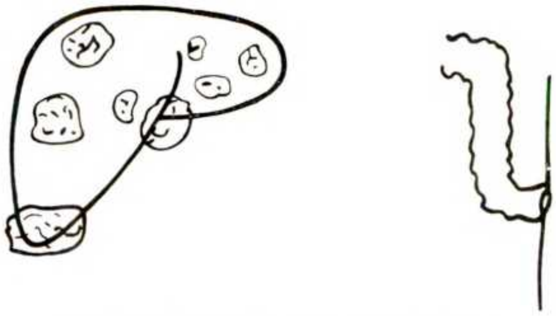

FIG. 13.—*Case* 3. Diagram of the operative findings.

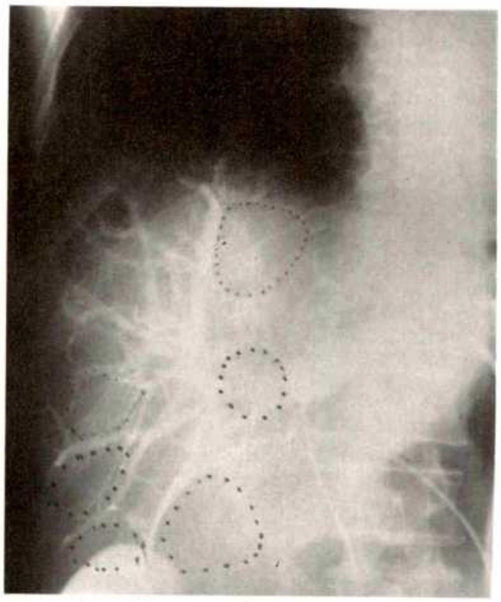

FIG. 14.—*Case* 3. Hepatogram showing the very large metastases. The obstructive jaundice was due to the deposit at the hilum.

Hepatography has not proved a completely reliable method of showing metastases, although large deposits are well demonstrated, and were seen to have decreased in size in *Cases* 2 and 3. It was difficult to visualize the smaller metastases, although Lavoie, Legare, and Viallet (1967) claim that metastases as small as 1 cm. in diameter can be detected in the venous phase. However, hepatography did show that the tip of the catheter was accurately sited in the left branch of the portal vein and that a trickle method will perfuse the whole liver. The liver scans also showed only the larger deposits, and care had to be taken to avoid false-positives. This was possible, as the liver was seen in each case at laparotomy and the metastases mapped. Liver scanning in *Case* 2 showed striking diminution in the size of the central deposits.

From the haematological studies none of the 4 patients developed leucopenia or thrombocytopenia. They received 5, 10, 15, and 10 g. of 5-fluoro-uracil respectively. Administered systemically, a dose of 5 g. in an average adult usually causes some degree of medullary depression.

The results of the liver-function tests were difficult to interpret as it was not always possible to distinguish the effects of the metastases from those of the 5-fluoro-uracil, and in *Case* 3 there was obstructive jaundice in addition. The results indicate that metastases have little effect on liver function unless jaundice occurs, although the alkaline phosphatase was a little raised before infusion in *Case* 2. In *Cases* 1, 2, and 4 the serum alkaline phosphatase and transaminases rose during the perfusion and there was a slight transient reduction in the serum albumin, with some elevation of the thymol turbidity. In view of this evidence of hepatocellular change it would seem that the perfusion had some deleterious effect on liver function in these 3 patients, but it was only of a temporary nature and to a mild degree. In *Case* 3 the severe initial derangement of the liver-function tests was presumably due to the deep obstructive jaundice, and as this faded with the perfusion the liver-function tests showed rapid improvement.

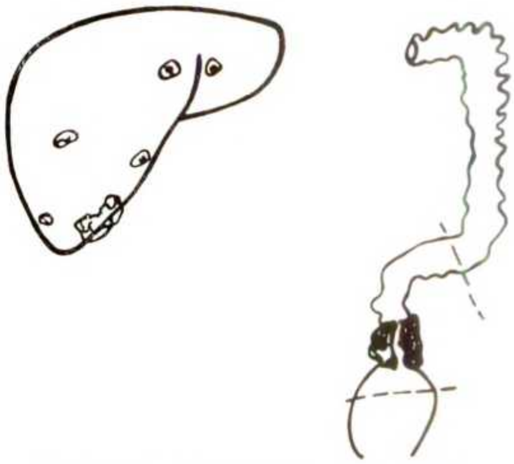

FIG. 15.—*Case* 4. Diagram of the operative findings.

In all 4 cases the perfusion had no effect on marrow function as judged by the haematological results. By introducing the cytotoxic agent directly into the portal system the liver appears to have taken the brunt of the reaction and to have had a cushioning effect on the bone-marrow, preventing haematopoietic medullary depression and allowing the patient to receive two or three times the normal intravenous dose of 5-fluoro-uracil. While this applies to the normal liver containing metastases the position is probably very different in cirrhosis. A patient not included in this series has subsequently been treated for multiple malignant hepatoma with cirrhosis by cytotoxic liver perfusion; he went into irreversible liver failure after receiving only 2 g. of 5-fluoro-uracil.

DISCUSSION

An attempt has been made to extend the treatment of carcinoma of the large bowel with liver metastases in the hope of an improved prognosis. The technique of liver perfusion by a cytotoxic agent via an umbilical vein cannula has proved straightforward to perform and the drip has been easy to maintain, comfortable for the patient, and with no serious side-effects apart from diarrhoea in 1 case. The cannula is turned off at a three-way tap and disconnected for periods during the day to allow full mobility, and there has been no difficulty in removing it without anaesthesia after 30 days.

The number of cases in this series is too small to justify conclusions but does perhaps show a trend. Comparison must be made with the survival time of patients treated by the conventional methods who fall into three groups: laparotomy only, laparotomy with palliative by-pass or colostomy, and palliative resection. From this point of view the figures quoted by Ellis (1971) are of interest and have been tabulated in *Table I*. The results of laparotomy alone and of palliative by-pass are poor, but one-third or more survive for more than 1 year after palliative resection. Of the 4 patients presented here, 3 were alive and well at 1 year, but 2 died during the next few months.

Table I.—RESULTS OF TREATMENT OF CARCINOMA OF THE LARGE BOWEL WITH LIVER METASTASES

AUTHORS	LAPAROTOMY ONLY	PALLIATIVE BY-PASS	PALLIATIVE RESECTION
Cady, Monson, and Swinton (1970)	—	—	33 per cent survived 1 year; 14 per cent survived 2 years
Ellis (1971)	All dead within 5 months	—	32 out of 86 cases survived for more than 1 year; longest survivor: 66 months
Flanagan and Foster (1967)	Average survival 6 months	—	—
Jaffe, Donegan, Watson, and Spratt (1968)	Average survival 5 weeks	—	—
McSherry, Cornell, and Glenn (1969)	Average survival 1·7 months	Average survival 8·9 months	Average survival 12·4 months

The only other report discovered of chemotherapy for hepatic neoplasms via the umbilical portal vein (Storer and Akin, 1966) gives depressing results; of 6 patients receiving 5-fluoro-uracil infusions, 4 had advanced hepatoma, 2 of these dying within a week and 2 showing some response. Two patients with carcinoma of the sigmoid colon and liver metastases were treated; 1 died 2 months after therapy and 1 was still alive at 5 months. It does seem that most of the patients in this series were at an advanced stage of terminal malignant disease.

The route of vascular access to the liver must be considered, as it has been claimed that the hepatic artery plays a more important part in the blood-supply to tumours of the liver than the portal vein. However, in 2 of the cases in the present series there was definite evidence that portal perfusion influenced the metastases; the deep jaundice disappeared in *Case* 3, and the metastases were seen to diminish on hepatography and liver scanning in *Case* 2. As metastases from carcinoma of the colon reach the liver via the portal blood it is logical that they may react to a cytotoxic drug introduced by the same route. Certainly an umbilical vein infusion is technically easier to institute and to maintain than a hepatic artery catheter which needs a major operation to insert and an apparatus producing supra-arterial pressure to bring about adequate liver perfusion. It may be suggested that the effect of portal vein perfusion is due to penetration of the drug into the systemic circulation, although some action on the liver must be allowed for, and it is likely that a cytotoxic agent passing through the liver is probably broken down fairly rapidly. Confirmatory evidence is supplied by the fact that far larger doses of 5-fluoro-uracil have been given via the umbilical vein without serious toxic side-effects than can be given systemically; in a recent patient not included in this series 24 g. were introduced into the portal vein in a 3-week period with no untoward complications. Further studies are needed to settle this point, with estimations of the level of the drug in the systemic blood. This method of treatment must be assessed in a much larger number of patients before its clinical value can be fully established. The present series can be regarded as a pilot study, demonstrating that the technique is practical and safe.

Other types of carcinoma of the gastro-intestinal tract with liver metastases may be suitable for treatment by umbilical vein perfusion, although carcinoma of the large bowel is the most appropriate as it not uncommonly metastasizes to the liver before producing local infiltration and lymph-node involvement. Carcinoma of the stomach and pancreas frequently show early infiltration and lymph-node involvement and only a few will be suitable for liver perfusion. Malignant hepatoma is another indication for this method of treatment, but has the disadvantage of a common association with cirrhosis, limiting the amount of cytotoxic agent that can be delivered to the liver, as in the case quoted above.

All 4 cases reported here had large metastases in the liver and there is obviously a limit to the regressive action of a cytotoxic drug on deposits of such dimensions. It is likely that smaller metastases would be more successfully dealt with, and microscopic aggregates of malignant cells might be eliminated if treated at an early stage. In *Case* 3 it seems probable that undetectable metastatic foci were present in the liver at the time of the original abdominoperineal resection, and these developed into the large metastases encountered 15 months later. This provides an argument for instituting a cytotoxic umbilical vein perfusion in all patients with operable carcinoma of the large bowel at the time of the primary resection. This method of treatment has now been embarked upon, but it will need some years and a large number of patients to assess whether the liver can be protected against metastases by this method. At the moment each patient is given 1 g. of 5-fluoro-uracil per day for 5 days after the operation. This does not delay discharge, and so far has not led to any side-effects or delay in healing.

A final point concerns the cytotoxic drug used, as there may be a better alternative to 5-fluoro-uracil. Melikian, Paton, Leeming, and Portman-Graham (1971) have shown that the liver plays an important part in folic acid metabolism, and absorption studies suggest that folic acid is converted into an active form in the liver, and this reaction may be depressed by 5-fluoro-uracil. Furthermore, 5-fluoro-uracil given in large doses can produce megaloblastic anaemia through inhibition of DNA–thymine synthesis, and macrocytosis with low serum-folate levels was recorded in 2 patients towards the end of chemotherapy which responded to folic acid. Thus, patients undergoing liver perfusion with this drug need to be given extra folic acid, especially if cirrhosis is present. Possibly, methotrexate may be preferable to 5-fluoro-uracil as its toxic effects can be reversed by folinic acid (Melikian, 1972).

Acknowledgements.—I should like to express my gratitude to Dr. A. Paton who indicated the possibility and uses of umbilical vein cannulation; to Dr. V. Melikian for his advice and encouragement, and for the metabolic studies he has done on patients with umbilical perfusions; to Mr. A. Clain, who referred *Case* 3; to Dr. P. Carpenter for the radiological studies and Dr. K. Chackett for the liver scans; to Dr. S. Kelly, who organized the investigations so competently; to Sister C. Walsh and the nursing staff for their care in looking after the perfusions; and to the patients for their willing co-operation.

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Addendum.—*Case* 2 died 24 months after treatment following a short terminal illness of a few weeks.

THE CHEMOFUSOR: A NEW APPARATUS FOR MAINTAINING CONTINUOUS INTRA-ARTERIAL INFUSION CHEMOTHERAPY

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SUMMARY

A new apparatus for continuous intra-arterial infusion cancer chemotherapy in ambulant patients is described.

CONTINUOUS intra-arterial infusion chemotherapy has now been in use for some years and has acquired a small but important role in the management of patients with malignant disease (Burn, Johnston, Davies, and Selwood, 1966). When the technique was first introduced, gravity was used to overcome arterial pressure and thus maintain a continuous forward flow. The chamber containing the infusate was set at a sufficient height above the cannulated artery to prevent back-flow.

The 'gravity-feed' method worked but it was cumbersome. Large volumes of infusate were necessary during each 24-hour period and mobility of the patient was restricted. With therapy often continuing for many weeks the disadvantages of the 'gravity-feed' method were prohibitive.

Later methods used to maintain constant intra-arterial flow included a variety of electrically driven slow-injection pumps and the portable Fenwall pressure infusor (Krant, Hall, Lloyd, and Pasterson, 1961). The former again had the disadvantage of confining the patient to bed or chair. The latter was a device in which the required pressure was transmitted to the container by means of an inflatable cuff. It allowed the patient mobility but required constant surveillance because the pressure within the inflated cuff dropped with use.

Subsequently, more refined apparatuses have been designed which obviate most of the previous disadvantages. The Watkins chronometric infusion pump, designed in the U.S.A., is an example whereby long-term continuous intra-arterial chemotherapy is possible in ambulatory patients (Watkins, 1963).

We have recently designed a small portable infusion pump which is easy to assemble, is reliable, can be safely used in out-patients, and is relatively inexpensive. We have named the apparatus the 'Chemofusor'.

THE CHEMOFUSOR

The Chemofusor is illustrated in *Figs.* 1 and 2. The outer casing (a) is of circular construction measuring 10·5 cm. in diameter by 4·5 cm. in depth. The casing is made of anodized aluminium with a Perspex cover plate (n). The cover screws on to three threaded locating pins (o). The assembled apparatus weighs 312 g.

The Chemofusor's power is supplied by a miniature mercury battery cell (g), manufactured by Mallory Batteries Ltd., No. RM 625-N. Two cells are used with a capacity of 300 mAH and weighing 8 g. each, with a minimum working life of 4 weeks. The voltage supply of 2·7 V. is fed through a dropping resistor to a transistorized circuit which stabilizes and boosts the pulsed supply to the motor unit. This motion is transmitted to a capstan positive-drive movement and then through nylon gear trains to the output shaft. A single roller (e) fixed to the drive plate rotates against the infusion tubing and creates the pumping action. Miniature stainless-steel ball races and jewelled bearings are used on the drive system. A clutch is incorporated to protect the movement from any misuse. The required rate of delivery of the infusate is predetermined within the range of 5–10 ml. every 24 hours as required. The movement has the fail-safe factor that if any component fails it is impossible for the pumping head to increase its speed.

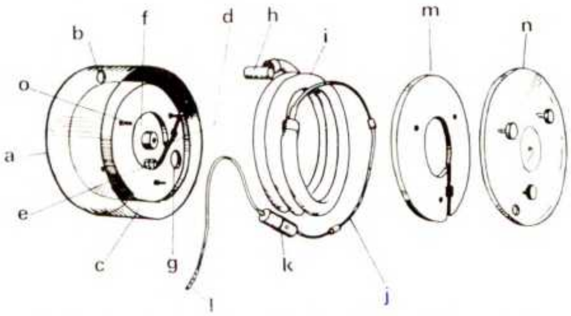

FIG. 1.—The components of the Chemofusor. a, Outer case. b, Reservoir location hole. c, Reservoir-containing space. d, Pump tube location. e, Pump roller. f, Bottom pump track. g, Battery recess. h, Self-sealing cap. i, Reservoir. j, Pump tube. k, Non-return valve. l, Graduated catheter. m, Top pump plate. n, Cover plate. o, Locating pins.

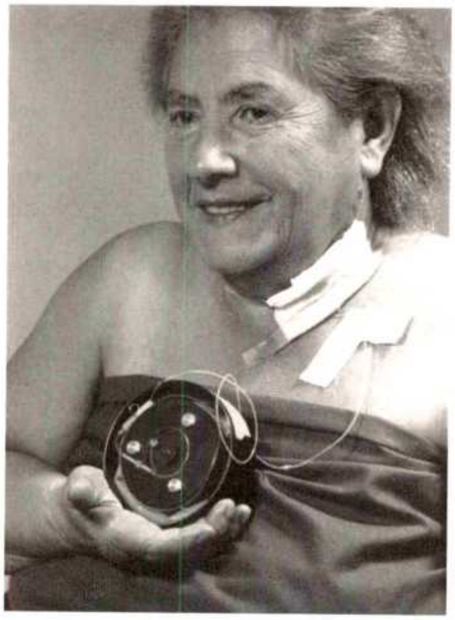

FIG. 3.—A patient undergoing continuous intra-arterial infusion chemotherapy for a carcinoma of the tongue.

The electromechanical movement and pump head are enclosed in a central metal container, measuring 7·7 cm. in diameter and 3·8 cm. in depth. This container is rigidly fixed inside the larger outer casing.

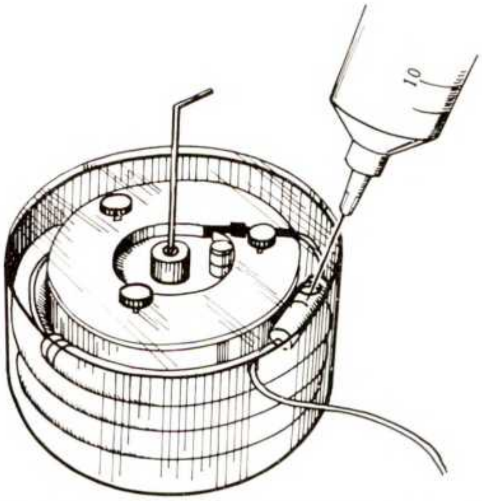

FIG. 2.—The complete Chemofusor, illustrating the self-sealing diaphragm on the non-return valve which can be used for independent injection. The central key shown on the figure is detachable and is used to prime the pumping tube manually when the cover plate is in position.

The cavity between the two containers (c) is used to house the drug-reservoir (i). This sac is made of 1-cm. diameter 'lay-flat' latex rubber tube and has a volume of 50 ml. One end of the reservoir has a self-sealing membrane (h) which is located on the underside hole of the outer casing (b). This enables the Chemofusor to be refilled without removal of the reservoir, which is retained in position until treatment is completed.

The drug reservoir is coiled into the cavity and its exit end connects to the pump tubing (j). This tubing, which is made of 1-mm.-bore silicone rubber, lies in the pump track (d) and is positioned by two locating sleeves.

The pump track is in two parts. The bottom track (f) is situated in the main pump container and the upper track (m) is removable. The pumping tube can be primed manually by rotating the roller (e). The sleeves on the pump tubing fit into the recessed locations in the separate halves of the pump track.

A special graduated intra-arterial catheter (l) made of PTFE is attached to a miniature disposable non-return valve (k). The valve is 3·2 cm. long and 6 mm. in diameter and it contains a self-sealing diaphragm for independent injection (*Fig.* 2). When connected to the pump tubing the valve is located in the undersurface of the cover plate (n).

The drug reservoir, pump tubing, intra-arterial catheter, and non-return valve are all provided prepacked by the C.S.S.D. These disposable components may be sterilized at 120° C., 15 p.s.i. in the autoclave or by gamma radiation.

When assembled the Chemofusor is worn by the patient in a carrying holder and the position can be adjusted for comfort. When in action the pump produces an unobtrusive ticking which indicates to the patient that the device is working. *Fig.* 3 shows a patient undergoing continuous infusion therapy for a malignant lesion of the tongue.

Acknowledgements.—We are grateful to Mr. P. Clark and Mr. G. Williams for the illustrations and to Miss D. Lippiatt for secretarial assistance.

The Chemofusor is manufactured by Keymex Engineering (Sales Ltd.), Oldfield Trading Estate, Sutton, Surrey (Tel. 01-644-7932). The batteries are supplied by Mallory Batteries Ltd., Gatwick Road, Crawley, Sussex.

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PERIPHERAL GANGRENE AS THE PRESENTATION OF MYELOPROLIFERATIVE DISORDERS

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SUMMARY

Six cases of myeloproliferative disorders (polycythaemia vera in 4, idiopathic thrombocythaemia in 2) are reported. In every case the presenting feature was pain associated with peripheral ischaemia and gangrene. Initial treatment by chemical sympathectomy affords symptomatic relief and improvement in foot circulation, though correction of the haematological abnormality is probably the most important factor in reversing the ischaemic process.

THE myeloproliferative diseases may be defined as disorders of myeloid tissue which result in the inappropriate and excessive production of one or more of the formed elements of the blood. They include such diseases as polycythaemia vera, idiopathic thrombocythaemia, and myeloid leukaemia.

Over the years since the original descriptions of polycythaemia vera as a clinical entity by Vaquez (1892) and Osler (1903) it has become increasingly recognized that this disease may be accompanied by complications involving the vascular system, and the incidence of such complications in polycythaemia vera is around 30 per cent (Brown and Griffin, 1930; Norman and Allen, 1937; Burris and Arrowsmith, 1953). Only a small proportion of cases, however, have been associated with peripheral vascular lesions of the limb vessels and it is rare for peripheral gangrene to be the presenting feature of the disease. Similarly, ischaemic necrosis of the extremities is an uncommon manifestation of idiopathic thrombocythaemia and only an occasional case report exists of peripheral gangrene as a presentation of either polycythaemia vera (Moore, Blaisdell, and Hall, 1964) or of the closely related disorder, idiopathic thrombocythaemia (Wellens, 1967).

This paper reports 6 patients with a myeloproliferative disorder (polycythaemia vera in 4, idiopathic thrombocythaemia in 2), all of whom presented within a 10-month period with peripheral gangrene as the initial manifestation of their disorder.

CASE REPORTS

Case 1.—J. C., a 37-year-old male, presented in April, 1970, with pain and a gangrenous plaque on the pulp of the left thumb. He was known to have had a right lumbar sympathectomy in 1964 for intermittent claudication and gangrene of the right great toe, but he had remained symptom-free thereafter. Examination revealed mild atrophic changes of the toes and fingers and a necrotic plaque 1·5 cm. in diameter in the pulp of the left thumb. The radial and ulnar pulses were absent in the right arm. Lower-limb examination showed the posterior tibial pulse to be diminished in the right leg and absent in the left leg. Dorsalis pedis pulses were absent. The pulse-rate was 64 per minute and the rhythm regular. The blood-pressure was 120/80 mm. Hg, the heart-sounds normal, and the electrocardiogram showed no abnormality. The chest radiograph was also normal. There was no splenomegaly. Blood examination showed the following results (*Table I*): haemoglobin, 18·9 g. per cent; packed-cell volume, 54 per cent; white-cell count, 11,700 per c.mm.; platelet count, 275,000 per c.mm. Random blood-sugars were 144 and 105 mg. per cent and the Wassermann reaction, Khan test, and Reiter complement-fixation test were negative.

Further blood examination in May, 1970, revealed a haemoglobin of 16·4 g. per cent and a packed-cell volume of 49 per cent. The patient was admitted in September, 1970, for further haematological investigations. Blood-volume studies by the ^{51}Cr method (*Table I*) revealed a red-cell mass of 41·38 ml. per kg., a plasma volume of 39·8 ml. per kg., and a total blood-volume of 81·2 ml. per kg.

A diagnosis of polycythaemia vera was made and venesection of 400 ml. of whole blood was performed; 5 m.c. of radioactive phosphorus (^{32}P) were then injected intravenously. Healing occurred with minimal loss of tissues and the patient remained symptom-free until February, 1971, when he presented with pain and gangrene of the tips of the middle and index fingers of the right hand (*Fig.* 1). Elevated haematological values were again found. Venesection was performed and a further 5 m.c. of ^{32}P were given intravenously. Although the haematological values were rapidly restored to normal, residual swelling and pain due to superadded infection in relation to the right middle finger prevented full symptomatic relief for several months.

Case 2.—C. W., a 74-year-old female, presented in May, 1970, with a 2-week history of pain, coldness, and cyanosis in the distal two phalanges of the index, middle, and ring fingers of the right hand. One transient similar episode had occurred 3 months previously. She had suffered from rheumatic fever 40 years previously. Examination showed a dusky cyanosis with punctate necrotic plaques in the pulps of the right second, third, and fourth fingers. Light touch sensation was absent in the distal phalanges of these fingers. All the pulses were palpable in both arms. The pulse-rate was 80 per minute and the rhythm regular. The blood-pressure was 200/100 mm. Hg, the heart-sounds were normal, and an electrocardiogram showed no abnormality. A chest radiograph was also normal. Blood examination showed the following results (*Table I*): haemoglobin, 18·2 g. per cent; packed-cell volume, 57 per cent; white-cell count, 11,300 per c.mm.; platelet count, 370,000 per c.mm. Blood-volume studies using the ^{51}Cr method revealed a red-cell mass of 36·5 ml. per kg., a plasma volume of 35·2 ml. per kg., and a total blood-volume of 71·7 ml. per kg. The Wassermann reaction, Khan test, and Reiter complement-fixation test were all negative. A diagnosis of polycythaemia vera was made. Venesection of 500 ml. of whole blood was performed and 4 m.c. ^{32}P were injected intravenously.

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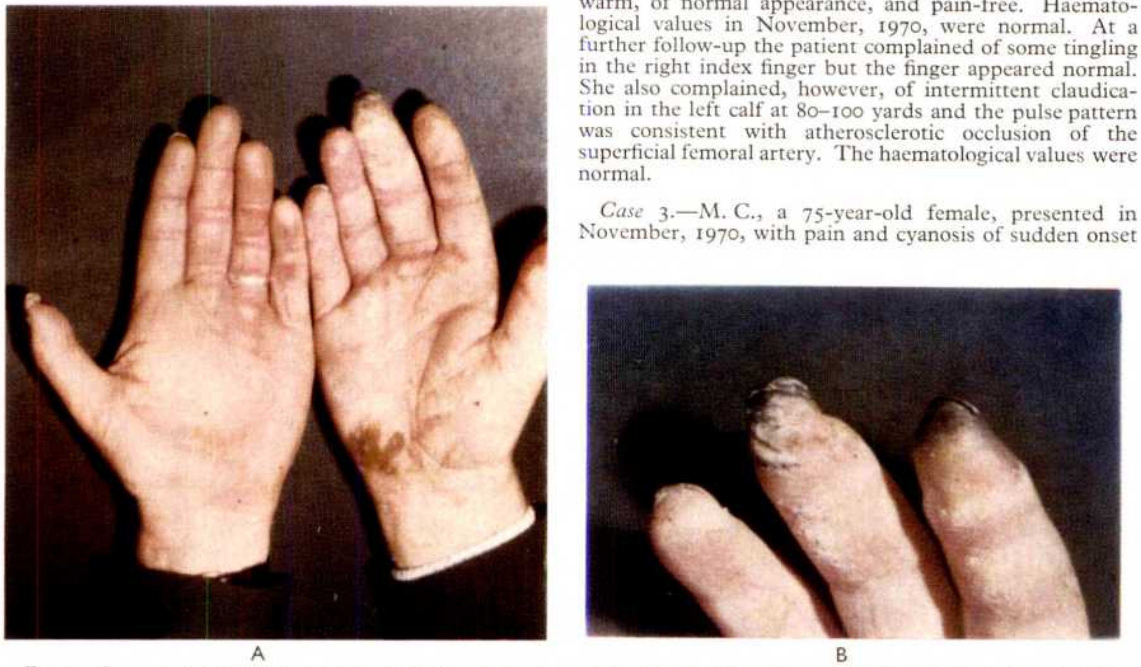

FIG. 1.—*Case* 1. A, The necrotic area at the tip of the middle finger of the right hand is shown at its early stage. Note that the earlier lesion at the tip of the left thumb has healed with minimal loss of pulp tissue. B, A few weeks later the line of demarcation of the necrotic tip of the right middle finger is evident. Gangrenous change is also evident in the index finger and a small necrotic plaque with a blister is seen at the tip of the ring finger.

Table I.—DETAILS OF 6 PATIENTS WITH MYELOPROLIFERATIVE DISEASE AND PERIPHERAL GANGRENE

CASE	AGE AND SEX	SITE OF GANGRENE	HAEMOGLOBIN (g. per cent)	PACKED-CELL VOLUME (per cent)	PLATELET COUNT (per c.mm.)	RED-CELL MASS* (mg. per kg.)	DIAGNOSIS
1. J. C.	37 M.	Upper limb	18·9	54	275,000	41·38	Polycythaemia vera
2. C. W.	74 F.	Upper limb	18·2	57	370,000	36·5	Polycythaemia vera
3. M. C.	75 F.	Lower limb	17·9	60	280,000	41·7	Polycythaemia vera
4. E. A.	62 M.	Lower limb	18·1	51	1,790,000	50·7	Polycythaemia vera and thrombocythaemia
5. J. F.	75 M.	Lower limb	12·3	36	1,500,000	—	Idiopathic thrombocythaemia
6. M. C.	67 M.	Lower limb	12·2	35	859,000	—	Idiopathic thrombocythaemia

* Upper limit of normal range for red-cell mass is 35 ml. per kg. for males and 30 ml. per kg. for females (Nadler, Hidalgo, and Bloch, 1962).

At follow-up review 1 month later the fingers were warm, of normal appearance, and pain-free. Haematological values in November, 1970, were normal. At a further follow-up the patient complained of some tingling in the right index finger but the finger appeared normal. She also complained, however, of intermittent claudication in the left calf at 80–100 yards and the pulse pattern was consistent with atherosclerotic occlusion of the superficial femoral artery. The haematological values were normal.

Case 3.—M. C., a 75-year-old female, presented in November, 1970, with pain and cyanosis of sudden onset in the left middle toe and a small area of gangrene of its pulp. There was also a painful gangrenous patch of skin, 2 cm. in diameter, over the lateral aspect of the left lower leg. Examination showed oedema of both ankles and pallor of the left foot on elevation. The left posterior tibial pulse, left dorsalis pedis pulse, and right posterior tibial pulse were absent. The right dorsalis pulse was present though diminished. An abdominal aortic bruit was audible at the aortic bifurcation consistent with stenosis due to atherosclerosis at that level. A plain radiograph revealed calcification of the abdominal aorta. The pulse-rate was 70 per minute and the rhythm regular. The blood-pressure was 150/75 mm. Hg, the heart sounds were normal, and an electrocardiogram showed no abnormality. A chest radiograph and intravenous pyelography were normal. Blood examination gave the following results (*Table I*): haemoglobin, 17·9 g. per cent; packed-cell volume, 60 per cent; white-cell count, 12,500 per c.mm.; platelet count, 280,000 per c.mm.; fasting blood sugar, 70 mg. per cent. Blood-volume studies using the ^{51}Cr method revealed a red-cell mass of 41·7 ml. per kg., a plasma volume of 34·7 ml. per kg., and a total blood-volume of 76·5 ml. per kg. A diagnosis of polycythaemia vera was made. Initial treatment was by left lumbar chemical sympathectomy by phenol injection and this resulted in pain relief and improvement in the foot circulation. Thereafter, venesection of 500 ml. of whole blood was performed and 5 m.c. of ^{32}P were given intravenously.

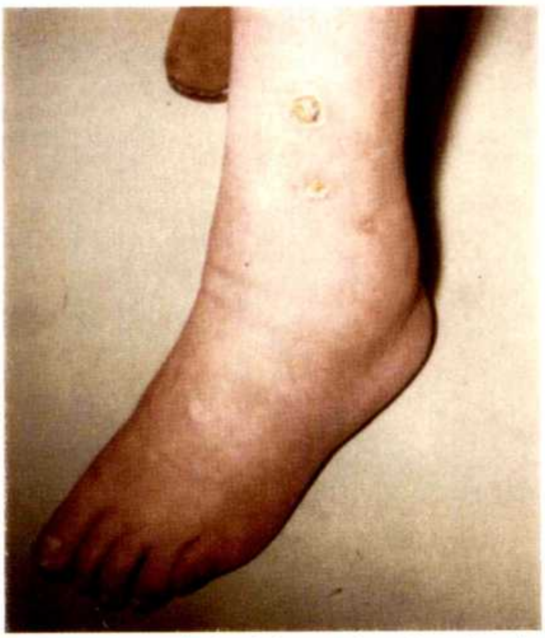

FIG. 2.—*Case* 3. The sharply demarcated area of necrosis on the lateral aspect of the left lower leg is seen in the healing phase. The left third toe has resumed a virtually normal appearance with minimal loss of tissue.

At follow-up in December, 1970, the foot was pain-free and the toe had healed with minimal loss of tissue. The area of necrosis in the lower left leg was pain-free and well localized (*Fig.* 2). In January, 1971, the haematological values were normal.

Case 4.—E. A., a 62-year-old male with plethoric facies, presented in September, 1970, with a 2-month history of rest pain in the left great toe and forefoot. There was no history of intermittent claudication. He had suffered from chronic bronchitis for 4 years. Examination showed a gangrenous plaque (1 × 0·75 cm.) on the tip of the left great toe and cyanosis of all the toes. There was no evidence of trophic changes. All the pulses were palpable in both legs though the dorsalis pedis pulses were diminished. The pulse-rate was 80 per minute and the rhythm regular. The blood-pressure was 150/100 mm. Hg, the heart-sounds were normal, and an electrocardiogram showed no abnormality. A chest radiograph showed changes of chronic bronchitis and emphysema. The tip of a firm spleen was palpable. Arteriography showed patency of all the main vessels including the tibial vessels in both limbs. Blood examination gave the following results (*Table I*): haemoglobin, 18·1 per cent; packed-cell volume, 51 per cent; white-cell count, 14,100 per c.mm.; platelet count, 1,790,000 per c.mm. Blood-volume studies using the ^{51}Cr method revealed a red-cell mass of 50·7 ml. per kg., a plasma volume of 48·8 ml. per kg., and a total blood-volume of 99·6 ml. per kg. Sternal marrow examination revealed normoblastic erythropoiesis, normoblastic granulopoiesis, and megakaryocyte hyperplasia. There was no evidence of Philadelphia chromosome.

A diagnosis of myeloproliferative disease with both polycythaemia and thrombocythaemia was made. Initial treatment by chemical sympathectomy of the left lumbar chain by phenol injection gave considerable relief from pain and, thereafter, venesection of 1000 ml. of whole blood was performed and 5 m.c. of ^{32}P were given intravenously.

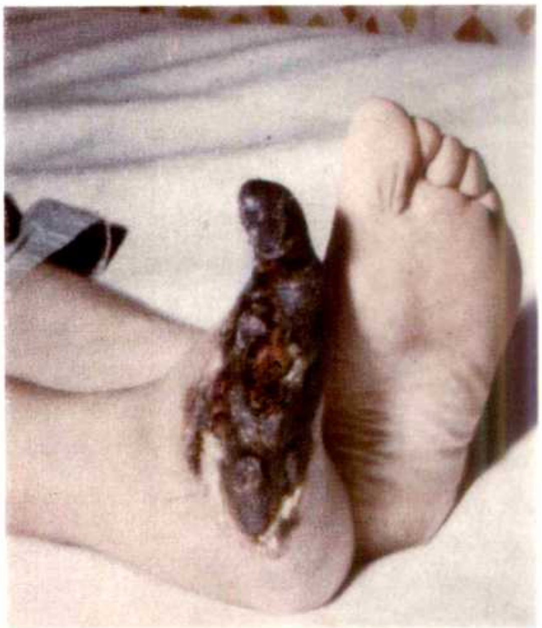

FIG. 3.—*Case* 5. Extensive gangrene of the right forefoot with loss of the lateral four toes.

At the follow-up review in January, 1971, the patient was pain-free and the left great toe had healed with minimal loss of tissue.

Case 5.—J. F., a 69-year-old male, presented in February 1970, with rest pain in the right foot of 2 months' duration. There was no history of intermittent claudication. Examination showed gangrene of the entire right third toe and signs of incipient gangrene in the fourth toe. All the lower limb pulses were palpable except for an absent right dorsalis pedis pulse. There were no atrophic changes and there was a good angle of vascular sufficiency. The pulse-rate was 96 per minute and the rhythm regular. The blood-pressure was 150/100 mm. Hg, the heart-sounds were normal, and an electrocardiogram showed no abnormality. A chest radiograph was also normal. The Wassermann reaction, Khan test, and Reiter complement-fixation test were all negative. Arteriography revealed a right proximal popliteal atherosclerotic occlusion but the distal vessels were patent. The left popliteal artery was narrowed but the distal vessels were patent. Blood examination gave the following results (*Table I*): haemoglobin, 12·3 g. per cent; packed-cell volume, 36 per cent; white-cell count, 7900 per c.mm.; platelet count, 1,500,000 per c.mm. Sternal marrow examination revealed normoblastic erythropoiesis, normal granulopoiesis, and well-marked megakaryocyte hyperplasia. A diagnosis of idiopathic thrombocythaemia was made. Initial treatment was by right lumbar chemical sympathectomy by phenol injection. Thereafter 3 m.c. of ^{32}P were given intravenously.

At follow-up in April, 1970, the platelet count had fallen to 603,000 and the pulse pattern remained unchanged. However, gangrene had spread to involve all of the toes, and although by July, 1970, the platelet count had fallen to 470,000, gangrene had extended to involve the lateral part of the forefoot (*Fig.* 3). Below-knee amputation was performed, and at operation all the stem arteries at the level of division bled briskly. In November, 1970, the patient was well and symptom-free but the platelet count was again markedly elevated, at 2,050,000 per c.mm. A further injection of 4 m.c. of ^{32}P was given intravenously. In January, 1971, he remained well and the platelet count was 460,000 per c.mm.

Case 6.—M. C., a 67-year-old male, presented in October, 1970, with pain and discoloration of the toes of both feet of 2 weeks' duration. The symptoms were worse on the left foot and had become more severe over the 2 days prior to presentation. Examination revealed purple discoloration of all the toes of the left foot which was more marked in the medial three toes, where there was loss of capillary flow, coldness, and loss of light touch sensation. The right foot showed cyanosis of the medial three toes and a gangrenous plaque, 1·5 cm. in diameter, on the pulp of the right great toe with loss of light touch sensation of the first and second toes. Apart from slightly diminished dorsalis pedis pulses all the limb pulses were present and normal. The pulse-rate was 112 per minute and the rhythm regular. The blood-pressure was 160/70 mm. Hg, the heart-sounds were normal, and an electrocardiogram showed sinus rhythm with right bundle branch block. A chest radiograph was normal. There was no splenomegaly. Blood examination gave the following results (*Table I*): haemoglobin, 12·2 g. per cent; packed-cell volume, 35 per cent; white-cell count, 8300 per c.mm. The platelet count on 9 Nov. was 859,000 and on 16 Nov. 775,000. A provisional diagnosis of idiopathic thrombocythaemia was made and initial treatment by chemical sympathectomy to the left lumbar chain by phenol injection afforded some relief of pain but did not materially alter the circulatory status of the foot. Two m.c. of ^{32}P were injected intravenously. However, before further investigations could be planned the patient died as a result of peritonitis from an unknown cause. Autopsy revealed minimal atherosclerosis and patency of all the arteries including those in the lower limbs.

DISCUSSION

Ischaemic gangrenous changes in the digits are most often seen in relation to arterial occlusions in atherosclerosis, but are also found in diabetes mellitus, rheumatoid arthritis, and scleroderma. Other causes include cervical rib, cardiac gangrene, drug-induced angiopathy, and syphilis. Much less common in producing gangrene of the extremities are polycythaemia vera and idiopathic thrombocythaemia. In particular, it is unusual for peripheral gangrene to be the presenting feature, although isolated case reports exist of this presentation of polycythaemia (Moore and others, 1964) and of idiopathic thrombocythaemia (Wellens, 1967).

The group of 6 patients reported here is unusua that they all presented within a 10-month period. the time of their presentation there was no histor a myeloproliferative disorder but routine bl examination indicated the diagnosis. A diagnosi polycythaemia may be suspected from elevated le for haemoglobin and packed-cell volume, but si these values may on occasions be only margin raised, or in the normal range, blood-volume stu to measure the red-cell mass are essential. interest in the present group of patients is the existence of atherosclerosis in every case, and it r be that for the full development of the periph ischaemia and necrosis a diseased arterial tree essential in addition to the myeloproliferative disor Nevertheless, this group of patients would not h been expected to suffer a threat to viability on basis of their arterial lesions alone.

The problem of management of these patient complex. Initial relief of pain and improvement local vascularity may be provided by chem sympathectomy, and in the present series symp matic relief was afforded to the patients with low limb ischaemia, all of whom received a phenol blo In these patients it is difficult to assess, therefore, respective parts played by chemical sympathecto as opposed to correction of the haematologi abnormality in the management of their sympto However, it is of interest that benefit followed resto tion of the haematological values to the norr range in the 2 patients with upper-limb ischaemia whom no sympathectomy was performed. It see likely, therefore, that correction of the blood abn mality may be the most important factor in reversi the ischaemic process.

Acknowledgements.—I wish to thank William Reid, Consultant Surgeon in charge of Peripheral Vascular Unit, Glasgow Royal Infirm and Belvidere Hospital, for his permission a encouragement to publish these case reports. I m also acknowledge the expert haematological adv freely given by Dr. MacDonald, Consultant Haematology, Glasgow Royal Infirmary. The help criticism provided by Mr. Reid and Dr. MacDon during preparation of the manuscript is mu appreciated.

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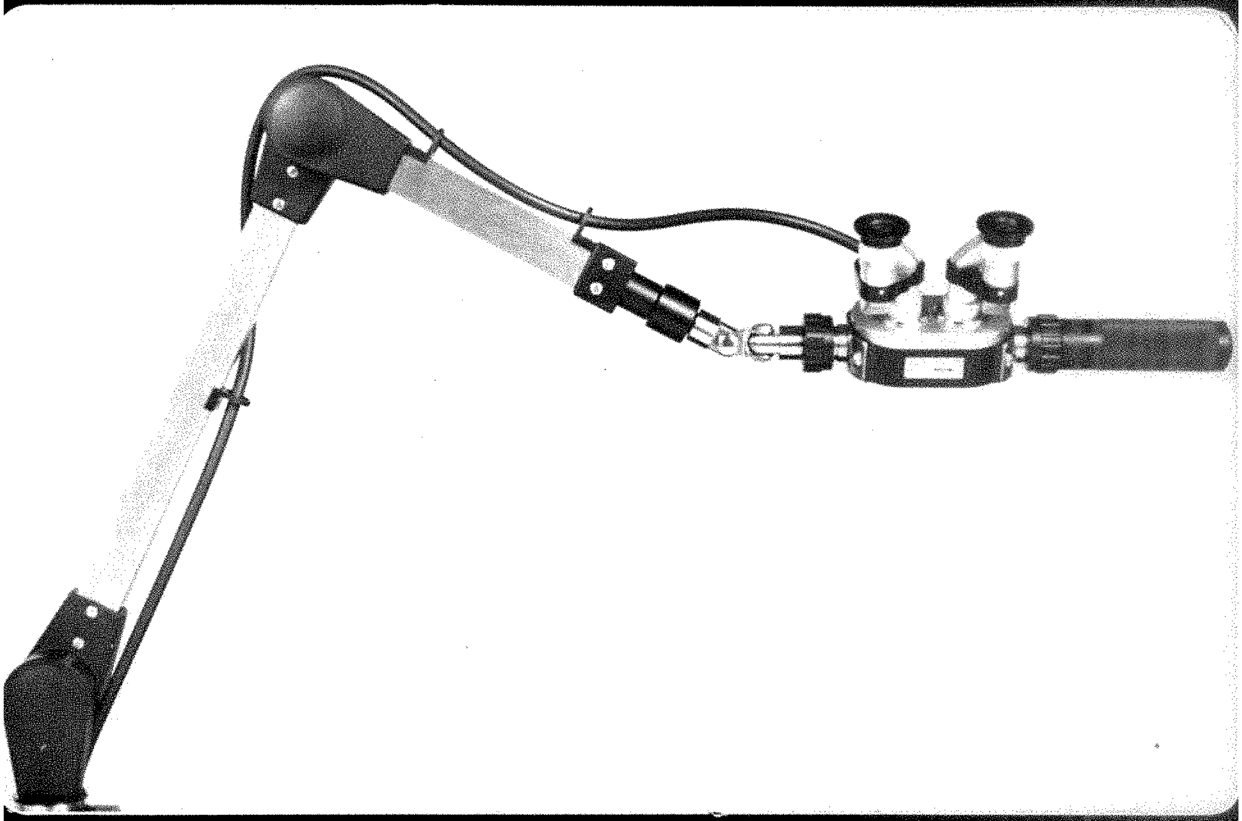

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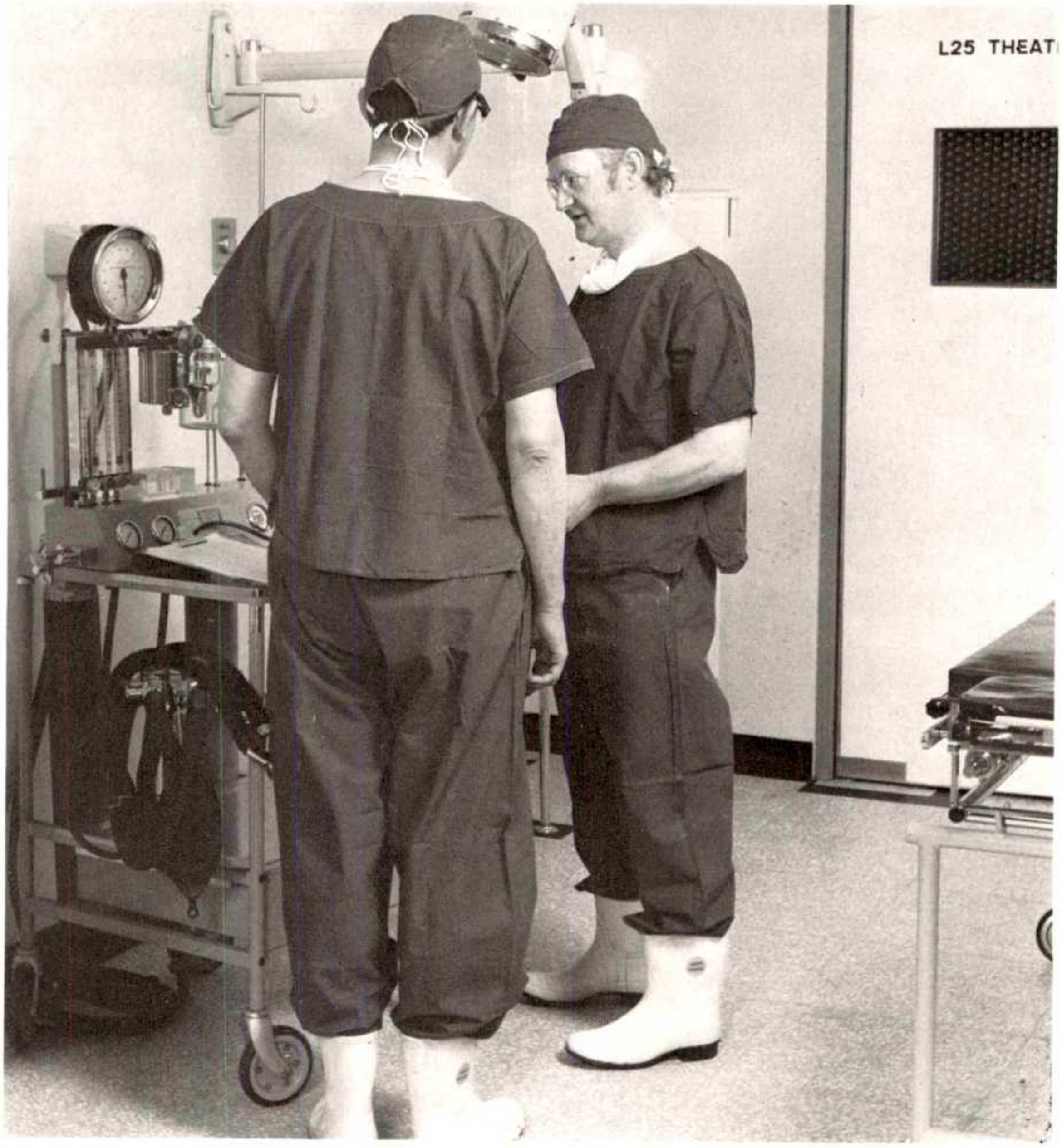

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MANAGEMENT OF THE THROMBOSED EXTERNAL AND INTERNAL ARTERIOVENOUS SHUNTS

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SUMMARY

Two methods for salvaging thrombosed internal and external arteriovenous shunts are described. Thrombosed external shunts have been cleared by phlebotomy or arteriotomy, while internal shunts have been reconstructed by end-to-end anastomosis of the artery and vein proximal to the occlusion.

LONG-TERM haemodialysis became possible when Quinton, Dillard, and Scribner (1960) introduced the external arteriovenous shunt: a Teflon Silastic conduit connecting a peripheral artery and vein. This means of access to the circulation has been well accepted, but problems are numerous (Byrne, Stevens, Weaver, Maxwell, and Reemtsma, 1971; Haimov, Singer, and Schupak, 1971; Klauber, Belinsky, Morehouse, and Mackinnon, 1971). Thrombosis in the arterial or venous cannula is common, often requiring resiting of the tip. The internal arteriovenous fistula introduced by Brescia, Cimino, Appel, and Hurwich (1966) is preferred, but thrombosis still occurs occasionally at the site of the fistula (Haimov and others, 1971; Hadjiyannakis, 1972).

Two methods are described for salvaging shunts which have thrombosed and which conventional methods have failed to clear. For external shunts the thrombus is removed via an incision in the vessel beyond the Teflon tip. A rather unusual case prompted the author to employ open thrombectomy and this method is described first. Thrombosed internal fistulae are refashioned by end-to-end anastomosis of the vessels proximal to the block. Seven initial cases are described in which these methods have been utilized.

THROMBOSED EXTERNAL TEFLON SILASTIC SHUNTS

Five external shunts were restored to normal function after conventional means had failed. Most thrombi, if recognized early, can be removed by heparinized saline and suction. Resistant thrombi can frequently be dispersed with urokinase; 5000 units are instilled into vessels and left for 1 hour, and suction is then applied with heparinized saline to rinse the vessel. If thrombi persist the shunt may still be salvaged by the following surgical manœuvres.

Method.—Angiograms were performed to establish the extent of the thrombosis (Berne, Turner, and Barbour, 1971). In all 5 cases the veins were thrombosed and in 2 there was also arterial thrombosis.

Under local anaesthesia a 2-cm. transverse skin incision was made over the site of the thrombosed vessel. A sphygmomanometer cuff was inflated to prevent embolization of the thrombus and to facilitate the phlebotomy. The vein was then opened transversely 0·5 cm. proximal to the thrombus. When the thrombus extended into a venous branch the phlebotomy was made above the junction to facilitate clearing (*Fig.* 1). The incision need only to be 2–3 mm. across the front of the vein. In the majority of cases the thrombus discharged itself spontaneously through the incision but this was aided by irrigation with heparinized saline via the Silastic tube of the shunt.

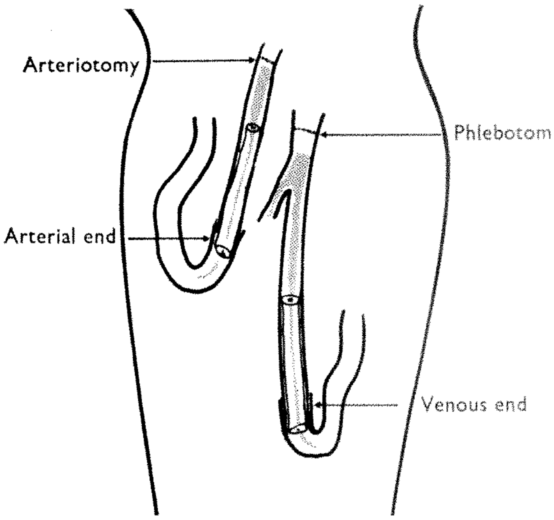

FIG. 1.—Technique of clearing thrombosed external shunts.

The transverse incision in the vein was closed with continuous 0000000 silk and the skin was closed with 0000 silk. To clear thrombi from the arterial side a similar incision was made, the vessel being occluded with a bulldog clamp proximal to the arteriotomy, and the artery was opened transversely 0·5 cm. proximal to the thrombus. The clot was removed by irrigation and the vessel closed with 0000000 silk.

CASE REPORTS.—Four of the 5 cases had had two or three previous revisions of shunts in the same forearm.

Case 1.—A 13-year-old girl with a 4-month-old Teflon Silastic shunt complained of acute pain at the venous end. Five minutes later blood started to ooze from the venous exit site. At the same time swelling of the arm was noted. By clamping the arterial end of the tube the haemorrhage was controlled. Under local anaesthesia the old wound was explored and it was found that the Teflon tip had been dislodged further up the vein and the Silastic tube was free in the subcutaneous tissues. The proximal part of the cephalic vein was ligated. Because of the swelling the exact position of the Teflon cannula could not be established. A new venous end was inserted higher up in an adjacent vein through a new incision but the flow was poor. A phlebogram showed that the missing Teflon tip was blocking the lateral branch of the main cephalic vein. Fortunately it had stopped near the elbow (*Fig.* 2). A 2-cm. transverse skin incision was made over the tip and a sphygmomanometer cuff was inflated. A 2-mm. transverse incision was made in the vein and the Teflon tip with a 4-cm. thrombus attached to it was removed. The incision was closed with 0000000 silk and the shunt remained patent for a further 3 months when the patient had a successful cadaveric renal transplant.

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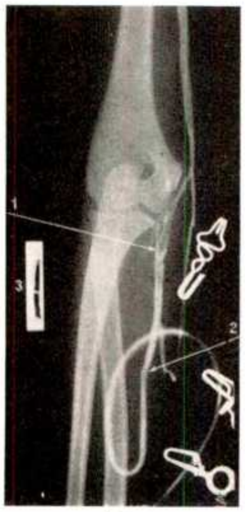

FIG. 2.

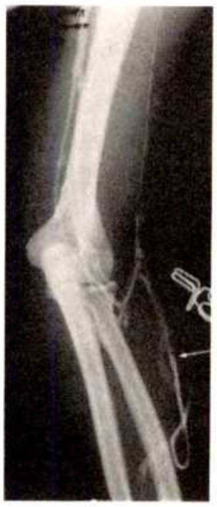

FIG. 3.

FIG. 2.—*Case* 1. Angiogram, showing (1) the dislodged Teflon tip blocking the adjacent vein, (2) the Teflon tip of the new shunt. (3) Photograph of the removed tip which is full of thrombus.

FIG. 3.—*Case* 3. Angiogram of the thrombosed vein.

The success in this patient led to the use of phlebotomy in the following cases.

Case 2.—A 21-year-old female had had a functioning external shunt for 2 years. Because of a thrombosis both arterial and venous ends had been revised and the tips were now near the elbow. Three months later the new shunt thrombosed. Angiography showed that both the artery and vein were thrombosed. The vein and artery were declotted by phlebotomy and arteriotomy. Four months later the shunt was still in use.

Case 3.—A 21-year-old female had had three revisions of an external shunt in her right arm. This shunt eventually thrombosed again and angiography showed extensive thrombus in the vein (*Fig.* 3). A thrombectomy was performed and the shunt functioned for 25 days. The patient was started on anticoagulants but the venous end of the shunt again thrombosed and was cleared twice by the above technique, each new incision being 0·5 cm. proximal to the previous one. Following this the vein remained patent for 3 months.

Case 4.—A 38-year-old female developed a thrombosis in an external shunt after 6 months, and 10 days after the construction of an internal fistula in the other arm. The artery was declotted easily with heparinized saline, and the vein was declotted via a phlebotomy (*Fig.* 1). One month later the shunt was still functioning.

THROMBOSED INTERNAL ARTERIOVENOUS FISTULAE

Of 40 internal fistulae constructed during the past 2 years, 4 thrombosed and local attempts to clear the vessels were consistently unsuccessful. Two further fistulae which thrombosed have been reconstructed by end-to-end anastomosis proximal to the occlusion by the following technique.

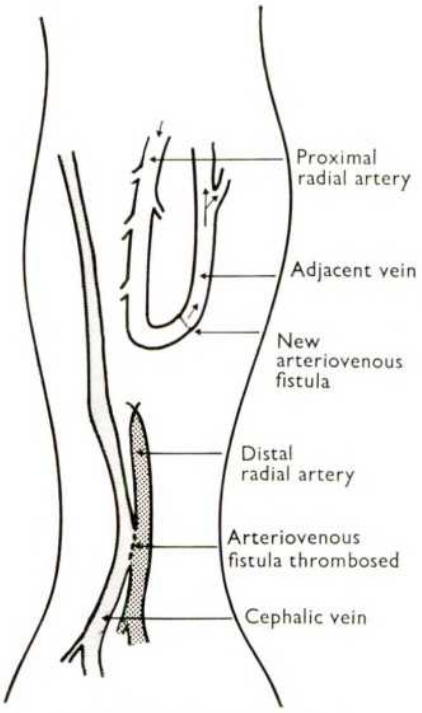

FIG. 4.—Technique used in *Case* 6.

Method.—Arterial and venous patterns were mapped out on the forearm. Under local anaesthesia a transverse incision was made 3–4 cm. proximal to the previous thrombosed fistula. In both cases the artery and vein were occluded. The artery was cleared and anastomosed end-to-end to an adjacent vein with 0000000 silk. The artery was formed into a loop, leaving the vein in a straight line.

A thrombosed vein can be used after declotting but it is recommended to utilize a fresh vein if there is one close by.

Cases 5, 6.—A 51-year-old male with chronic renal failure and congestive cardiac failure was started on home dialysis. He had had a functioning internal fistula for 7 months and an external shunt in the other arm which had been revised twice. The venous end of the shunt thrombosed and was declotted via a phlebotomy (*Case* 5). Twenty days later during a hypercoagulation episode (platelets over 1 million per c. mm.) both the internal and external shunts thrombosed. The patient arrived at hospital 48 hours later and it was not possible to salvage the external shunt. A transverse incision was made above the thrombosed internal fistula. Both the artery and vein contained clots. The adjacent vein was found and anastomosed end-to-end to the proximal part of the thrombosed artery (*Fig.* 4). One week later the fistula was

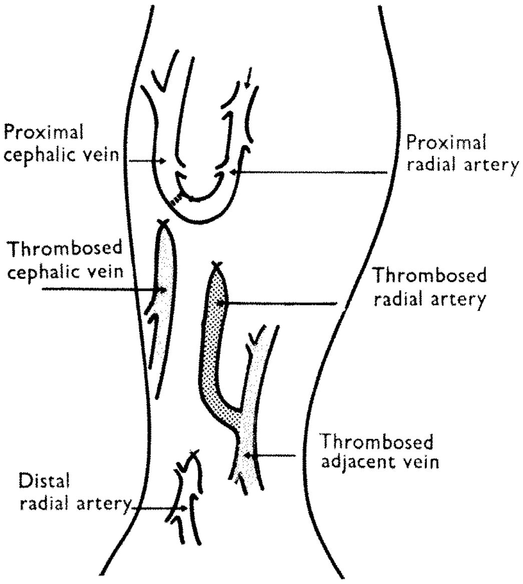

FIG. 5.—Technique used in *Case* 7.

used and 3 months later it was still functioning very well.

Case 7.—A 38-year-old female had an end-to-side radial artery internal fistula which never functioned. Ten days later an end-to-end arteriovenous fistula was created after declotting the cephalic vein which was the only vein in the vicinity (*Fig.* 5). Five days later this fistula was used and was still functioning after the patient had received a cadaveric kidney graft.

Acknowledgements.—I wish to thank Professor R. Y. Calne of the Department of Surgery, University of Cambridge, for permission to perform these techniques on his patients; the Radiology and Photographic Departments of Addenbrooke's Hospital, Cambridge, for their support and help, and Miss Patricia Hagan for secretarial assistance.

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THE AUTOGENOUS SAPHENOUS VEIN LOOP FOR HAEMODIALYSIS

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SUMMARY

Eleven autogenous saphenous vein loops have been used in 9 patients on haemodialysis in order to gain access to the circulation. All the patients lacked peripheral vessels available for alternative procedures. These grafts have functioned satisfactorily for over 18 months and have proved technically easy to construct and efficient to use. Three loops thrombosed after successful renal transplantation, and 1 developed an aneurysm which was repaired. One vein loop failed during dialysis. In 1 patient the graft enlarged considerably and she died of congestive cardiac failure; the part played by the graft in the development of the cardiac failure remains uncertain.

PRIOR to the introduction of the Cimino-Brescia fistula for regular haemodialysis (Brescia, Cimino, Appel, and Hurwich, 1966) access to the circulation was usually achieved by the Quinton-Scribner shunt (Quinton, Dillard, and Scribner, 1960). Although the external shunt was found to be satisfactory for haemodialysis its use was limited by the number of peripheral vessels available. In consequence a group of patients presented after several years of successful dialysis with a lack of shunt sites. The wider use of the Cimino-Brescia arteriovenous fistula from the time of commencement of haemodialysis has largely eliminated this problem. Unfortunately, however, a proportion of patients remain in whom the lack of peripheral vessels prevents the construction of a suitable arteriovenous fistula. These patients usually have had numerous arteriovenous shunts previously inserted, or have a failed renal transplant with a thrombosed fistula. May, Tiller, Johnson, Stuart, and Sheil (1969) introduced the use of saphenous vein loops in these difficult patients, and other reports have followed (Girardet, Hackett, Goodwin, and Friedman, 1970; Moses, Hurwich, Adar, Eliahov, and Bogokowsky, 1970; Perez-Alvarez, Vargus-Rosendo, Gutierrez-Bosque, Matos Diaz-Ordaz, and Santo-Atherton, 1970; Ton That, Lazorthes, Conte, Gouzi, Escat, and Suc, 1970; Hehrlein, Abe, and Goubeaud, 1971). This paper reports on the construction, usefulness, and complications of such loops in 9 patients.

PATIENT SELECTION

During the past 2 years 9 patients on regular dialysis therapy have required saphenous vein autotransplants to provide continued access to the circulation. The 9 patients were from the three dialysis units in Glasgow, the total dialysis population during this period being 74. Five of the patients were female and 4 male with an age range of 18–41 years. In 6 of the patients the vein loop was in situ prior to transplantation and of these, 4 have subsequently had a renal transplant. In 3 patients the vein loop was inserted following failure of a renal transplant, 1 of whom has had a total of 3 loops inserted.

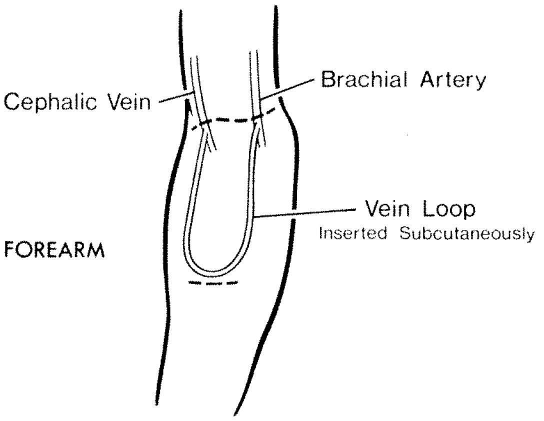

FIG. 1.—Method of subcutaneous insertion of a saphenous vein loop.

Table I.—FUNCTIONAL RESULTS AND COMPLICATIONS FOLLOWING SAPHENOUS VEIN LOOP INSERTION

PATIENT	DIALYSIS	LENGTH OF TIME (mth.)	COMPLICATIONS
R. P.	Good	18	Clotted after transplantation
A. A.	Good	18*	Aneurysm
H. B.	Good	5	Clotted after transplantation
M. McC.†			
1	Good initially	12	High venous back pressure; clotted
2	Clotted	1	Haemorrhage
3	Good	2*	—
M. McM.	Good	12	Clotted after transplantation; high venous back pressure
M. L.	Good initially	8	Patient died in congestive cardiac failure
C. D.	Good	6*	—
G. W.	Good	3*	—
C. R.	Good	2*	—

* Continues to function at present time.
† This patient required 3 autogenous vein-grafts.

OPERATIVE TECHNIQUE (*Fig.* 1)

Under general anaesthesia an oblique incision is made in the antecubital fossa to allow access to the brachial artery and a suitable vein. Both vessels are mobilized over a distance of about 6 cm. and controlled with appropriate slings.

A long saphenous vein is next removed from the groin to the knee and its branches ligated. The vein is distended with heparinized saline and excess adventitia removed. The vessel is next reversed and laid on the front of the forearm under slight tension in the form of a loop. A small incision is made at the base of the projected course of the vein, and using artery forceps, subcutaneous tunnels are developed. The vein is then pulled into the tunnel so that its ends lie opposite the brachial artery and the chosen vein.

At this stage the patient is given 5000 U. of heparin intravenously, and the brachial artery is clamped. A longitudinal arteriotomy is made and the vessels are anastomosed end to side using continuous 000000 silk. At the conclusion of this anastomosis the arterial clamp is temporarily released to ensure that the graft is not twisted. The venous end of the vein loop is then completed in the same fashion. The patency of the chosen vein should be checked prior to the anastomosis. This is performed by passing a No. 3 Fogarty embolectomy catheter proximally into the vein. Following the procedure, the patient should be anticoagulated for 24 hours with heparin (5000 U., 6-hourly).

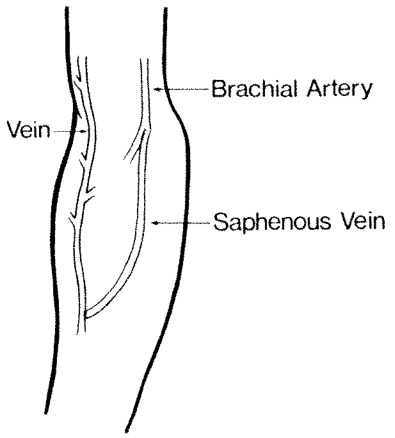

FIG. 2.—Alternative method of insertion of a saphenous vein as a straight segment. This procedure may be modified according to the availability of the venous drainage.

In 2 patients, because of the lack of a suitable vein in the antecubital region, the saphenous vein was sutured from the brachial artery to a small forearm vein in 1 case (C. R.) and to a vein in the upper arm in the second patient (M. McC.) (*Fig.* 2).

RESULTS

The autogenous saphenous vein loops have functioned satisfactorily for up to 18 months (*Table I*) for the purposes of haemodialysis in all except 1 patient (M. McC.). In general, unless the need is urgent the graft should not be used for dialysis purposes for 6 weeks. This interval allows the vessel to become arterialized and minimizes subsequent damage from repeated puncture. Because of this the operation should be planned several weeks prior to use.

The dialysis technique is similar to that employed with internal arteriovenous fistulae, the needles being inserted into the ascending and descending limbs of the loops. Following cannulation, satisfactory flow rates in excess of 300 ml. per minute have been achieved in most patients and blood-urea and creatinine figures confirm that the dialysis is as efficient as when an arteriovenous fistula or shunt is used. Excessive venous back pressure has been a problem in 2 cases and will be discussed later.

COMPLICATIONS

1. Clotting.—None of the loops clotted in the immediate postoperative period, but 3 thrombosed several months after a successful renal transplant. The reason for this phenomenon is not clear but it is known also to occur with conventional arteriovenous fistulae. The vein loop in 1 patient (M. McC.) thrombosed during dialysis.

2. Aneurysm Formation.—Repeated needling for dialysis has resulted in aneurysm formation in 1 patient (A. A.). A saccular aneurysm formed when the loop was needled for blood sampling shortly after its insertion. This aneurysm proved simple to repair under local anaesthesia and did not compromise the future of the use of the loop.

3. High Venous Back Pressure.—This occurred in 2 patients, though it did not decrease the efficiency of the dialysis. Arteriograms in these patients (M. McC. and M. McM.) (*Fig.* 3) show stenosis of the vessels distal to the anastomosis. These areas of narrowing were probably present prior to the creation of the vein loop and an alternative vein should have been used. Both vein loops subsequently clotted, one after transplantation and the other during a dialysis.

4. Dilatation of the Vein Loop.—In 1 patient (M. L.) the saphenous vein was noticed to be moderately varicosed. Several weeks after insertion it began to increase in diameter, eventually reaching a size of 2·5 cm. The cardiac output in this patient was estimated at 13 litres per minute and the patient subsequently died in congestive cardiac failure. The contribution which the loop made to the cardiac failure is difficult to assess.

5. Failure during Dialysis.—Failure during dialysis occurred in 1 patient (M. McC.). This patient had a high venous back pressure and the graft thrombosed after functioning satisfactorily for 1 year. Embolectomy under local anaesthesia restored the patency for a further 4 months, after which it clotted completely. A second loop was therefore performed in the other arm and unfortunately became infected, with subsequent haemorrhage necessitating ligation of the brachial artery above the loop. In this patient, and in 1 other (C. R.) where suitable antecubital veins were not available, the saphenous vein was anastomosed to the brachial artery and to a vein lower in the forearm. Although technically more difficult this procedure had the advantage of allowing other venous channels in the forearm to become arterialized and therefore available for cannulation.

DISCUSSION

The problem of access to the circulation will continue to be a challenge to surgeons who are associated with a regular dialysis programme. Fortunately, the use of arteriovenous fistulae has obviated many of the earlier difficulties with shunts, and they continue to function well in the long term. However, a small percentage of patients (in our series 12 per cent) will require alternative procedures. Autogenous saphenous veins have been used for many years in peripheral vascular surgery, with a 5-year patency of around 60 per cent (De Weese and Rob, 1971). Although we have used the long saphenous vein, arterialized by anastomosis to the brachial artery, the technique is versatile and can be adapted to suit available arteries and veins. Moses and others (1970), for example, used the ulnar artery at the wrist and a vein in the antecubital fossa, and Girardet and others (1970) have described the use of very long grafts, from the ulnar artery to the cephalic vein at the upper third of the arm. In 2 of our patients straight grafts rather than vein loops were required.

In the long term it will be important to know the useful life of these grafts. The longest period reported is 12 months (Girardet and others, 1970), and our own results show that they may be used for periods of up to 18 months. Two factors are probably important in securing long-term patency. First, the graft should not be used for a period of 6–8 weeks until it has become arterialized. This time allows the vein wall to thicken and thus contract when the needle is removed after dialysis. Secondly, care should be taken to ensure that the vein draining the loop is not narrowed by previous thrombophlebitis. Preoperative venography may be used to assess the patency of the venous drainage or, alternatively, a Fogarty embolectomy catheter may be used for direct evaluation at operation.

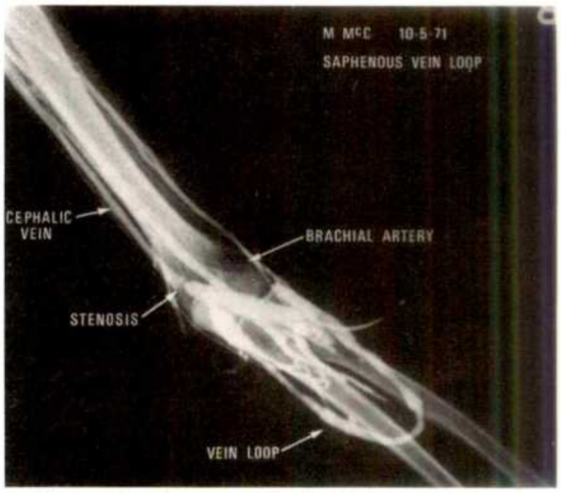

FIG. 3.—Arteriogram via the brachial artery, showing the vein loop and a stenosis at the venous end proximal to the anastomosis.

One patient in this series died in cardiac failure with a functioning graft (M. L.). The vein loop was dilated and a shunt of this size could conceivably have added considerably to the cardiac output. In retrospect the vessel should not have been used in this patient; it was moderately varicose and we would not use such a vessel in the future. Johnston and Blythe (1970) have shown that conventional arteriovenous fistulae normally used for dialysis do result in an increased cardiac output. We are currently assessing the importance of these loops on the haemodynamics of patients on regular dialysis.

Other potential drawbacks such as subacute bacterial endocarditis (Hook, Hainer, McGee, and Fellers, 1957) or ischaemic syndromes of the hand (Storey, George, Stewart, Tiller, May, and Sheil, 1969) have not been observed in our patients.

Although our experience with autogenous saphenous vein loops has been very satisfactory they should be looked upon principally as a method to be used on those patients with no alternative method of gaining access to the circulation. We believe, therefore, that the Cimino-Brescia fistula remains the procedure of choice in patients commencing regular haemodialysis, because of its ease of construction and reliability for long-term use.

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FACTORS INFLUENCING PROGNOSIS IN THE SURGERY OF PERIPHERAL VASCULAR DISEASE: PLATELET ADHESIVENESS, PLASMA FIBRINOGEN, AND FIBRINOLYSIS*

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SUMMARY

A study of 76 patients having aorto-iliac (46) and femoropopliteal (30) surgery for atherosclerosis has shown a significant correlation between increased platelet adhesiveness, prolonged clot lysis, and failure of the reconstruction between 3 months and 5 years after operation. In addition, a raised plasma-fibrinogen level, persisting 1 year after reconstruction, is often associated with failure. Patients having predominantly femoropopliteal disease show a significantly higher plasma-fibrinogen level than those with localized aorto-iliac disease. This correlation is such that when a high plasma-fibrinogen level is found in a patient with the clinical features of aorto-iliac disease it may be inferred that the femoropopliteal segment is also involved.

ADVANCES in the technical management of occlusive arterial disease are increasingly accompanied by efforts to understand the processes responsible for failure of arterial reconstruction. Failures which occur immediately after operation are usually related to faulty surgical technique (DeBakey, Crawford, Morris, Cooley, and Garrett, 1964) or to an abrupt fall in cardiac output. It is often more difficult to account for failure at a later date.

While our efforts are being directed at the complications, rather than the underlying nature, of atherosclerotic disease, we must expect to encounter failures associated with recurrent disease (Szilagyi, Smith, and Whitney, 1964) and new distal or proximal disease. Lesions resembling atheroma may develop in autogenous vein-grafts (Butzner, 1947), and Walton (1972) has demonstrated lipoprotein deposits in the interstices of prosthetic fabric grafts.

Although long-term results of proximal (aorto-iliac) surgery are better than those of distal (femoropopliteal) surgery (DeBakey and others, 1964), prolonged patency of vein-grafts under conditions of low blood-flow has been described by Mannick, Jackson, Coffman, and Hume (1967). This resistance to thrombosis may be related to the intrinsic fibrinolytic activity of vein tissue (Pandolfi, Nilsson, Robertson, and Isaacson, 1967). We have histochemical evidence of plasminogen activation in a vein-graft removed after several years as a substitute artery.

Blood containing excessively adhesive platelets has been found in patients with atherosclerosis of coronary arteries by McDonald and Edgill (1957) and in patients showing late thrombosis of femoropopliteal by-pass grafts (Evans and Irvine, 1966; Evans and Mustard, 1968).

Nestel (1960) found diminished fibrinolytic activity of the blood in patients with coronary artery and peripheral vascular stigmata of atherosclerosis.

In the context of this study 'early' graft failure is that which occurs during the first 3 postoperative months, subsequent failures being regarded as 'late'. We have studied the blood of patients subjected to aorto-iliac and femoropopliteal surgery, with the intention of seeking a correlation between late graft failure, platelet adhesiveness, plasma fibrinogen, and levels of serum fibrinolytic activity.

PATIENTS AND METHODS

Seventy-six patients were investigated, 46 having aorto-iliac surgery and 30 reconstruction of the femoropopliteal segment. The blood of 68 patients was examined preoperatively, venepuncture of non-congested veins being performed with the patient under basal conditions, including abstinence from smoking. Haematological study of the remaining 8 patients was carried out retrospectively, from 2 to $4\frac{1}{2}$ years after operation.

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* Based on a paper presented to the Surgical Research Society in July, 1971, and to a symposium on 'Recent Advances in the Surgery of Peripheral Vascular Disease' at the Royal Postgraduate Medical School in November, 1971.

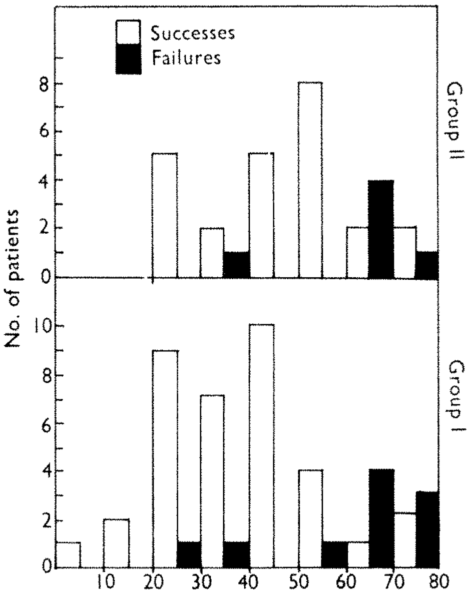

FIG. 1.—Patients having successful and failed grafts in relation to platelet adhesiveness.

Of the 30 femoropopliteal reconstructions, all were autogenous vein by-pass grafts. In the aorto-iliac group, 11 patients had thrombo-endarterectomies performed, and the remaining 35 had by-pass grafts using 'Dacron' or 'Teflon' prostheses.

No patient in whom reconstruction failed during the first 3 postoperative months has been included.

The mean postoperative follow-up period was 28 months, with a range from 6 to 62 months.

Platelet adhesiveness was measured using the rotating glass-bulb technique introduced by Wright (1941). Platelet counts were performed by hand to an accuracy of ±5 per cent. Platelet adhesiveness is defined as the difference in platelet count before and after rotation for 20 minutes expressed as a percentage of the initial count.

Total plasma fibrinogen was measured colorimetrically, as described by Varley (1967), and the heparin-precipitable fraction (H.P.F.) estimated by the method of Smith (1957).

Fibrinolytic activity was estimated by measuring dilute clot lysis times (Fearnley, Balmforth, and Fearnley, 1957) and euglobulin lysis times (von Kaulla, 1963).

RESULTS

The results of surgical treatment and mean ages of patients in group I (femoropopliteal by-pass grafts) and group II (aorto-iliac reconstruction) are summarized in *Table I*. Patients whose grafts were found to have failed during the follow-up period will be described as 'failures' and those with patent reconstructions as 'successes'. The even distribution of patients by age is noteworthy.

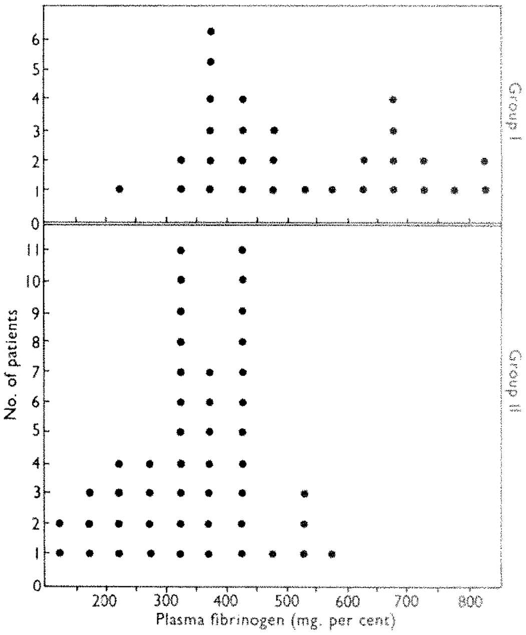

FIG. 2.—Distribution of plasma-fibrinogen level in both groups.

Table I.—NO. OF PATIENTS IN EACH GROUP

GROUP	OVERALL TOTAL		SUCCESSES		FAILURES	
	No. of Patients	Mean Age (yr.)	No. of Patients	Mean Age (yr.)	No. of Patients	Mean Age (yr.)
I	30	59·3	24	58·3	6	63·3
II	46	55·6	36	55·9	10	54·4
Total	76		60		16	

Platelet Adhesiveness.—*Fig.* 1 shows the distribution of patients in groups I and II, and illustrates that in both groups most failures lie in the range of high adhesiveness. Statistical separation of successes and failures is shown in *Table II*, confirming that the platelets of patients whose operations fail lie in a significantly higher adhesive range than those of the successes.

The mean level for all patients in group I was 50·4 per cent, which is significantly higher than the 43·8 per cent found in group II ($P < 0·01$).

Plasma Fibrinogen.—The overall mean level for the population studied was 422·6 mg. per cent. Histograms for both groups (*Fig.* 2) illustrate a group separation, but with considerable overlap. Further analysis of these data (*Table III*) reveals a significant overall difference in plasma fibrinogen between groups I and II ($P < 0·001$).

No difference in the plasma-fibrinogen level was demonstrated between successes and failures in

61 patients followed up from 3 to 12 months postoperatively. However, patients followed up for *more* than 12 months have been studied separately, and of 15 cases in this category, 8 successes showed a mean plasma fibrinogen level of 276 mg. per cent while 7 failures had a significantly higher level of 452·0 mg. per cent ($P < 0{\cdot}01$). It seems possible then that a high level of fibrinogen in the plasma may only prove of prognostic significance when a graft has functioned successfully for at least 12 months.

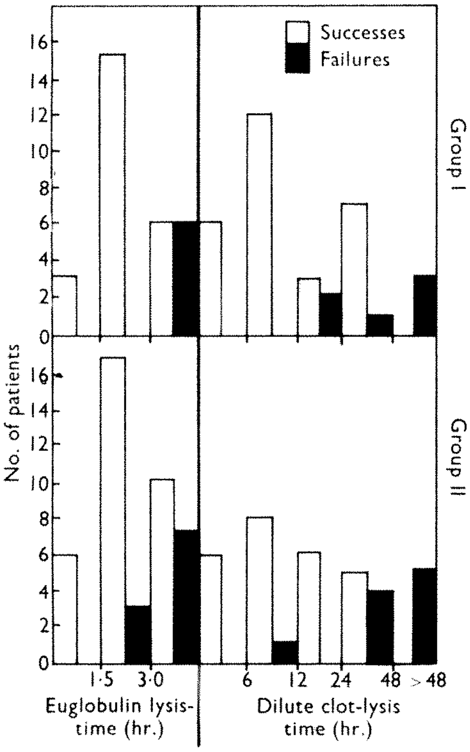

FIG. 3.—Clot-lysis times for patients in group I (above) and group II (below).

Heparin-precipitable Fraction of Fibrinogen (Smith and von Korff, 1957).—While the overall mean values for H.P.F. show no significant separation between groups (*Table IV*) the high value for failures in group II (123·9 mg. per cent) is conspicuous.

Fibrinolysis.—Estimation of clot-lysis times in both groups, using dilute clot lysis and euglobulin lysis methods (*Fig.* 3), shows a clear distribution of patients with 'failed' operations in the slow lysis ranges. While many patients whose operations succeeded showed rapid clot lysis, this was not observed in any patient in the 'failed' category. When the values for the whole series of 76 patients were examined the successes showed significantly more rapid lysis times than the failures ($P < 0{\cdot}01$). There was no apparent overall difference between groups I and II.

Association between Platelet Adhesiveness and Plasma Fibrinogen.—Quadrant analysis of values for these parameters, examining low and high ranges divided at their means, revealed a statistically significant correlation between high levels of adhesiveness and high plasma fibrinogen ($\chi^2 = 12{\cdot}4$; $P < 0{\cdot}001$).

DISCUSSION

The incidence of failure after arterial reconstruction during the late postoperative period in this small series is similar to that previously reported (Szilagyi, Smith, Elliot, and Allen, 1965; Baddeley, Ashton, Slaney, and Barnes, 1970; DeWeese and Rob, 1971) but we should point out a degree of bias in favour of our success rate since not all the patients have been followed for 5 years, and several which have been documented here as successes may subsequently 'fall' into the failure category. As has been pointed out (DeWeese and Rob, 1971), 50 per cent of patients having femoropopliteal vein by-pass grafts are likely to die from sequelae of atherosclerosis before reaching the 5-year follow-up stage, and we may expect a reduced number of 'successes' when assessment is made after 5 years. This reduction in size of each group will, therefore, tend to balance the failures taking place during the 1–5-year period.

Table II.—MEAN VALUES FOR PLATELET ADHESIVENESS AND SIGNIFICANCE OF SEPARATION FOR SUCCESS AND FAILURE

GROUP	PLATELET ADHESIVENESS PERCENTAGE (MEAN)		
	Successes	Failures	*P*
I	47·8	61·0	<0·01
II	39·9	58·0	<0·01

Table III.—PLASMA FIBRINOGEN

GROUP	MEAN PLASMA FIBRINOGEN (mg. per cent)					
	Overall		*Successes*		*Failures*	
	Amount	No. of Cases	Amount	No. of Cases	Amount	No. of Cases
I	532·4	30	523·9	24	566·5	6
II	351·0	46	342·3	36	382·4	10
	$P < 0{\cdot}001$					

Table IV.—HEPARIN-PRECIPITABLE FIBRINOGEN

GROUP	MEAN VALUES FOR HEPARIN PRECIPITABLE FIBRINOGEN (mg. per cent)		
	Overall	*Successes*	*Failures*
I	80·1	84·4	62·8
II	93·2	85·5	123·9
	$P > 25$ (N.S.)		

Our observations showing a correlation between the late failure of femoropopliteal by-pass grafts and increased platelet adhesiveness are complementary to those reported previously concerning aorto-iliac reconstructions (Hamer, 1972) and support the findings of other workers (Evans and Irvine, 1966; Evans and Mustard, 1968). Although we have found an association between high platelet adhesiveness and elevated plasma fibrinogen, the latter parameter appears to be a less reliable prognostic indicator, despite the striking observation that occlusion taking place after 12 months of successful function is frequently associated with high plasma-fibrinogen levels.

Of considerable interest is the observation that patients in group I showed markedly raised levels of plasma fibrinogen. Of the 30 patients in this group, 27 showed no obvious evidence of proximal arterial disease. Conversely, of 4 patients in group II showing plasma-fibrinogen levels exceeding 500 mg. per cent, radiological evidence of tibial atherosclerosis was found in 3 cases. It appears that a high level of plasma fibrinogen is frequently associated with the presence of peripherally situated arterial disease and we suggest that measurement of this parameter is of value in drawing attention to unsuspected distal lesions in patients presenting with predominantly aorto-iliac disease. The source of fibrinogen in patients with peripheral disease has not yet been positively identified, but we have recently reported the early results of an experimental study suggesting that a marked rise in plasma fibrinogen follows deposition of fibrin within *and* outside blood-vessels, there being an associated release of fibrin degradation products (F.D.P.) which may or may not be detectable in the serum (Farrell, Hamer, and Wolf, 1972). We share with Young and Kolmen (1970) the opinion that thrombolysis may provide a stimulus to release of fibrinogen from the liver or platelets, and it is possible that thrombosis and thrombolysis taking place within small peripheral arteries may account for the high plasma fibrinogen observed in patients in group I. The surface area of diseased vessel exposed to circulating blood in patients with small-vessel disease is far greater than that in patients with aorto-iliac disease. This aspect of our work awaits confirmation and is the subject of further study.

Although the results of this investigation suggest that preoperative identification of abnormally adhesive platelets and defective fibrinolytic capability should encourage a guarded long-term prognosis, we would seldom advise against reconstructive surgery in the presence of clear positive clinical indications.

Acknowledgements.—This study was generously supported by a grant from the Endowment Research Fund of the United Birmingham Hospitals. We acknowledge the technical help given by Miss N. Pejhan and Mrs. K. McCann, and wish to thank Mrs. P. Prior for her help with statistical analyses.

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GASTRIC ULCER TREATED BY VAGOTOMY, PYLOROPLASTY, AND ULCERECTOMY

BY H. A. DANIELS AND A. W. B. STRACHAN

BARROW AND FURNESS GROUP OF HOSPITALS

SUMMARY

Sixty-two patients with gastric ulcers have been treated by vagotomy, pyloroplasty, and excision of the ulcers from 1963 to 1971. There has been only 1 recurrence.

It is suggested that excision of the ulcer is an important step in conservative surgery for gastric ulcer.

No one really knows why partial gastrectomy prevents the recurrence of gastric ulcers. The operation (1) improves the drainage, (2) reduces the acidity, and (3) usually removes the ulcer. Up to 1962 this was the standard operation for gastric ulcer in Barrow but by that time vagotomy and pyloroplasty had become the operation of choice for duodenal ulcer and we felt that it might be reasonable to use the latter procedure in cases of gastric ulceration. This would improve stomach drainage and reduce acidity. If ulcerectomy were added it would provide the third factor and ensure that a carcinoma was not being missed.

Since then the majority of gastric ulcers have been treated by this method. Partial gastrectomy has been used in some cases of doubt regarding carcinomas and also in some cases of antral ulcers. Vagotomy was sometimes added. In other patients, where the ulcer appeared to be healed or very small, vagotomy and pyloroplasty only were carried out.

TECHNIQUE

The vagotomy has been truncal in most of the cases. Selective vagotomy adds considerably to the difficulty of the operation especially with an indurated lesser-curve ulcer, and we have not been convinced it makes much difference to the incidence of severe diarrhoea.

Table I.—TYPE OF OPERATION FOR 107 GASTRIC ULCERS TREATED SURGICALLY

Type of Operation	*No. of Cases*
Vagotomy, pyloroplasty, and ulcerectomy	62
Vagotomy and pyloroplasty	23
Partial gastrectomy ± vagotomy	22

Table II.—COMPLICATED GASTRIC ULCERS

TYPE OF GASTRIC ULCER	NO. OF CASES	TREATMENT	NO. OF DEATHS
Perforated gastric ulcer	6	5 Vagotomy, pyloroplasty, and ulcerectomy 1 Vagotomy, pyloroplasty, and suture	0 0
Bleeding gastric ulcer	12	8 Vagotomy, pyloroplasty, and ulcerectomy 2 Vagotomy and pyloroplasty 2 Partial gastrectomy	1 1 1

Table III.—RESULTS OF THE VARIOUS OPERATIONS

RESULT	VAGOTOMY, PYLOROPLASTY, AND ULCERECTOMY	VAGOTOMY AND PYLOROPLASTY	PARTIAL GASTRECTOMY
Visick grade 1	46	14	15
Visick grade 2	9	4	4
Visick grade 3	1	1	1
Visick grade 4	1	—	—
Deaths	4 (6 per cent)	2 (9 per cent)	2 (9 per cent)*
Percentage of satisfactory results	96	95	95

* 8 per cent overall.

Lesser-curve ulcers are easy to excise and it is often unnecessary to clear the lesser curve of vessels and fat. The stomach is opened close to the ulcer, the crater is inspected, and if benign (apparently) it is excised working from the mucosal surface. In this way it is possible to keep close to the ulcer margin.

The ulcer can sometimes be cored out of the thickness of the stomach wall with a relatively small opening in the stomach. The hole left is, however, surprisingly large. It is closed with catgut in two layers. If there is much fibrous thickening the deep layer takes the mucosa only and the seromuscular layer approximates the thickened wall without inversion.

Large posterior ulcers are more difficult and sometimes it is necessary to make an anterior gastrostomy in order to inspect them. This is most important if any doubt about malignancy exists. It is much easier to spot a benign ulcer with its punched out edges and fibrous floor in this way. The posterior ulcer can then be excised working through the gastrostomy if approach through the lesser sac is difficult.

An ulcer that appears malignant from the outside may well prove benign when seen from the inside. Radical gastrectomies for simple ulcers should be avoided at all costs.

For the past 2 years Ryle's tubes have been removed at the end of the operation and very rarely need to be reinserted.

MATERIAL

The number of gastric ulcers treated from 1963 to 1971 was 107 (*Table I*). Of these, 62 were treated by vagotomy, pyloroplasty, and ulcerectomy, 23 by vagotomy and pyloroplasty, and 22 by partial gastrectomy, sometimes with added vagotomy.

Table IV.—TYPE OF OPERATION COMPARED WITH THE CAUSE AND TIME OF DEATH IN 8 CASES

OPERATION	CAUSE OF DEATH	TIME OF DEATH (Day after Operation)	AGE (yr.)	COMMENT
Vagotomy, pyloroplasty, and ulcerectomy	Pulmonary embolus	5	74	Bleeding gastric ulcer. No postoperative bleeding
Vagotomy, pyloroplasty, and ulcerectomy	Pulmonary embolus	6	56	—
Vagotomy, pyloroplasty, and ulcerectomy	Coronary thrombosis	4	51	—
Vagotomy, pyloroplasty, and ulcerectomy	Diarrhoea	7	56	Staphylococcal enteritis
Vagotomy and pyloroplasty	Persistent bleeding	2	83	Bleeding never stopped
Vagotomy and pyloroplasty	Persistent bleeding	14	67	Ulcer oversewn; bleeding recurred; ulcer excised on the day before death
Partial gastrectomy	Persistent bleeding	1	56	Bleeding splenic artery; 13 pints of blood transfused on the day of operation
Gastrectomy	Oesophageal leak	7	46	Total gastrectomy for a supposed malignant ulcer high up. Leak from oesophagus 1 cm. above suture line

Twenty-two gastric ulcers were associated with duodenal ulcers. This is a minimal figure as it is likely that not every duodenal ulcer scar was mentioned in the notes when the immediate concern was with a gastric ulcer.

Table II shows that 6 of the gastric ulcers presented as acute perforations and were dealt with by vagotomy, pyloroplasty, and ulcerectomy in 5 cases and by vagotomy, pyloroplasty, and suture in 1 case. None of these patients died.

There were 12 bleeding gastric ulcers which did not fare as well as the perforations. Eight were dealt with by vagotomy, pyloroplasty, and ulcerectomy with 1 death, 2 by vagotomy, pyloroplasty, and suture with 1 death, and 2 by partial gastrectomy with 1 death. Details of these deaths will be dealt with later.

The results of the operations are shown in *Table III*, each type of operation showing about a 95 per cent satisfactory result (Visick grades 1 and 2). Three patients were lost to follow-up but none of these was having symptoms when last seen. Only 1 patient of the vagotomy, pyloroplasty, and ulcerectomy series has not been followed up. He was an Indian seaman with a perforated gastric ulcer who returned to India after the operation. One patient developed a recurrence of her gastric ulcer. It was a high lesser-curvature ulcer treated by selective vagotomy, pyloroplasty, and ulcerectomy in 1969. It recurred in 1972 and has been dealt with by a high Billroth-I partial gastrectomy. The recurrence was in the scar where the ulcer had been previously excised.

The causes of death are shown on *Table IV*. Of the vagotomy, pyloroplasty, and ulcerectomy cases, 2 died from emboli and 1 from coronary thrombosis. The fourth patient had diarrhoea, thought to be of staphylococcal origin, and died of bronchopneumonia, probably from excess fluid replacement. Of the vagotomy and pyloroplasty deaths, both were due to persistent bleeding in patients operated on as emergencies for bleeding ulcers.

One of the partial gastrectomy patients who died was also operated on for bleeding, the source being the splenic artery in the floor of a large posterior ulcer.

The second gastrectomy death was the result of misdiagnosing a high posterior gastric ulcer as malignant and carrying out total gastrectomy. The ulcer was in fact benign. Death was from an oesophageal leak about 1 cm. above the suture line, possibly the result of a cut-out suture.

DISCUSSION

There seems to be considerable discrepancy between the reported results of gastric ulcers treated by vagotomy and pyloroplasty. Hendry and Bahrani (1965) treated all types of gastric ulcer by vagotomy and pyloroplasty, and followed their patients carefully until healing, as judged radiologically, was achieved. They reported 98 per cent satisfactory results in patients followed for 6 months to 6 years.

On the other hand, Duthie, Moor, Bardsley, and Clark (1970) and Douglas and Duthie (1971) found that ulcers of the body of the stomach treated by vagotomy and pyloroplasty showed a high recurrence rate, only 79 per cent of cases being satisfactorily cured, while combined duodenal ulcer and gastric ulcer cases showed a 97 per cent satisfactory rate after vagotomy and pyloroplasty.

Clarke, Lewis, and Williams (1972) reported 4 recurrences after vagotomy and pyloroplasty for gastric ulcer, 3 of them being in patients with combined duodenal and gastric ulcers. They concluded that vagotomy and pyloroplasty comprise a sound operation for a high ulcer or a bleeding ulcer but not for combined ulcers.

Kennedy, Kelly, and George (1972) also reported 4 recurrences in 66 patients treated by vagotomy and pyloroplasty, 3 of them being in patients with ulcers of the body or lesser curve of the stomach. They suggested that vagotomy and pyloroplasty are suitable for antral or combined ulcers but not for high ulcers.

In the present series 62 patients had vagotomy, pyloroplasty, and ulcerectomy with 1 recurrence. It is suggested that excision of the ulcer is important in the prevention of recurrence.

A feature of gastric ulcers which is not often stressed is their tendency to inhabit one particular site in the stomach. If the ulcer heals and recurs it is found in the same place each time.

It is unusual at operation to see more than one gastric ulcer or the scars of other gastric ulcers that have healed. If conditions favourable to the formation of gastric ulcers obtain one could expect more than one ulcer to form or if healing occurred recurrence could be expected anywhere in the stomach. This is what happens in the duodenum where it is common to find more than one active ulcer and perhaps the scars of two or three others in the first 3·5 cm. of the duodenum.

It therefore seems likely that there is some local factor at the actual site of the gastric ulcer which causes the ulcer to form repeatedly at the same site. If there is a locus minoris resistentiae, then excision of this area might well be important in the prevention of recurrence of gastric ulcers. When Billroth-I gastrectomy is carried out for gastric ulcer surgeons go to considerable pains to remove the ulcer and only leave it behind if it is situated adjacent to the oesophagus. If the same care was taken to excise the ulcer when vagotomy and pyloroplasty was carried out it is suggested that recurrence would be rare.

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A CIRCULATING DEPRESSANT EFFECT FOLLOWING CANINE HAEMORRHAGIC SHOCK

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SUMMARY

Following periods of 1 or 3½ hours of haemorrhagic shock in 12 anaesthetized ventilated greyhounds, ultrafiltrates of plasma taken 4 hours after retransfusion exibited significantly increased depressant activity on guinea-pig atrium *in vitro*. This effect was significantly greater following prolonged hypotension and could not be accounted for by changes in electrolyte composition. It is suggested that this effect may be related to defective myocardial function following haemorrhagic shock.

SEVERAL investigators have described impaired performance of the heart following canine haemorrhagic shock (Gomez and Hamilton, 1964; Siegel and Downing, 1970). Lefer and his colleagues (Brand and Lefer, 1966; Lefer, 1970; Lefer and Martin, 1970) have postulated that this effect is due to a circulating peptide present in the post-shock plasma of cats and dogs following haemorrhagic, endotoxic, and cardiogenic shock. In spite of the potentially important clinical implications this observation has not received independent substantiation. The following study presents the results of a continuing investigation in dogs.

MATERIALS AND METHODS

Twelve greyhounds (weight range 23–32 kg.) were anaesthetized and ventilated and subjected to controlled haemorrhage into a reservoir until the mean arterial blood-pressure was 35–40 mm. Hg. The arterial pressure was maintained at this value for 3½ hours in 6 dogs and for 1 hour in another 6 animals. Following the period of hypotension in both groups of dogs all the remaining shed blood was retransfused. The animals were then observed for a further period of 4 hours. The haemodynamic and metabolic results of these studies are reported in detail elsewhere (Ledingham, Heimbach, Hutton, and McArdle, 1971; Heimbach, Fisher, Hutton, McArdle, and Ledingham, 1972).

Processing of Plasma.—Arterial blood-samples (50 ml.) were removed prior to haemorrhage (control) and at the conclusion of each experiment, i.e., 4 hours after the retransfusion of the shed blood (post-hypotension). The blood samples were placed immediately in ice-cold heparinized centrifuge tubes containing 1 per cent v./v. dextran 70 and spun at 4° C. for 20 minutes at 2000 × *g* and the supernatant plasma was frozen until required. Samples of plasma were filtered at 4° C. through a Diaflo (Amicon Corp., Lexington, U.S.A.) filter UM-10 (cut off M.W. 10,000). The resultant ultrafiltrates were then assayed.

Assay.—Guinea-pigs were killed and the left atrium was removed rapidly and placed in modified Krebs-Henseleit buffer (Lefer, 1966) previously equilibrated with 95 per cent O_2/5 per cent CO_2. The atrium was mounted on the positive electrode in a 5-ml. organ bath at 33° C. and suspended under 600 mg. of tension on a Nihon Kohden (Tokyo, Japan) force-displacement transducer attached to a Devices recorder (Devices Instruments Ltd., Welwyn Garden City). The atrium was stimulated supramaximally with a square-wave stimulator at 2 Hz. Samples for assay were brought to bath temperature and equilibrated with 95 per cent O_2/5 per cent CO_2, following which the *p*H fell to 7·35. When a stable developed tension had been obtained the bath was emptied and the sample added. The activity of the atrium was then followed until a new stable developed

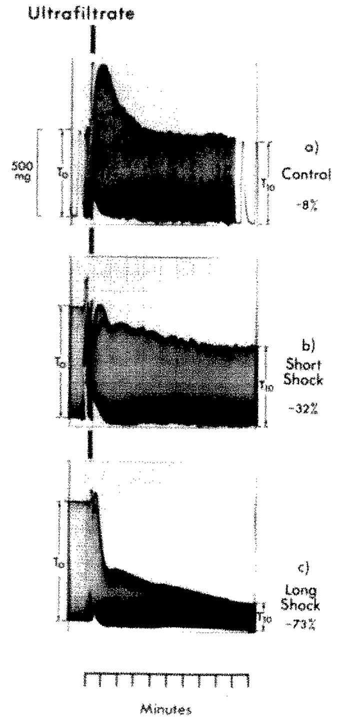

FIG. 1.—Tracings of assays of 3 ultrafiltrates from (a) control sample and post-hypotension samples (b) following 1 hour of hypotension (short shock) and (c) following 3½ hours of hypotension (long shock). The values of developed atrial tension at 10 minutes (T_{10}) were expressed as a percentage of the developed tension in Krebs-Henseleit buffer (T_0). The percentage depressions for each assay are shown.

tension had been achieved and the percentage change in developed tension at 10 minutes was recorded.

Samples of ultrafiltrates of control and post-hypotension blood were also analysed to determine their electrolyte content; sodium and potassium by flame ionization photometry, chloride by titration, calcium and magnesium by atomic absorption spectrometry.

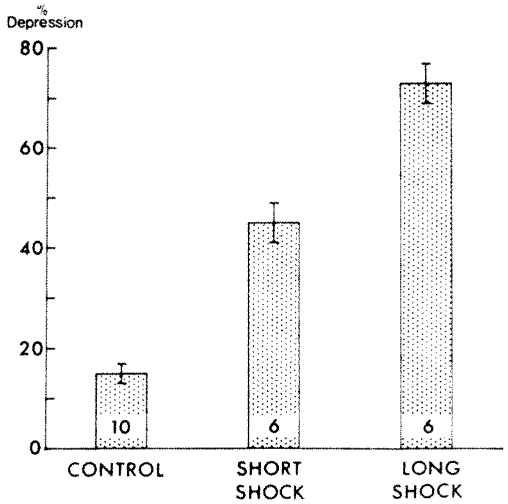

FIG. 2.—Mean percentage depression and standard error of the mean of samples of control ultrafiltrates and post-hypotension ultrafiltrates following 1 hour (short shock) and 3½ hours (long shock) of hypotension. Figures are the number of dogs in each group.

Table I.—ELECTROLYTE COMPOSITION OF THE ULTRAFILTRATE FROM 6 CONTROL AND 6 POST-HYPOTENSION (3½ HOURS' DURATION) DOGS

ELECTROLYTE	CONTROL GROUP (mEq./l.)	POST-HYPOTENSION GROUP (mEq./l.)
Sodium	161 ± 9	151 ± 9
Potassium	4·0 ± 0·2	6·2 ± 0·9
Chloride	104 ± 12	74 ± 3
Calcium	2·1 ± 0·3	1·7 ± 0·2
Magnesium	0·96 ± 0·08	1·74 ± 0·14

RESULTS

Typical tracings of assays of a control ultrafiltrate and of post-hypotension ultrafiltrates from each of the two groups of animals are shown in *Fig.* 1. A variable but consistent initial increase in developed tension occurred after the addition of all the ultrafiltrates but in the shock samples it was masked by the magnitude of the atrial depression. The initial increase in developed tension after addition of the ultrafiltrate is the result of exposure of the atrium on emptying the organ bath. The mean percentage depression of developed tension in the control group and both groups of bled animals is shown in *Fig.* 2. Control samples exerted a depression of 15 ± 2 per cent (mean ± standard error of the mean). Following 1 hour of hypotension the depression had increased to 45 ± 4 per cent ($P < 0{\cdot}001$) and had increased significantly further after 3½ hours' shock to 73 ± 4 per cent ($P < 0{\cdot}005$).

A sample from 1 dog subjected to 3½ hours of hypotension was diluted in varying amounts of Krebs-Henseleit buffer. These dilutions were then assayed. The results are shown in *Fig.* 3. An exponential regression was obtained ($r = 0{\cdot}95$).

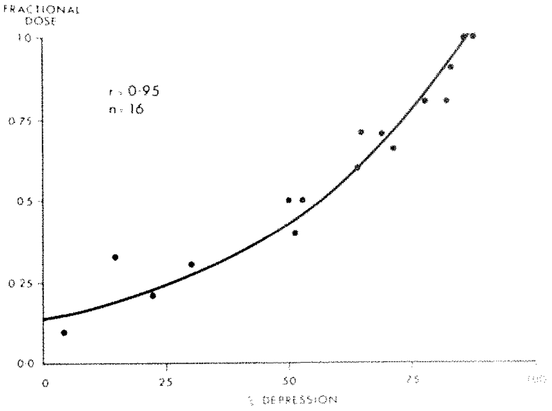

FIG. 3.—Exponential regression analysis of dilutions in Krebs-Henseleit buffer of an ultrafiltrate from an animal subjected to 3½ hours of hypotension against the percentage depression obtained in assays of each dilution.

The electrolyte composition of 6 control and 6 post-hypotension (3½ hours' duration) ultrafiltrates is shown in *Table I*. Sodium concentration did not change (161 ± 9 and 151 ± 9 mEq./l. in control and post-hypotension samples respectively); calcium concentration was also unchanged (2·1 ± 0·3 and 1·7 ± 0·2 mEq./l. respectively). There was a rise after hypotension in both potassium (4·0 ± 0·2 to 6·2 ± 0·9 mEq./l.; $P < 0{\cdot}05$) and magnesium (0·96 ± 0·08 to 1·74 ± 0·14 mEq./l.; $P < 0{\cdot}001$) concentrations and a fall in chloride concentration (104 ± 12 to 74 ± 3 mEq./l.; $P < 0{\cdot}05$).

DISCUSSION

It has been reported that prolongation of hypotension results in diminished myocardial contractility (Regan, LaForce, Teres, Block, and Hellems, 1965). In our experimental model prolongation of hypotension resulted in an increase in the depressant activity of resuscitation plasma. The values following 3½ hours of hypotension corresponded to that found by Wangensteen, DeHoll, Kiechel, Martin, and Lefer (1970), using a different assay system but with a similar degree of hypotension. The possibility of electrolyte changes contributing to this effect was considered. Although there was a rise in potassium concentration the value following hypotension corresponded to that of the Krebs-Henseleit buffer. However, the rise in magnesium concentration did not reach the concentration in the Krebs-Henseleit buffer. As protein-bound calcium is removed by ultrafiltration the ultrafiltrate calcium concentration was lower than plasma total calcium concentration and also Krebs-Henseleit buffer calcium concentration. This might have contributed to the small but consistent depression of developed atrial tension found in the control ultrafiltrate; it is unlikely, however, to have represented more than a minor fraction of the depression observed in the post-hypotension ultrafiltrates. Lefer and his co-workers (Brand, Cowgill, and Lefer, 1969; Lefer, Cowgill, Marshall, Hall, and Brand, 1967) have investigated other substances present in plasma following shock and found no major depressant effects. These results thus support the view that a substance is appearing in increasing quantities in the plasma of dogs subjected to hypotension of increasing duration. Further support was found in the dose–response curve (*Fig.* 3) which showed an exponential relationship between response and dilutions of ultrafiltrate.

These results are consistent with the appearance in plasma of a compound of low molecular weight in increasing quantity with the prolongation of shock. Its *in vitro* effects on myocardial contractility would agree with the finding of defective myocardial performance in the resuscitation phase of experimental haemorrhagic shock.

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HYPERBARIC OXYGEN AND WOUND HEALING IN POST-IRRADIATION HEAD AND NECK SURGERY

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SUMMARY

Irradiation impairs wound healing owing to reduced vascularity with an increased susceptibility to infection. The case histories of 4 patients with carcinoma of the larynx who have had irradiation and subsequent laryngectomies followed by hyperbaric oxygen therapy are described. It is the authors' clinical impression that skin healing in these patients has been improved by hyperbaric oxygen therapy. The skin changes following ionizing radiation, the rationale of hyperbaric oxygen, and its method of use are described.

MANY patients who undergo head and neck surgery for cancer have previously received radiotherapy. The complications of wound breakdown and infection in such cases are well known. These complications frequently prolong the patient's stay in hospital and may require further reconstructive procedures.

These sequelae are often due to the inability of irradiated tissues to heal normally and to resist infection as a result of reduced vascularity and the resultant tissue hypoxia. If the arterial Po_2 is increased, hypoxia is reduced, encouraging healing and reducing the liability to infection. This may be done by exposing the patient to an atmosphere of hyperbaric oxygen. Hyperbaric oxygen has been used with some success in the treatment of ischaemic skin-flaps (Perrins, 1966; Niinikoski, 1970) and in varicose ulceration (Slack, Thomas, and De Jode, 1966). It has had palliative success in peripheral vascular disease (Illingworth, Smith, Lawson, Ledingham, Sharp, Griffiths, and Henderson, 1961; Schraibman, and Ledingham, 1969; Watt, 1971). Particular success has been noted in the treatment of anaerobic infections, especially gas gangrene (Boerema and Groeneveld, 1970; Cooke, 1971; Watt, 1971). Hyperbaric oxygen also has an inhibiting effect on aerobic organisms (McAllister, 1966).

Hyperbaric oxygen has been used in conjunction with radiotherapy in the treatment of cancer (Van den Brenk, 1961; Wildermuth, 1965; Churchill-Davidson, Foster, Wiernik, Collins, Pizey, Skeggs, and Purser, 1966), but its use in wound healing in irradiated patients has not apparently been reported before.

Four patients who had undergone post-irradiation head and neck surgery and who subsequently developed wound-healing problems have been treated with hyperbaric oxygen.

CASE REPORTS

Case 1.—Mrs. R. C., aged 50 years, presented in November, 1968, with a right supraglottic squamous-cell carcinoma (T2 No Mo). She underwent radiotherapy, receiving 6360 rad. from a cobalt unit. Three months later there was residual disease and she underwent total laryngectomy with standard block dissection in the neck in April, 1970. On the third and fourth postoperative days wound infection became evident with necrosis of the edge of the skin-flaps. A pharyngocutaneous fistula developed. A bacteriological culture grew *Proteus mirabilis* and *Pseudomonas aeruginosa*. The patient underwent hyperbaric oxygen therapy from the twelfth to the twenty-seventh postoperative days, receiving a total treatment time of

48 hours 45 minutes over 15 days at 2 atmospheres absolute (A.T.A.) (15 lb. per in.^{2} or 1·1 kg. per cm.^{2}). During this time there was very rapid improvement in healing although a small fistula remained. This persisted and was excised in August, 1970. She received further hyperbaric oxygen after this excision for 31 hours 50 minutes over 7 days at 2 A.T.A. Healing was complete and she has remained well since.

Case 2.—Mr. R. F., aged 55 years, presented at another hospital in January, 1970, with a poorly differentiated squamous-cell carcinoma in the region of the left aryteno-epiglottic fold extending into the pyriform fossa. He was treated with a course of radiotherapy, receiving a total of 4500 rad which was intended as a preoperative course in a combined régime. Operation was, however, delayed and the patient was transferred to the Westminster Hospital where he underwent total laryngectomy and standard block dissection of the neck in May, 1970. During the first postoperative week he developed a wound infection with fluctuation under the skin-flaps. A culture grew anaerobic streptococci. He was treated with hyperbaric oxygen, receiving a total treatment time of 52 hours 15 minutes over 16 days at 2 A.T.A. The infection resolved rapidly. The patient died over a year later of systemic metastases.

Case 3.—Mr. A. U., a Turkish patient aged 50 years, presented in 1965 with a squamous-cell carcinoma of the left vocal cord extending to the anterior commissure and to the subglottic region (T3 N1 M0). In a course of radiotheraphy he received 6714 rad from a cobalt-60 unit. Two years later the disease recurred. The patient refused surgery and received a further course of 4800 rad. Following this he received intravenous methotrexate. In 1971 the patient agreed to surgery and underwent palliative total laryngectomy in June. He then developed a wound infection with wound breakdown. Healing was slow and a fistula persisted. During the eighth postoperative week the fistula was curetted but failed to heal. Curettage was repeated 3 weeks later and on this occasion the patient was exposed to hyperbaric oxygen for a total of 54 hours over 14 days at 3 A.T.A. At the end of this time the wound was healed and dry and remained so until the patient's discharge from hospital. No further follow-up is available.

Case 4.—Mrs. M. C., aged 52 years, presented in 1969 with a squamous-cell carcinoma of the right vallecular region extending to the right pharyngeal wall. She received a course of radiotherapy of 7200 rad from a cobalt-60 unit. She underwent total laryngectomy with removal of the posterior one-third of the tongue in 1971 for recurrent disease, and developed wound breakdown and a pharyngocutaneous fistula postoperatively. She underwent a course of hyperbaric oxygen for 46 hours from the twentieth postoperative day over 12 days at 3 A.T.A. At the completion of treatment the wound and fistula had completely healed.

All the patients received full supportive treatment and appropriate antibiotics.

DISCUSSION

Pathology of Radiation Changes.—Therapeutic doses of radiation may produce a mild erythema of the skin with degeneration of the sweat-glands and hair follicles. The initial reaction settles within 6–8 weeks. Subsequently the epithelium becomes atrophic, epilation persists, and there is pigmentation or depigmentation and telangiectasia.

In the blood-vessels the endothelium becomes oedematous, and there may be arrest of circulation in small vessels and a narrowing of the lumen in those of moderate size. There is atrophy of the muscular coat, fibrosis, and a thickening of the vessel walls, the end-result being an obliterative endarteritis (Gillies and McIndoe, 1933; McIndoe, 1947; Cade, 1948). Such changes have been considered to be changes in the vessels themselves (Ackerman and Del Regato, 1970), although there is evidence to suggest that they may be secondary to those in the surrounding connective tissue (Rhoades, 1948). The changes in the skin and blood-vessels are progressive (Cade, 1948). Their effect, associated with the direct effect of radiation on the viability of individual cells, is to reduce the regenerative and recuperative powers of the tissues; they are less able to sustain infection and trauma and their healing powers are impaired (McIndoe, 1947).

There is experimental evidence to confirm the delaying effect of radiation on wound healing (Ritchie, 1933; Grillo and Potsaid, 1961).

Effect on Subsequent Surgery.—The surgical problems encountered during operation and in the healing of wounds in patients who have been previously irradiated are within the experience of most surgeons. Work (1959) reviewed these problems. He considered that the majority of patients operated on within 12 months of radiation have few problems although occasional cases may present difficulties during surgery or healing. However, he stated: 'Surgery of the neck in patients who have been irradiated 12 months or more previously for cancer of the larynx is fraught with many difficulties. The surgeon experiences these during the performance of the surgery and during the postoperative care of the patient. This is true whether there is persistent cancer or not in these patients.'

Whilst up-to-date, supervoltage radiotherapy may have gone some way to reduce these problems they nevertheless still exist.

Theories and Methods of Hyperbaric Oxygenation.—It has been noted by several users of hyperbaric oxygen that a beneficial effect is obtained in the healing of ischaemic skin-flaps (Perrins, 1966), infected varicose ulcers (Slack and others, 1966), and to a lesser extent in limbs with ischaemic trophic changes and ulcers (Kidokoro, Sakakibara, Takao, Nihei, Hibi, Sakakibara, Washizu, Takahashi, Koike, Kawamura, Kobayashi, and Konishi, 1970). In view of the fact that irradiation to the skin causes local hypoxia, it would therefore seem logical to assess the effect of hyperbaric oxygenation in patients who are awaiting healing of irradiated skin areas which may or may not be infected. It has also been noted in dogs that the healing of traumatized skin is improved in hyperbaric oxygen. This has been assessed by measuring the tensile strength of the wound and it has been found that an increase as great as 43 per cent in the tensile strength of the wound has been achieved (Beckham and Hitchcock, 1965).

Hyperbaric oxygenation has been used for some time for the therapy of resistant infections with considerable success. Its effect on anaerobic organisms is well known, particularly on *Clostridium welchii* (Boerema and Groeneveld, 1970). However, it may also be used with good effect in aerobic infections (Goulon, Rapin, Letournel, and Barois, 1966; Ollodart, 1966). It exerts its effect in two ways: by reducing hypoxia in infected tissues, thereby increasing the host's own active resistance to infection and by a direct toxic effect on the micro-organism (McAllister, Stark, Norman, and Ross, 1965). It has been shown by Winter and Perrins (1970) that in healthy pigs whose skin has been traumatized the acceleration of epithelial cells across a wound is increased in hyperbaric oxygen as also is the number of mitotic figures in these cells. The rate of epithelization is proportional to the level of oxygen. At 1·1 kg. per sq. cm. (15 lb. per sq. in., 2 A.T.A.) the rate is almost double that at 1 A.T.A. In tissue culture it has been demonstrated that mitosis and cell movement are dependent on the oxygen tension (Medawar, 1948).

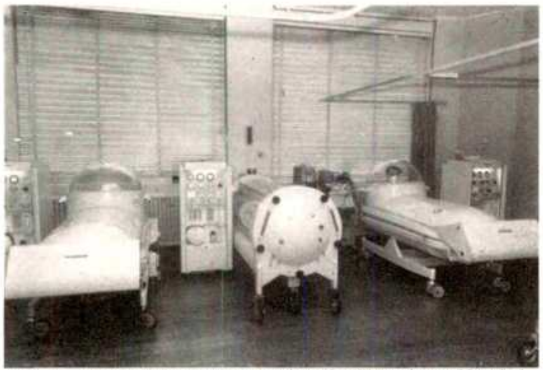

FIG. 1.—The hyperbaric oxygen unit at the Westminster Hospital.

The most satisfactory way of administering the oxygen is by the use of a one-person, hyperbaric chamber (*Fig.* 1). For the patients reported here the Vickers hyperbaric bed and cylinder have been used which are capable of administering oxygen at pressures of 1·1 kg. per sq. cm. (15 lb. per sq. in., 2 A.T.A.) or 2·2 kg. per sq. cm. (30 lb. per sq. in., 3 A.T.A.) respectively. As the patient is totally immersed in oxygen, the oxygen reaches the tissues directly by solution in the tissue fluids and via the lungs and thence via the systemic circulation. The oxygen is conditioned for humidity and temperature. Carbon-dioxide levels are controlled by use of soda-lime filters. Cardiac monitoring and artificial ventilation can be carried out, if necessary, within the chamber. During the course of therapy a patient receives 2 hours' hyperbaric oxygen twice a day at 2 or preferably 3 A.T.A.

At normal temperature and pressure the atmosphere has a partial pressure of oxygen of about 150 mm. Hg but the partial pressure of oxygen in the alveoli is only about 105 mm. Hg. This difference is accounted for by the presence of water vapour and expired carbon dioxide. However, there is also a loss of oxygen across the alveolar–capillary membrane, leaving a figure of 98–100 mm. Hg in the arterial blood. In normal people breathing air at normal temperature and pressure 19·4 ml. of oxygen per 100 ml. of blood are carried combined with haemoglobin and 0·3 ml. is dissolved in simple solution in the plasma. Estimates based on physiological principles of the partial pressure of oxygen in the arterial blood of patients breathing pure oxygen at 1, 2, and 3 A.T.A. are 650, 1400, and 2000 mm. Hg respectively. This constitutes a very considerable increase in the oxygen tension. If, however, the patient is anaemic the anaemia will not interfere with oxygenation at hyperbaric pressures. This is explained as follows: at pressures of 1, 2, and 3 A.T.A. of pure oxygen 2, 4·3, and 6·5 ml. of oxygen per 100 ml. of blood respectively are dissolved in simple solution. At rest the tissues of a patient extract 6·0 ml. of oxygen per 100 ml. of blood passing through. It can therefore be seen that at 3 A.T.A. the patient could survive without any haemoglobin (Boerema, Meijne, Brummelkamp, Bouma, Mensh, Kamermans, Sternhane, and Van Aalderen, 1960).

It has also been shown that high levels of Po_2 result in a reduction of blood-flow through tissues (Bird and Telfer, 1965). This is more than compensated for by the increase in Po_2, so that the oxygen delivery to the tissues is still increased and in the one-person chamber the skin will also be receiving increased oxygen directly from the ambient atmosphere.

There is no standardized period of treatment as this depends on the rate of healing. Treatment is stopped when healing is complete. Nevertheless, a course of treatment should not last for more than 3 weeks because of the potential toxic effects of oxygen therapy. Provided that these limits are enforced toxic effects are very rare, but the individual patient may have a lower threshold than average for these effects so that each patient must be observed carefully and treatment stopped if there is any suspicion of toxicity. The commonest manifestations are mild confusion and tingling of the extremities. Middle-ear pressure problems are occasionally encountered but are seldom severe. Pain can generally be relieved by a temporary decompression.

The favourable clinical impression in the case histories presented here suggests that the practice of using hyperbaric oxygen in head and neck surgery after irradiation is rational. Statistically significant clinical trials are impracticable, so that animal experiments are being conducted to test this hypothesis.

Acknowledgements.—The authors would like to thank Mr. E. H. Miles Foxen and Mr. C. A. Holborow for permission to report their cases; Dr. C. J. Gavey, Mr. C. E. Drew, and Dr. J. G. B. Thurston for their helpful advice; Messrs. Vickers (Medical) Engineering Limited for the loan of hyperbaric chambers; the Department of Medical Photography, Westminster Hospital, for the illustration, and Miss Stevens for secretarial assistance.

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THE AETIOLOGY OF CYSTIC ARTERIAL DISEASE

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SUMMARY

Two cases of cystic arterial disease of the popliteal artery are described in which a communication with the capsule of the knee-joint was demonstrated. The importance of this finding in the aetiology of the condition is discussed.

Cystic adventitial disease is a condition characterized by the presence in the adventitial coat of the artery of multiple cystic spaces containing a viscid gel with surrounding fibrosis. About 40 cases have been documented (Haid, Conn, and Bergan, 1970) since it was first described in 1946. The majority of these have involved the midpopliteal artery and it is a rare cause of unilateral calf claudication. The other arteries that have been affected are the common iliac artery (Atkins and Key, 1946; Jaquet and Meyer-Burgdorff, 1960) and the radial and ulnar arteries (Parkes, 1961; Bäckström, Linell, and Ostberg, 1965).

The aetiology of the condition has been much discussed and, as stressed by Little and Goodman (1970) in their review of the literature, no conclusive evidence has been presented to support any of the theories postulated. We report 2 cases of cystic arterial disease of the popliteal artery in which the findings suggest the possible aetiology of the condition.

CASE REPORTS

Case 1.—Mr. J. S., a storeman aged 43, presented with a history of exercise pain (intermittent claudication) in the right calf for 8 months. The onset had been sudden and the symptoms gradually progressive. His walking distance was about 400 yards. He had no other symptoms of peripheral ischaemia and was otherwise well. He was a non-smoker and there was no relevant family or past history.

On examination he was a fit-looking man of normal build. There was no abnormality to be found in his chest or abdomen. He was normotensive. In his legs the pulse state was normal before and after exercise and no bruits were detected. The circulatory and nutritional states of his feet and his toes were satisfactory.

In view of the definite and persistent history of exercise pain right femoral arteriography was carried out and this showed a smooth indentation in the upper part of the popliteal artery (*Fig.* 1) with a normal lumen above and below. There was no evidence of atherosclerosis and a provisional diagnosis of cystic adventitial disease was made.

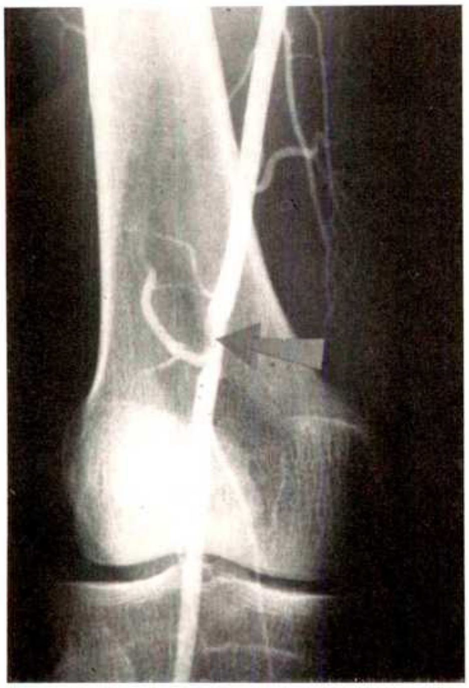

FIG. 1.—*Case* 1. Arteriogram showing indentation of the popliteal artery (arrowed).

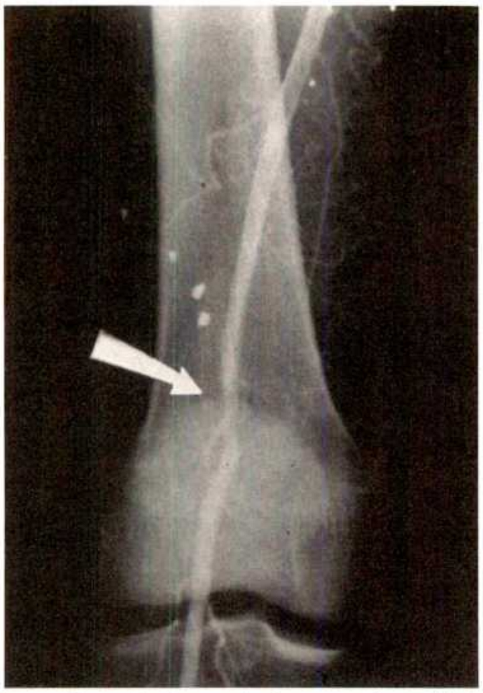

FIG. 3.—*Case* 2. Arteriogram showing compression and deviation of the popliteal artery (arrowed).

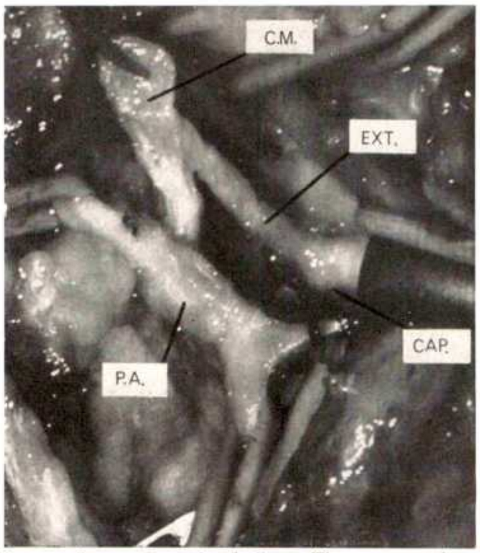

FIG. 2.—*Case* 1. Operative findings. The empty cystic mass (**C.M.**) enucleated from the popliteal artery (**P.A.**) with the extension (**EXT.**) passing from it to the capsule of the knee-joint (**CAP.**).

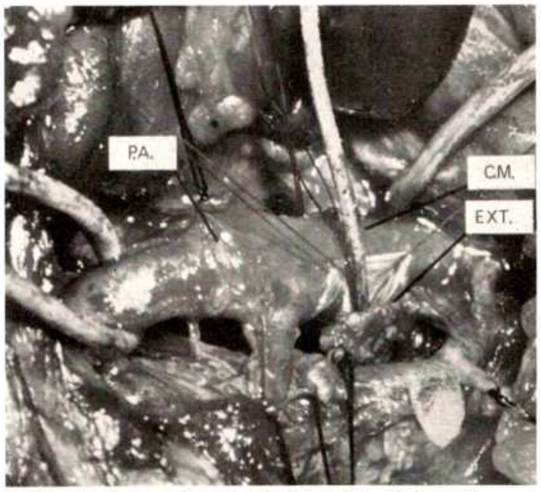

FIG. 4.—*Case* 2. Operative findings. Part of the cystic mass (**C.M.**) in and around the popliteal artery (**P.A.**) with a probe in the extension (**EXT.**) passing to the capsule of the knee-joint.

At operation a posterior approach revealed marked fibrosis and adhesions around the artery in the popliteal fossa. Careful dissection showed a collection of cysts around the artery, especially on its deep surface, involving about 3 cm. of its length. On further dissection an extension from the cystic segment was found to pass to the posterior capsule of the knee-joint to which it was firmly attached. The extension contained a viscid gel similar to that found in the cystic segment. The cysts were carefully peeled off the artery and removed, together with the extension, without damaging the artery (*Fig*. 2). The popliteal artery expanded to a normal calibre with improvement of the pulse distally.

Postoperatively his recovery was uneventful until the sixth day when he suffered a minor pulmonary embolus which was confirmed by lung scan. This was treated by anticoagulants. He recovered well and was discharged on the seventeenth day. He was soon able to resume normal activities and return to his work symptom-free. At follow-up 1 year after operation he was completely free of exercise pain with satisfactory peripheral pulses.

Histological examination of the periarterial cysts showed that the wall consisted of thick fibrous tissue lined in parts by a layer of flattened epithelial cells. Cross-sections of the extension to the knee-joint showed a normal genicular artery with, on one side, a layer of fibrous tissue in which there was a cleft lined by a layer of flattened cells similar to that seen in the cysts surrounding the popliteal artery. There was no elastic tissue to be seen in the cysts or extension.

Case 2.—Mr. L. P., a market gardener aged 55, gradually over a period of 8 months developed exercise pain in the right calf muscles. The pain had become troublesome at his work, which was an active outdoor job, and he had noted coldness in his right foot. There were no other symptoms of peripheral ischaemia and he was otherwise well. He was a moderate smoker and drinker and had been in good health previously.

On examination he was generally fit and of a normal build. He had mild hypertension. There was no abnormality to be found in his chest or abdomen. At rest he had normal pulses in both legs with a faint bruit in the right popliteal fossa. After limited exercise there was diminution of the right pedal pulses and a harsher popliteal bruit. The skin circulation and nutrition of his foot and toes were satisfactory. Routine blood screening revealed no abnormality.

A provisional diagnosis of popliteal stenosis due to cystic adventitial disease was made and arteriography carried out. A right femoral arteriogram showed kinking and compression of the midpopliteal artery with normal-looking vessels above and below (*Fig.* 3).

At operation the popliteal artery was exposed through a posterior approach. Fibrosis and multiple cysts were found around a segment of the artery, especially on its medial and deep aspects, for about 2·5 cm. of its length. A small pressure gradient was found across the segment. From the posterior aspect of the affected segment an extension about 5 mm. across was found to pass to the posterior capsule of the knee-joint to which it was firmly adherent (*Fig.* 4). The extension contained viscid gel similar to that in the cysts around the artery.

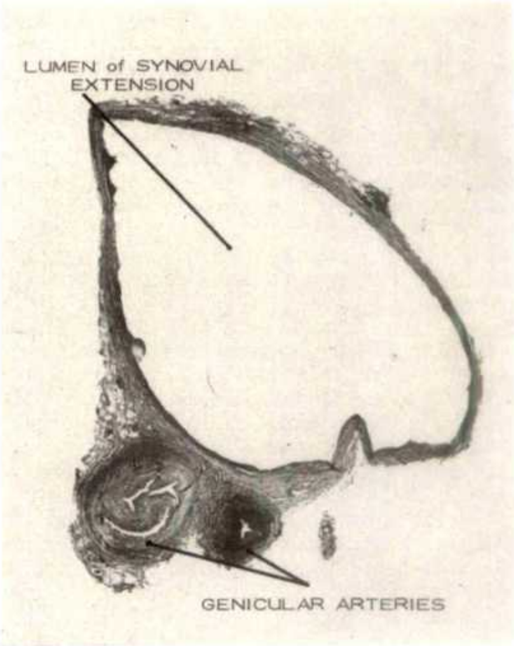

FIG. 5.—*Case* 2. Cross-section of the extension from the cystic popliteal artery to the capsule of the knee-joint.

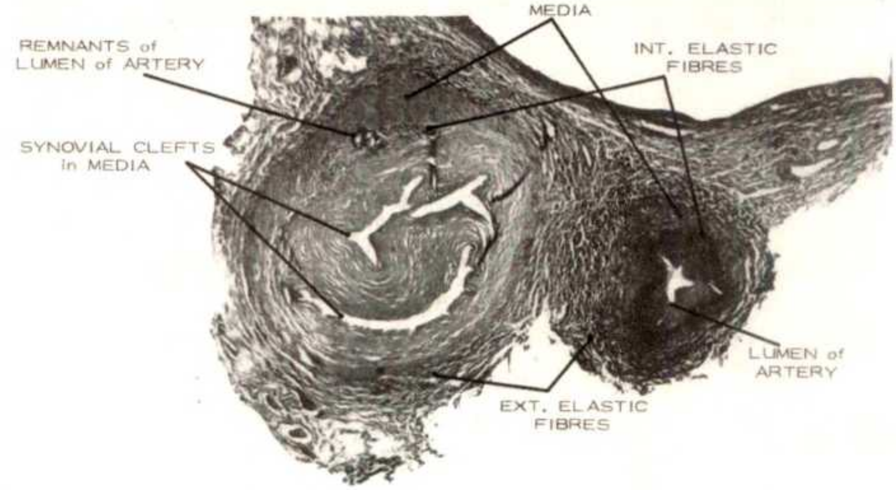

FIG. 6.—*Case* 2. Magnified cross-section of the genicular arteries shown in *Fig.* 5.

The involvement of the arterial wall by the cystic disease was such that enucleation was not possible. After systemic heparinization the affected segment was resected together with the extension and its attachment to the capsule of the knee-joint. No communication with the cavity of the knee-joint was demonstrated. The arterial defect was repaired by a graft from the long saphenous vein. A satisfactory restoration of the distal circulation was obtained with good pedal pulses.

Postoperatively the patient's progress was uneventful and he was discharged on the tenth day. He soon returned to his work and at follow-up 6 months after operation he was fully active and symptom-free with normal peripheral pulses. His hypertension was controlled by Aldomet.

Histological examination was similar to that seen in *Case* 1. The fibrous-walled cystic spaces, with a patchy inner lining of flattened epithelial-like cells and a mucinous content, had the features of a ganglion. The cystic extension to the knee-joint showed in its fibrous wall small arteries and remnants of elastic and plain muscle-tissue. One section showed expansion of part of an artery by cystic spaces lying in its muscular coats and pushing the lumen and internal elastic lamina to one side (*Figs.* 5, 6).

DISCUSSION

The clinical picture of cystic adventitial disease of the popliteal artery is of the sudden onset of unilateral intermittent calf claudication in a 30–40-year-old man, usually with a progressive course (Lewis, Douglas, Reid, and Kennedy Watt, 1967; Haid and others, 1970; Little and Goodman, 1970). On examination there is no clinical evidence of generalized cardiovascular disease. The femoral pulses are always normal whilst the popliteal and pedal pulses may be diminished at rest and may disappear after exercise, though these are not constant features (Ishikawa, Mishima, and Kobayashi, 1961). Our cases illustrate the variable clinical signs that may be encountered.

Arteriography is essential in establishing the diagnosis. A limited segment of the artery is involved by a smooth filling defect with a normal lumen above and below. The clinical and radiographic appearances are such that a differential diagnosis of the popliteal entrapment syndrome must be borne in mind (Leading Article, 1970).

Exploration is indicated in order to establish the diagnosis and to correct the defect. The only effective long-term treatment is either complete stripping of the adventitial coat and its cysts from the vessel wall or resection of the affected segment and graft replacement. Histological examination of the cysts shows them to be lined by fibrous tissue sometimes with an epithelial synovial-like lining. The cysts contain a gelatinous fluid similar both physically and chemically to that found in the common ganglion. These facts were demonstrated in our cases.

The current concepts of aetiology have recently been reviewed by Haid and others (1970) and are:—

1. Repeated minor trauma from stretching and distortion of the artery, owing to its proximity to the knee-joint, producing cystic degeneration of the adventitia.
2. Myxomatous degeneration in the adventitial coat of the artery as part of a generalized disorder of connective tissue. This theory is unlikely.
3. Developmental inclusion of mucin-secreting cells in the arterial wall. McEvedy (1962) in his thesis on simple ganglia advocated that these lesions arose as extensions of so-called 'capsular cysts' in the capsule of the neighbouring joint. These cysts were lined by synovial membrane and enlarge as a result of repeated minor trauma to form simple ganglia. Histological and biochemical comparisons between ganglia and adventitial cysts are similar (Leaf, 1967; Lewis and others, 1967).

It has been postulated that these two conditions might be similar in origin (Lewis and others, 1967). Richards (1963) suggested that more definite evidence of such an origin would be the demonstration of a communication between the cysts and the neighbouring joint. Such a connexion has been demonstrated in both our cases. This has not been reported before in relation to the popliteal artery, although Parkes (1961) noted connexions between cysts of the radial and ulnar arteries and the carpal joints.

The operative and histological findings in our cases support the synovial cellular inclusion theory and that the pathogenesis is similar to that of a simple ganglion. Either capsular synovial cysts enlarge and probably track along a genicular artery to involve the adventitia of the popliteal artery or synovial rests are sequestrated during development into the arterial wall, there to secrete, enlarge, and extend over many years. The interesting histological findings in our second case in which synovial clefts were found within the media of the genicular artery suggests sequestration rather than tracking along such a resistant layer.

In the first patient the cysts were entirely adventitial and were readily removed, leaving an intact popliteal artery. In the second patient enucleation was impossible because the cysts were both adventitial and in the media of the artery. Resection of the affected segment of artery was therefore required. These operative findings confirm the probable dual aetiological mechanism of tracking and sequestration from a common synovial source. Anatomically the cystic condition is not entirely adventitial in its distribution but also involves the media. It would therefore be more correct to call it 'cystic arterial disease'.

Careful dissection in other cases may reveal similar communications between the popliteal artery and the adjacent capsule of the knee-joint. Removal of the cysts and their connexion is probably important in the eradication of the condition and the prevention of a recurrence.

Acknowledgements.—We are grateful to Dr. E. H. Hemsted for his detailed histological studies and advice and to Mr. L. Williams of the Photographic Department of the Royal Berkshire Hospital for the illustrations.

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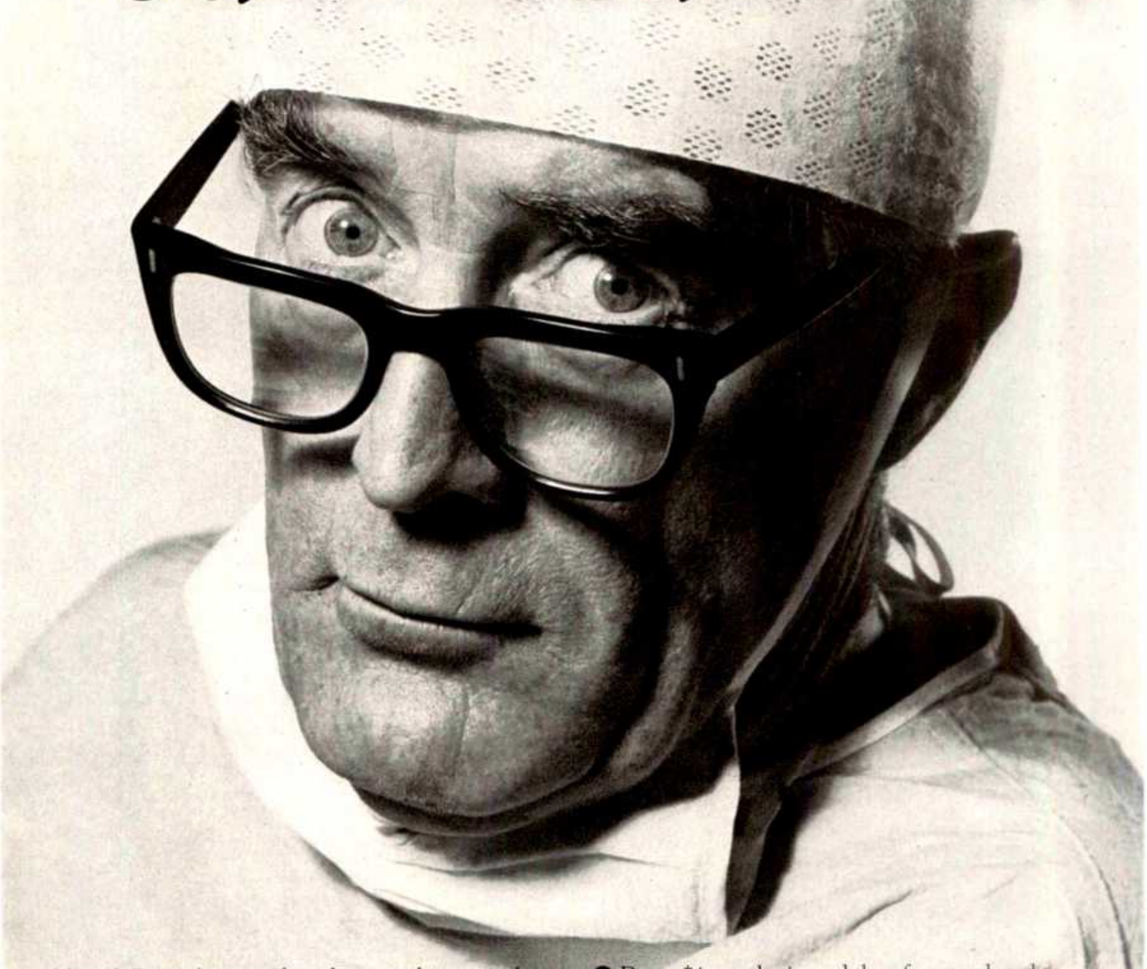

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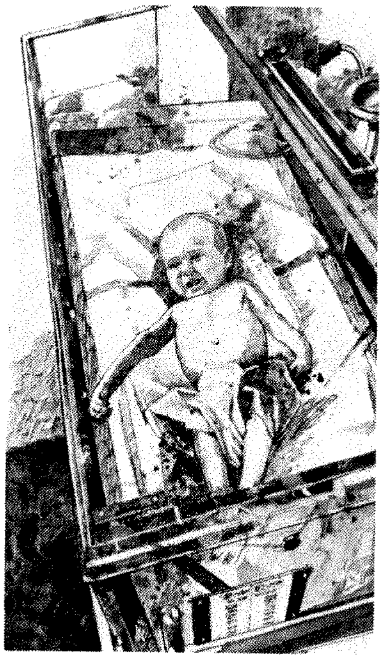

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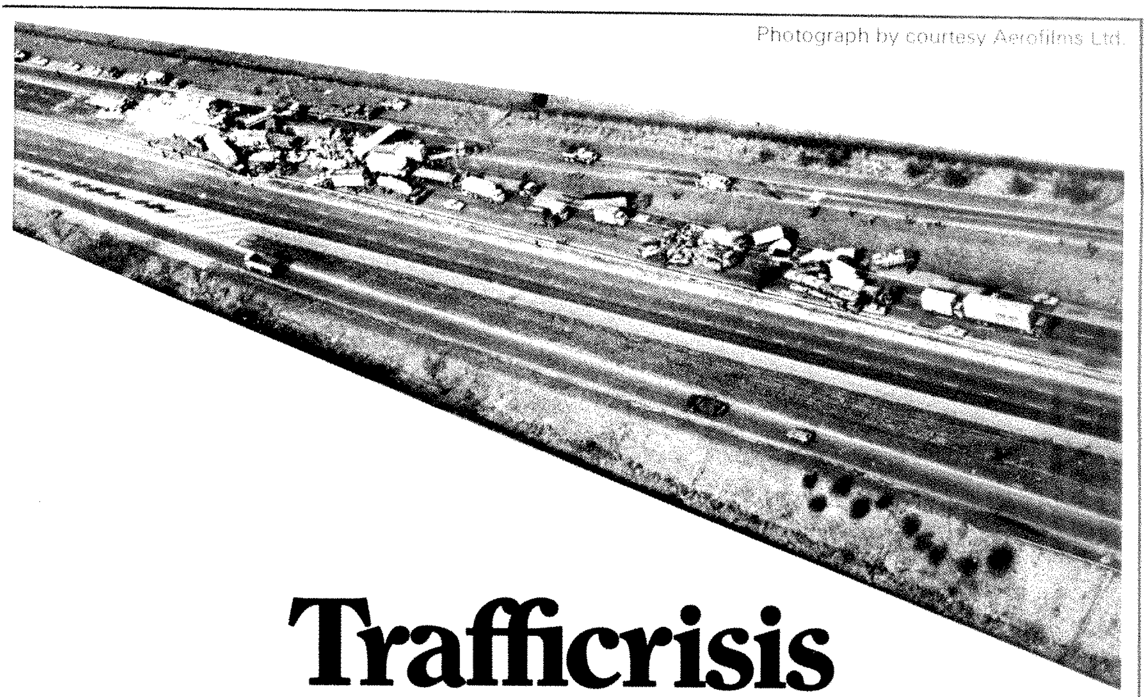
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MOUSSEAU-BARBIN TUBES FOR THE TREATMENT OF CARCINOMA OF THE LOWER TWO-THIRDS OF THE OESOPHAGUS

RESULTS AND OPERATIVE TECHNIQUES

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SUMMARY

Twenty-three patients have undergone insertion of a Mousseau-Barbin tube for the correction of dysphagia due to inoperable carcinoma of the stomach or the oesophagus. All the patients obtained relief of their symptoms and there was no postoperative mortality or infection.

Technical details are discussed which are designed to reduce the occurrence of obstruction of the tube and erosion of the mucosa of stomach and oesophagus, and to facilitate insertion of the tube in difficult cases.

MOUSSEAU, Le Forrestier, Barbin, and Hardy (1956) first described their tube 17 years ago. Since then a technique has been evolved in the Department of Cardiothoracic Surgery, University of Leeds, which during the past 4 years has produced very successful results without postoperative mortality.

MATERIALS AND METHODS

During the past 4 years (Feb., 1968, to Feb., 1972) 23 patients have undergone insertion of Mousseau-Barbin tubes in an attempt to relieve dysphagia caused by inoperable carcinoma of the gastro-oesophageal junction and the lower and middle thirds of the oesophagus.

The indication for insertion of the tube was the presence of a growth which could not be removed or by-passed satisfactorily, or if the patient was too ill to withstand major surgery when there was no hope of a cure, particularly if secondary deposits were present.

Oesophagoscopy should always be performed immediately prior to performing the laparotomy to assess the size and state of the oesophagus and the extent of the growth. A nasogastric tube can then be passed through the obstructed lumen under direct vision into the stomach. This procedure should never be performed blindly because the oesophagus adjacent to the growth is very friable and is easily perforated.

1. Carcinoma of the Lower Third of the Oesophagus and Gastro-oesophageal Junction.—Packs are placed around the stomach to absorb any overspill of the gastric contents. The stomach is opened through a longitudinal incision with diathermy, between supporting stay-sutures, sufficient to allow entry of the whole hand. When a large, craggy growth is present at the gastro-oesophageal junction it may be almost impossible to define the entrance to the oesophagus which is necessary if a nasogastric tube could not be passed successfully from above. In such cases the index finger is inserted into the oesophagus and a gum-elastic bougie is passed along the groove between the index and second (middle) fingers and thus more easily into the oesophagus.

If the gastrostomy requires extension in difficult cases it should be made paradoxically towards the pylorus. This facilitates closure ultimately without undue retraction being necessary both on the stomach and the laparotomy; it also reduces efflux of gastric contents into the subphrenic spaces.

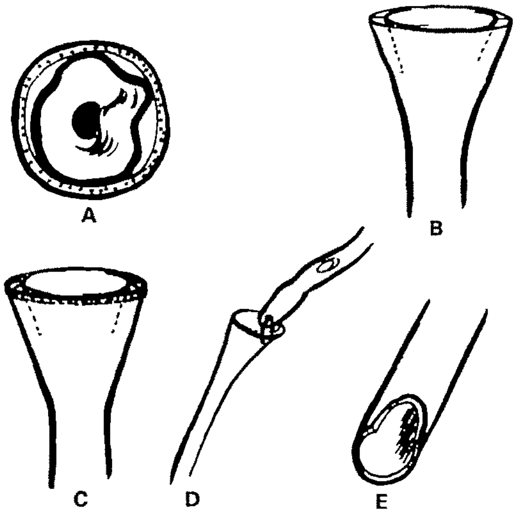

FIG. 1.—A, View of proximal, funnel end of the tube demonstrating the disparity between its circumference and that of the oesophagus. B, C, Demonstrating the rounded edges of the funnel end after it has been cut to fit the oesophagus. D, Suture of the tail end of the tube to the end of 'rail-roading' vehicle. E, Distal end of the tube tailored to increase opening area and reduce possibility of obstruction.

Before the Mousseau-Barbin tube is given to the anaesthetist the surgeon should trim its funnel end in order to provide a snug fit in the oesophagus. If the diameter of the funnel is greater than that of the oesophageal lumen then folds will occur in the funnel (*Fig.* 1 A) in which food will collect, producing oesophagitis, ulceration, and infection. This scalloping of the funnel margin also reduces the area of entrance to the tube. When the funnel is trimmed to size the sharp edge (*Fig.* 1 B) should be rounded with scissors (*Fig.* 1 C) in an attempt to reduce trauma to the mucosa.

The thin end of the Mousseau-Barbin tube is attached to the end of the nasogastric tube or gum-elastic bougie with a suture placed by the anaesthetist. The suture should be placed as near to the end of both tubes as possible in order to minimize trauma in transit (*Fig.* 1 D).

When pulling the tube into place it should be pulled slowly and firmly by holding a long swab in the hand in an attempt to keep the operating field clean.

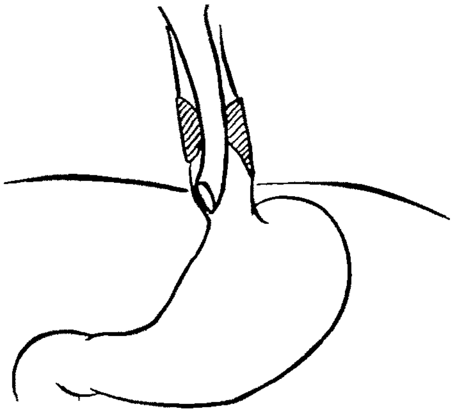

FIG. 2.—Malposition of the distal end of the tube in the lower oesophagus causing obstruction. The tube has slipped upwards out of the stomach.

Occasionally slight difficulty will be experienced at the cricopharyngeal level. The anaesthetist can check with a laryngscope that all is well, but we have not found it necessary to trim the tube for this reason as suggested by Dean (1969).

When the tube rests firmly on the growth excess length is removed using angled bone-cutters. Three cm. is sufficient length of tube to remain in the stomach. If more remains the tube will impinge upon the greater curvature of the stomach, producing ulceration, haemorrhage, or perforation, and also obstruction to the downward passage of food through the tube.

To reduce the possibility of obstruction a flap should be cut out of the end of the tube as shown in *Fig.* 1 E. This also doubles the area of outlet. Again any sharp edges should be rounded with bone-cutters.

It is not necessary to suture the tube in place or to perform temporary gastrostomy, as suggested by Dave (1971).

2. Carcinoma of the Middle Third of the Oesophagus.—The same methods apply here except that the tube is pulled into place through a longitudinal oesophagotomy. The distal end of the tube is cut so that it is 3 cm. above the cardia in order to prevent it becoming misplaced as shown in *Fig.* 2 with the likelihood that it will become obstructed.

DISCUSSION

The age range of the 23 patients was 42–87 years (mean 67 years). They all obtained complete relief of their symptoms and surprisingly none of them experienced unpleasant symptoms due to the presence of this tubular splint.

Reflux oesophagitis results if the patients lie flat and this can have severe consequences (Holden and Wooler, 1971) if acid reflux is not controlled. All the patients are advised to eat liquidized food and to avoid fish and bread. However, many of them disregard this advice and some admit to having no dietary restrictions.

Postoperatively antibiotics (Ampiclox 500 mg., 6-hourly i.m.) are prescribed for 2 days and with this régime no infection has followed this very unsterile operation.

Three of the patients were in the 'middle third' category. One of them had the tube pulled into place via a gastrotomy. The tube slipped up into the oesophagus and became malpositioned (*Fig.* 2) and irremediable blockage followed, requiring removal of the tube. This was easily performed by making four longitudinal slits down the funnel using endoscopic scissors. The collapsed tube could then be removed without trauma to the upper alimentary tract.

The tube is not suitable for tumours above the level of the aortic arch because the proximity of the funnel to the pharynx causes the tube to be displaced upwards owing to the longitudinal shortening of the oesophagus during swallowing.

CONCLUSIONS

The Mousseau-Barbin tube is of great benefit to patients who have dysphagia caused by inoperable carcinoma of the stomach or the oesophagus or who are too ill to undergo major surgery. It can be introduced safely in all patients by any surgeon whose training permits them to perform a laparotomy, particularly if the above suggestions are employed.

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OESOPHAGEAL INTUBATION IN OBSTRUCTIVE LESIONS OF THE OESOPHAGUS

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SUMMARY

In a study of the relative merits of the Mousseau-Barbin and Celestin tubes used for palliation in 60 patients with dysphagia due to mechanical obstruction of the oesophagus by cancer or stricture, the Celestin tube emerged as a better palliative measure than the Mousseau-Barbin tube in so far as operative morbidity and mortality are concerned. In the assessment of the quality of life after intubation the Celestin tube again appears to be the better tube in the early postoperative period but in the later stages there appears to be no significant difference in the quality of life between the two tubes.

The quality of life as defined in this paper appears to have little relation to the duration of survival.

OESOPHAGEAL intubation has become a common palliative procedure for patients with inoperable lesions of the oesophagus and cardia of the stomach. It is usually indicated where the lesion has been shown to be incurable or the general state of the patient is too poor for major surgery. In general the expectation of life of these patients is limited and the primary objective of intubation is therefore the restoration of trouble-free swallowing.

In this survey of 60 patients intubated at the Royal United Hospital, Bath, the majority had a carcinoma of the oesophagus or stomach (91·6 per cent) and the remainder had benign strictures associated with peptic oesophagitis. Most of the patients in the series had oesophageal lesions, but those with high gastric lesions have also been included where tubes have been used to overcome the obstruction to swallowing.

Two types of tubes have been used in this group of patients, the Mousseau-Barbin and Celestin tubes, and all the operations were performed by one consultant surgeon over a period of 7 years from 1966 to 1972. The objectives of this study were twofold: to compare the effectiveness of these two types of tube and to evaluate the quality of life experienced by these patients after intubation.

HISTORICAL BACKGROUND

The first but unsuccessful attempt at oesophageal intubation was made in the year 1845 by Leroy d'Etiolles of France who used decalcified ivory as the material for his tube (Celestin, 1959). The first successful intubation was reported by Sir Charles Symmonds in 1885; initially he used an oesophageal tube fixed to a boxwood funnel, but later he improved the tube by using ivory, silver, and finally gum-elastic, fixing the tube in place by threads brought out through the mouth and tied to the ear. About this time Hill (Souttar, 1924) introduced a probe, made of silver wire covered by a fine rubber tube which was left in situ and around which some food was able to pass. In 1914 Guisez, using a De-Pezzer-like catheter, introduced a tube for the first time under direct vision with the help of an oesophagoscope. After the introduction by Sir Henry Souttar in 1924 of a tube made of German silver wire with an expanded top, inserted through the oesophagoscope (Souttar, 1924, 1927) interest in the field died down until 1949 when Brown produced an improved tube made of silver. Plastic materials were used for the first time by Coyas (1955) in Athens and by Triboulet-Piton in France in 1954 (Lortat-Jacob and Triboulet-Piton, 1955) in the form of a tube made with a radio-opaque ring at both ends. In the same year Kropff designed a tube made of polythene which was inserted through a cervical oesophagotomy. These tubes had disadvantages and a major advance was made in 1956 when Mousseau and Barbin introduced the Mousseau-Barbin tube made of Neoplex, and Barbin first described the 'pull-through' method of inserting the tube through a high gastrotomy. The final development occurred in 1959 when Celestin described a tube based on the Mousseau-Barbin tube but made in two parts: a hollow oesophageal tube and a detachable pilot bougie made of solid polythene. The upper end of the Celestin tube was formed into a barrel shape so that the tube fitted the oesophagus better and was therefore less likely to pass through the stricture or to become obstructed. This particular tube was also less liable to produce pressure necrosis of the oesophageal wall, and at a later stage Celestin incorporated a radio-opaque strip in the tube.

METHOD OF SURVEY

The information used in this survey has been obtained in three main ways. First, by examination of the clinical history, clinical findings, investigations, operations, and postoperative complications from the hospital records. Secondly, the patient's general practitioner was contacted and asked for his observations on the patient's condition after intubation. Thirdly, in the case of surviving patients, direct interviews were sought with both the patient and relatives, or where the patient had subsequently died the close relatives were interviewed in order to obtain information and opinions about the success of the procedure.

PATIENTS

Sixty patients are included in this series, 55 of whom had carcinomas and 5 had benign strictures of the oesophagus. Of the malignant lesions, 58 per cent were in males and 42 per cent in females. The eldest patient was a 97-year-old female and the youngest a 48-year-old female. The highest incidence of carcinoma was in the age-group 60–90 years. The lesions have been classified into four groups: the first three according to the level of the oesophagus involved, i.e., upper third, middle third, and lower third, and the fourth group includes lesions of the cardia and other gastric cancers causing obstruction of the oesophagus.

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The investigations used for diagnosis and localization of the lesion in this series have been barium-swallow examination, oesophagoscopy, and biopsy. The highest incidence of carcinoma of the oesophagus was in the lower-third region. In all the patients the state of operability of the lesion was established and the extent of the disease delineated before intubation was undertaken. The age and sex distributions of the patients are shown in *Table I* and the sites of the lesions are shown in detail in *Table II*.

Table I.—AGE AND SEX DISTRIBUTIONS OF PATIENTS WITH MALIGNANT LESIONS

AGE-GROUP (yr.)	MALE (58 per cent)		FEMALE (42 per cent)		COMBINED (100 per cent)	
	No.	Percentage of Group	No.	Percentage of Group	No.	Percentage of Group
91 upwards	1	3·1	1	4 2	2	3 6
89–90	9	28	8	35	17	31
79–70	7	22	7	31	14	25 5
69–60	12	37·5	5	21·7	17	31
59–50	3	9·3	1	4·2	4	7·2
49–40	—	—	1	4 2	1	1 8
Total	32		23		55	

Table II.—SITE OF THE MALIGNANT LESIONS

SITE OF LESION	NO	PERCENTAGE
Upper third of the oesophagus	1	1·8
Middle third of the oesophagus	17	30 8
Lower third of the oesophagus	23	41 8
Cardia, fundal (high gastric)	14	25 4

OPERATIVE PROCEDURES

The operations were performed by one consultant surgeon over a period of 7 years, using the 'pull-through' method of intubation. All the patients had a preliminary oesophagoscopy and biopsy except 2 patients, both more than 90 years of age, where intubation was done in one stage. In 6 patients the inoperability of the lesion was established after exploratory thoracotomy and in a further 8 patients after exploratory laparotomy.

Two methods of intubation have been used in this study. In the more usual of these methods a small-bore gum-elastic bougie is passed through the narrowed area under direct vision using the oesophagoscope. The tip of the bougie is recovered from the stomach through a high gastrotomy made through a small, left upper paramedian incision. The distal end of the Mousseau-Barbin tube, or in the case of the Celestin tube the distal end of the pilot bougie, is tied to the gum-elastic bougie at the mouth end and the main oesophageal tube is guided through the oesophageal stenosis to the stomach. The tube is then drawn through and impacted at the proximal end of the obstructing lesion and the tube is cut off at a suitable length in the stomach.

In the second method retrograde bouginage is undertaken via the gastrotomy incision in cases where the stricture is difficult to pass from above or where a laparotomy has been undertaken for assessment of operability. Once the bougie is in position through the obstruction the procedure is the same as with the first method. A small corrugated rubber drain is usually used to guard against leakage from the closed gastrotomy wound. The tube has not been fixed to the stomach in this series and in no patient has a pyloroplasty been done as has been suggested by Celestin. On the day following operation a radiograph of the chest is obtained and if there is no evidence of oesophageal perforation the patient is allowed fluids by mouth; from the second day a gradual return to a normal diet has been usual and most patients are eating solid food by the third postoperative day. All the patients were instructed about taking an effervescent drink, such as Enos or Andrews Salts, should the tube become blocked by solid food impacted in it.

COMPLICATIONS

Of the 60 patients, 36 had a Mousseau-Barbin tube inserted and 24 a Celestin tube, the Mousseau-Barbin tube being used from 1966 to 1969 and the Celestin tube from 1970 to 1972 (*Table III*). The patients in general were in the older age-groups and were usually in a poor general condition presenting a considerable anaesthetic and surgical risk. Although many of the complications could be attributed to anaesthesia they have all been grouped as postoperative complications associated with oesophageal intubation. It has proved difficult to distinguish between anaesthetic and operative complications in this group of patients.

Table III.—TYPE OF TUBES USED

TYPE OF TUBE	NO	PERCENTAGE	PERIOD
Mousseau–Barbin	36	60	1965–69
Celestin	24	40	1970–71

The commonest complication was bronchopneumonia. This is particularly significant because the incidence was notably higher in our patients than in postoperative patients of the same sex and age distribution undergoing other surgical procedures. The overall incidence of bronchopneumonia in this series was 30 per cent; in the Mousseau-Barbin group it was 32·7 per cent and in the Celestin tube group 29·1 per cent.

The other immediate postoperative complications were pulmonary collapse, pleural effusion, haemorrhage from the oesophagus, perforation of the oesophagus and mediastinitis, coronary thrombosis, and peritonitis. The late complications were wound infection, a persistent gastric fistula, oesophageal haemorrhage, and, in the long-term, frequent episodes of blocking of the tube. The details of these complications are shown in *Table IV*.

MORTALITY

As in the differentiation of the cause of the complications it was difficult to distinguish between the mortality due to operation and that due to anaesthesia. We have accepted that all the patients who died in the immediate postoperative period died from the operation irrespective of whether they died from operative or anaesthetic complications. We have arbitrarily defined a postoperative death as one which occurred within 7 days of the operation as we estimate that most of the patients who had complications due to surgery died within this period. The overall operative mortality was 20 per cent. However, in the Mousseau-Barbin tube series it was 25 per cent but was only 12·5 per cent in the Celestin tube patients. As would be expected from the incidence of post-operative complications, the commonest cause o death was bronchopneumonia. Other causes of death were haemorrhage from the oesophagus or stomach, perforation of the oesophagus with mediastinitis, and coronary thrombosis (*Table V*).

Table IV.—COMPLICATIONS

COMPLICATION	IN-PATIENTS WITH TUBES				TOTAL NO OF CASES		NO. OF DEATHS				
	Mousseau–Barbin		*Celestin*				*Celestin*		*Mousseau–Barbin*		*Total No.*
	No	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	No	Percentage	
Immediate											
Bronchopneumonia	11	32·7	7	29·1	18	30·0	2	8·3	5	13·9	7
Pulmonary collapse	5	13·9	4	16·6	9	15	—	—	—	—	—
Pleural effusion	4	11·1	3	12·5	7	11·6	—	—	—	—	—
Haemorrhage	3	8·3	2	8·3	5	8·3	—	—	2	5·5	2
Perforated oesophagus and mediastinitis	1	2·8	1	4·2	2	3·3	1	4·2	1	2·8	2
Coronary thrombosis	1	2·8	0	—	1	1·66	—	—	—		
Peritonitis	—	—	1	4·2	1	1·66	—	—	—	—	—
Late											
Wound infection	6	16·6	6	25	12	20	—	—	—	—	—
Persistent fistula	1	2·8	1	4·2	2	3·3					
Haemorrhage	1	2·8	1	4·2	2	3·3	1	—	1	—	2

Table V.—OPERATIVE MORTALITY (DEATH WITHIN 7 DAYS) AND CAUSE OF DEATH

TYPE OF TUBE	NO OF CASES	OPERATIVE MORTALITY	PERCENTAGE MORTALITY	CAUSE OF DEATH							
				Broncho-pneumonia		*Haemorrhage*		*Perforated Oesophagus and Mediastinitis*		*Coronary Thrombosis*	
				No	Percentage	No	Percentage	No.	Percentage	No.	Percentage
Mousseau-Barbin	36	9	25	5	13·9	2	5·5	1	2·8	1	2·8
Celestin	24	3	12·5	2	8·3	—	—	1	4·2	—	—

THE QUALITY OF LIFE OF INTUBATED PATIENTS

The stimulus for this survey was a curiosity about the quality of life of patients after intubation because the purpose of intubation was the relief of dysphagia. We were interested in how these patients lived with their tube and how their post-intubation existence compared with their preoperative state. We have attempted to review their day-to-day life from both the physical and mental aspects, particularly with regard to their ability to enjoy life to some degree. In order to evaluate this degree of palliation we had first to find a standard against which the quality of life in individual patients could be compared. It proved to be difficult because so many factors were involved, i.e., different types of patients with different types of lesions at different stages and treated with two different types of tube. Since treatment was palliative in all the cases with the objective of relief of dysphagia, relief of preoperative symptoms seemed to us to be the best criterion. The commonest presenting symptoms were dysphagia and loss of weight, so that our criteria were based on the postoperative ability to swallow and the maintenance or gain of body-weight. We also added the incidence of blockage of the tube.

Table VI.—GRADES USED FOR ASSESSING QUALITY OF LIFE IN THIS SERIES

GRADE	SWALLOWING	BLOCKAGE OF TUBE	WEIGHT
I (very good)	Solid	Nil or minimum	Gain
II (good)	Solid	Occasional	Steady
III (fair)	Semi-solid	Occasional	Steady
IV (bad)	Liquid	Often	Loss

Table VII.—QUALITY OF LIFE COMPARED WITH THE TYPE OF TUBE USED

GRADE	CELESTIN TYPE		MOUSSEAU-BARBIN TYPE	
	No of Cases	Percentage of Total	No. of Cases	Percentage of Total
I	5	20·8	2	5·5
II	10	41·6	4	11·1
III	3	12·5	15	41·6
IV	3	12·5	6	16·6

As far as swallowing was concerned, we divided foods into three types (solid, semi-solid, and liquid) in order to compare the patient's ability to swallow. We have used meat, such as steak, and salad and apple as our examples of solid food, mincemeat, rice pudding, soft-boiled egg, or bread softened in milk for semi-solid food. Because loss of weight is such a common presenting symptom, the surviving patients were weighed routinely as a measure of their ability to maintain their body-weight or even to gain weight.

Blockage of the tube proved to be a very common postoperative incident in the lives of these patients and we regarded a blockage as significant when the patient or his relatives were worried, the patient had to abandon the meal, the attentions of the patient's doctor were required, or the patient needed admission to hospital. On admission, the tube quite frequently spontaneously unblocked itself, but if it failed to do so the tube was unblocked either by the passage of a Levin's tube or by oesophagoscopy and endoscopic removal of the food mass.

Accordingly the quality of life for these patients in the postoperative period was judged as one of four grades (*Tables VI, VII*).

Table VIII.—LENGTH OF SURVIVAL AFTER INTUBATION COMPARED WITH THE TYPE OF TUBE USED

TIME AFTER INTUBATION (mth)	MORTALITY (per cent)	
	Mousseau-Barbin Tube	Celestin Tube
0–3	47	25
4–6	11	21
7–9	2 8	8 3
10–12	5 6	—
13–15	2 8	—
16–18	—	—
19–30	5 6	—

Grade I (very good): Able to swallow solid food without blockage of the tube, associated with a steady weight-gain.

Grade II (good): Initially able to swallow solid food but later able to swallow semi-solids only with occasional blockage of the tube although maintaining a steady body-weight.

Grade III (fair): Able to swallow semi-solids onl with occasional blockage of tube, but with maintenanc of body-weight.

Grade IV (bad): Able to swallow liquids only wit frequent blocking of the tube and a steady loss o body-weight.

We found that the quality of life was related to som degree with the period of survival (*Table VIII*) bu the relationship was by no means a direct one.

The patients in grade I did not survive for th longest periods and only in grade IV patients was ther a direct relation between the quality of life and th survival period. All the patients in this group di uniformly badly and died within a month or so o intubation. On the other hand, grade I and I patients tended to die within 3 or 4 months o intubation whereas patients in grade III survived fo longer periods. As might be expected, as time o survival increased the patients in grades I and I tended to descend into grade III or IV.

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In Memoriam

Charles F. M. Saint, C.B.E., F.R.C.S.

(1886–1973)

BORN on 14 August, 1886, at Bedlington, Northumberland, Charles F. M. Saint was educated at King Edward VI Grammar School, Morpeth, and the University of Durham, Newcastle upon Tyne. His academic record as a student was absolutely brilliant. After graduating M.B., B.S. in 1908 Charles Saint became intimately associated with Professor Rutherford Morison, first as house-surgeon and later as surgical registrar and private assistant. He spent much of his time preparing Morison's later work for publication, in particular that well-known book, *An Introduction to Surgery*. In 1912 he obtained the M.D., M.S. with first-class honours, and in 1913 he became a Fellow of the Royal College of Surgeons of England.

Soon after the outbreak of World War I he joined the Royal Army Medical Corps and was drafted to France, where he distinguished himself as a surgeon in charge of various forward surgical units. For his military work he was awarded the C.B.E. and the Médaille d'Honneur in gold. In 1919 he returned with the rank of Major and resumed his pre-war appointments.

Such was the man who came to Cape Town in March, 1920, at the age of 33 years as the first Professor of Surgery in the first School of Medicine in South Africa. The principles of surgery formed the basis of Professor Saint's approach to the practice and teaching of surgery, and when he retired in 1946 he had moulded and inspired the surgical ideas which, developing in the Cape Town School, permeated far through Southern Africa and spread beyond the seas. Indeed, his dynamic influence has continued to live and flourish through his students, for what was once said of Morison can equally well be said of him: 'Because he was a great man as well as a great surgeon, he handed on the spirit as well as the letter of his creed and became one of the greatest disseminators of surgical thought and makers of surgeons.'

Charlie Saint, as he was known to his students, gave top priority to teaching, but he was also a superb clinician, a master surgeon, and a widely respected man who possessed those unique qualities found only in truly great men: leadership and the ability to inspire. Although he moved to Sark in 1960 he continued to take a keen interest in medical schools and to offer wise counsel to many, and as he grew older we saw more of Saint the philosopher and classical scholar. His aphorisms—all pearls of wisdom—have become the by-words of many and in 1967, aged 81 years, he delivered a stirring address entitled 'Another Look Around' in which he reiterated his lifelong philosophy of looking outwards, forwards, and upwards and through this achieving 'happiness which is the most important thing in life'.

SHORT NOTES OF RARE OR OBSCURE CASES

DUODENO-URETERIC FISTULA*

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SUMMARY

A case of a duodeno-ureteric fistula in a man of 46 years is described. This is a rare condition, only 2 previous cases having been reported. The patient did not agree to operation and no tissue is available for histological examination. However, reasons are given for believing this to be the first case in which the primary pathology is in the duodenum.

CASE REPORT

Mr. W. M., a fitter, first began to get attacks of abdominal pain in 1961 at the age of 35 years. He had no significant previous medical history. The patient described his initial attacks as 'gastric' in type. On his first admission to New End Hospital in July, 1967, the character of the pain had changed and suggested a right renal colic. He had been investigated for pain in the right hypochondrium between 1965 and 1967 at another hospital. In 1966 an intravenous pyelogram and cholecystogram had been normal and a further intravenous pyelogram in June, 1967, was also normal (*Fig.* 1). After 1967 his attacks of pain remained predominantly in the right abdomen. Sometimes his symptoms suggested a peptic ulcer, the pain being aggravated by food and relieved by milk. The pain occasionally woke him at night and was sometimes associated with the vomiting of food. He had no disturbance of bowel habit. His symptoms were exacerbated by a high alcohol intake. At other times his symptoms were more characteristic of a renal colic with pain in the right loin radiating to the right groin. Usually he had no urinary symptoms, but occasionally he had frequency and dysuria.

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* Paper presented to the Clinical Section of the Royal Society of Medicine on 12 Nov., 1971.

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In April, 1969, he had a severe exacerbation of his symptoms which required admission to hospital. He had pain in the right side of his abdomen which radiated to his right loin and right testicle. He had no urinary symptoms, but his right testicle was mildly swollen and tender. An intravenous pyelogram on this occasion was abnormal, showing a mild hydronephrosis of the right kidney. A barium-meal examination showed that the second part of the duodenum was narrowed. A combined liver and pancreatic scan was normal, which made a diagnosis of carcinoma of the head of the pancreas unlikely, but primary carcinoma of the duodenum could not be excluded. This and the severity and duration of his symptoms were indications for operation, but on the day of the proposed operation the patient discharged himself. Since that time the patient has had many admissions with attacks of pain. On each occasion he steadfastly refused operation and was given symptomatic treatment only. Despite this, however, the patient put on over 6½ kg. in weight and the frequency and severity of the attacks diminished.

In September, 1969, a further intravenous pyelogram again showed a hydronephrosis, but for the first time a

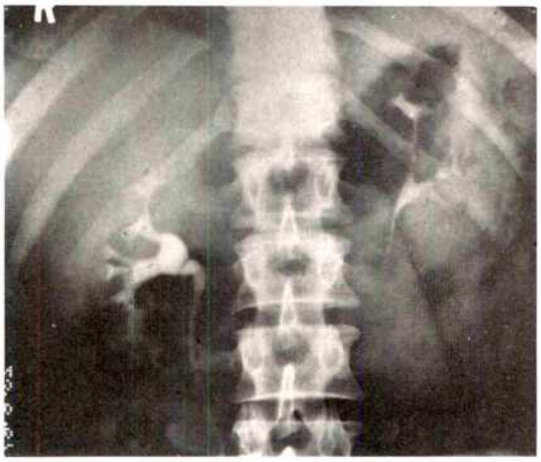
FIG. 1.—Normal intravenous pyelogram in June, 1967.

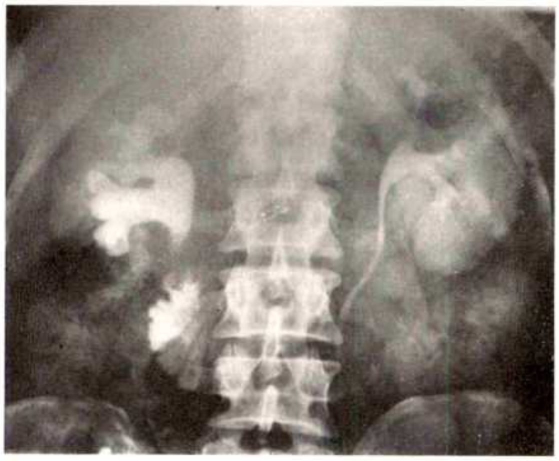
FIG. 2.—Intravenous pyelogram in September, 1969, showing hydronephrosis of the right kidney and passage of contrast into the second part of the duodenum.

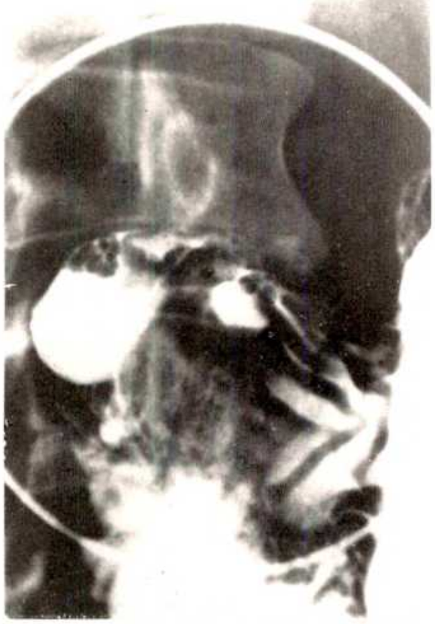
FIG. 3.—Barium-meal examination in September, 1969. Coned view of the duodenum showing narrowing of the second part of the duodenum with a small ulcer crater. A further ulcer crater is seen in the prepyloric area.

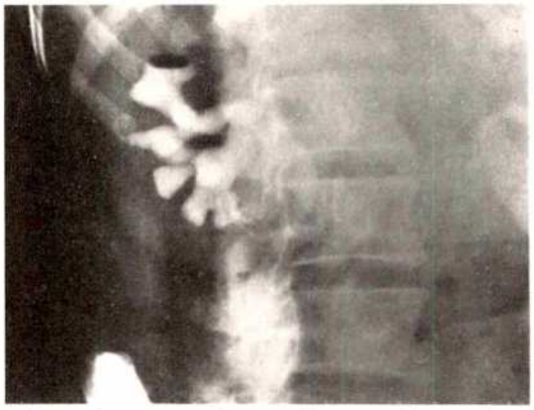
FIG. 4.—Intravenous pyelogram in May, 1971. Oblique view of the right kidney showing an air-bubble in the superior calix.

fistula was shown between the upper ureter, 1 cm. below the pelvi-ureteric junction, and the second part of the duodenum (*Fig.* 2).

A barium-meal examination showed a small ulcer crater at the lower end of the narrowed duodenal segment and in addition a prepyloric ulcer (*Fig.* 3). A combined intravenous pyelogram and barium-meal examination showed the fistula to be related to the lower part of the narrowed duodenal segment. The ureter distal to the fistula could not be demonstrated. On questioning the patient after this investigation it was established that he had had pneumaturia intermittently for some time, but had paid little attention to it.

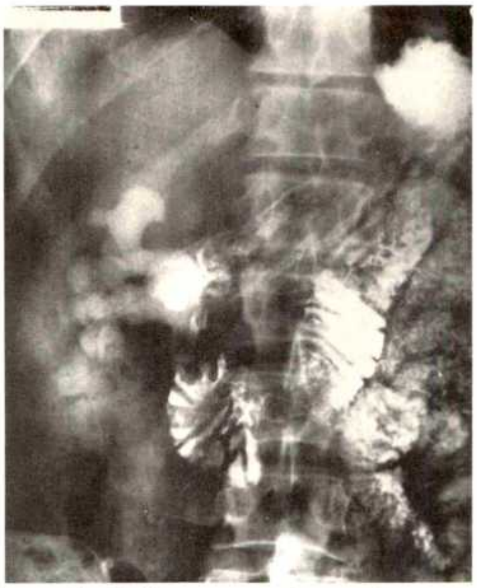

FIG. 5.—Combined intravenous pyelogram and barium-meal examination in May, 1971, showing the ureter related to the lower end of the narrowed duodenal segment. Note the bubble of air in the ureter.

Further barium-meal and intravenous pyelogram examinations in May, 1971, showed little change from 1969. Air-bubbles were clearly seen in the urinary tract (*Figs.* 4, 5). In addition, a further cholecystogram was normal.

In the absence of biopsy material obtained by operation, attempts were made to obtain this endoscopically. It was possible to visualize the stomach and a small prepyloric ulcer was seen, but the patient did not tolerate passage of the instrument into the duodenum. An attempt to biopsy the duodenum using a Crosby capsule was thwarted by the patient discharging himself yet again. However, duodenal intubation revealed the intriguing information that the duodenal content had a urea concentration of 14 mg. per 100 ml.

At the present time the patient is still getting attacks of pain and occasionally requires admission to hospital. He is well nourished and his weight remains steady. He still refuses to consider operation.

A summary of his other investigations are as follows:—

Normal values for: haemoglobin, white-blood count, erythrocyte-sedimentation rate, vitamin B_{12}, folate, urea, electrolytes, sugar, alkaline phosphatase, aspartate transaminase, bilirubin, amylase, plasma proteins, calcium, and phosphate.

Urine contained no blood, protein, sugar, or bile; specific gravity 1010–1020; *p*H 5·5–9·0.

Midstream urine, occasional growth of *Escherichia coli*, *Streptococcus faecalis*, *Proteus*, or *Klebsiella*. Early morning specimens of urine (× 6), negative cultures for tubercle bacilli. Urine calcium (24 hours), normal. Endogenous creatinine clearance, normal.

Stools, occult blood was occasionally positive.

Mantoux test, weakly positive.

Wassermann reaction, negative.

Pentagastrin test: before pentagastrin, 1·5 mEq. acid per hour; after pentagastrin, 23·22 mEq. acid per hour. Fasting plasma gastrin, 107 pg. per ml. (normal).

DISCUSSION

There have been only 2 previous reports of duodeno-ureteric fistula. Davis (1918), in the days before the use of the intravenous pyelogram, demonstrated a fistula by retrograde catheterization of the right ureter. Bile-like fluid was seen discharging from the right ureteric orifice and retrograde injections of contrast showed the fistula to be at the pelvi-ureteric junction. The second case was reported by Deslesaver (1969). An intravenous pyelogram showed a functioning right kidney, but the contrast passed into the second part of the duodenum through a fistula 3 cm. below the pelvi-ureteric junction. Both cases were treated by nephrectomy and suturing of the duodenum and the histology in both cases was chronic renal infection.

Pyelo- or nephroduodenal fistula is more common, and is almost always between the second part of the duodenum and the right kidney, although at least 1 case involved the left kidney and the terminal duodenum (Arendt and Brockmann, 1934). About 30 cases have been recorded and without exception the pathological process has always begun in the kidney. In a recent review McEwan (1968) recorded 23 cases. Biondi (1935) described a case which he thought was secondary to a duodenal ulcer, but the tuberculous right kidney removed at operation was almost certainly the primary pathology (King, 1950). Prior to effective chemotherapy tuberculosis was a common cause of pyeloduodenal fistula, but now chronic renal infection with or without stones is the commonest pathology. The renal infection causes a perinephritis, which involves the duodenal wall with subsequent fistula formation. This is analogous to the cholecystoduodenal fistula associated with cholecystitis and stones, which may occasionally lead to gall-stone ileus. However, there has as yet been no recorded case of renal stone ileus.

The present case is interesting in that the symptoms preceded the demonstration of the fistula by 7 years. In fact in 1961 the initial symptoms were described by the patient as 'gastric' in type with nothing to suggest a renal pathology. In 1967 after symptoms had been present for 6 years the intravenous pyelogram was still normal. Even when the fistula was demonstrated in 1969 the kidney was still shown on the intravenous pyelogram to function normally, and, apart from the mild hydronephrosis, appeared to have a normal anatomy. No evidence of renal tuberculosis has been found and the occasional urinary infection can be explained by the passage of small amounts of duodenal content into the urine, as is evidenced by the pneumaturia. No renal stones were seen on the intravenous pyelogram in 1967 and this makes unlikely the possibility of a stone becoming arrested in the upper ureter and ulcerating through into the duodenum. Therefore, although no histological proof is at present available it would seem that the primary pathology was in the duodenum.

The exact duodenal pathology, however, must be a matter for speculation. The commonest duodenal lesion is a duodenal ulcer. This patient's gastric secretion of 23 mEq. acid per hour after pentagastrin stimulation is within normal limits although it would be compatible with the diagnosis of duodenal ulcer. A prepyloric ulcer was demonstrated radiologically and visualized endoscopically and it is known that these may be associated with ulcers in the duodenum. However, the duodenal ulcer demonstrated by barium-meal examination was located in the second part of the duodenum which is an unusual location. A diagnosis of Zollinger-Ellison syndrome was considered, but this was ruled out by the low resting acid output and the normal fasting plasma-gastrin level. It is conceivable that the patient may have had a sealed-off perforation of a posterior duodenal ulcer causing a localized abscess. Its subsequent rupture into the upper ureter and duodenum could result in the formation of a fistula. The 'ulcer' seen in the second part of the duodenum may not be an ulcer in the accepted sense but may simply represent the mucosal defect at the entry point of the fistula.

A primary malignant tumour of the duodenum is unlikely in view of the length of history and the lack of progression of the disease, while a benign tumour is unlikely to ulcerate the duodenal wall.

Any inflammatory lesion which could cause a periduodenitis with adherence of the duodenum to the ureter could theoretically cause a fistula.

Perforated diverticula of the duodenum have been recorded causing fistula into the gall-bladder and colon (Munnell and Preston, 1966). Swallowed sharp foreign bodies have caused pyeloduodenal fistula (Abeshouse, 1949) and pancreatitis may occur in an annular pancreas (Hope and Gibbons, 1954). All these conditions are uncommon and no evidence can be produced for any of these diagnoses in this patient.

Retroperitoneal fibrosis often causes ureteric obstruction, but usually at the level of the fourth lumbar vertebra. It has also been reported causing duodenal obstruction (Schneider, 1964). However, the fibrosis constricts but does not infiltrate and fistula formation is unlikely.

Crohn's disease is well known for its tendency to form fistulae. It occurs in the duodenum in less than 5 per cent of cases and is almost always associated with disease elsewhere in the bowel (Fielding, Toye, Beton, and Cooke, 1970). The present patient had no evidence of disease on follow-through examination of the small intestine and no diarrhoea or evidence of malabsorption. Crohn's disease has been diagnosed by per-oral duodenal biopsy techniques (Hermos, Cooper, Kramer, and Trier, 1970).

This case still presents a diagnostic problem, but it is felt that its unique nature justifies this report. An exact diagnosis can probably only be obtained by laparotomy which is at present not possible and, since the patient is maintaining reasonable health, perhaps not even justifiable.

Acknowledgements.—I should like to thank Mr. M. J. Lange for his permission to publish this case, and Dr. C. E. Mackintosh who undertook the most recent radiological studies. Professor C. G. Clark kindly arranged for the plasma-gastrin assay to be done in the Department of Surgery at University College Hospital, London.

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AN UNUSUAL THYROID GLAND

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SUMMARY

A patient is described in whom the only thyroid tissue present was a mass approximately 4 cm. in diameter situated high up in the neck and just lateral to the laryngeal prominence of the thyroid cartilage. Degenerative changes in this ectopic gland were marked. An ectopic gland in such a position has not previously been described in euthyroid adults. The embryological development, functional activity, and pathology of ectopic thyroid glands are discussed.

ABNORMALITIES of the thyroid gland and its embryological remnants are not uncommon. Cysts along the track of the thyroglossal duct can for various reasons require surgical treatment. A case is presented in which the thyroid gland was represented solely by a small area of functioning thyroid tissue in an ectopic position. Originally a tentative diagnosis of thyroglossal cyst had been entertained. However, careful clinical assessment in association with detailed thyroid-function tests revealed the true nature of the cervical swelling preoperatively.

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CASE REPORT

HISTORY.—M. L., a 17-year-old schoolgirl, presented in September, 1970, with a painless swelling in the neck, which had first been noted a month previously. She had no dysphagia, dysphonia, cough, or dyspnoea, and direct questioning revealed no symptoms of systemic thyroid dysfunction. Past history and family history were unremarkable.

EXAMINATION.—The patient was clinically euthyroid and general examination was normal. She had a firm, roughly circular swelling approximately 4 cm. in diameter in the left anterior triangle of the neck just lateral to the upper border of the laryngeal prominence of the thyroid cartilage. It moved with swallowing but not with protrusion of the tongue and was freely mobile. There was no thyroid tissue palpable in the normal position.

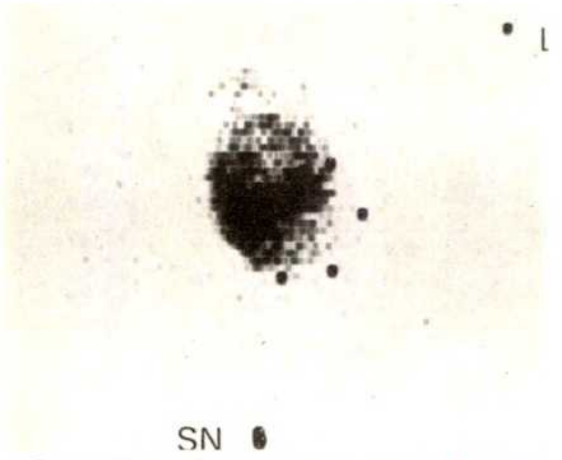

FIG. 1.—^{131}I scan of the neck, showing uptake by the ectopic thyroid with an area of diminished uptake superiorly. S.N., Sternal notch.

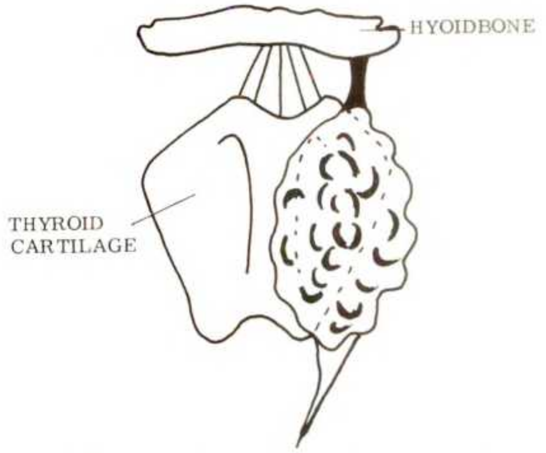

FIG. 2.—Diagram showing the anatomical relationships of the ectopic gland.

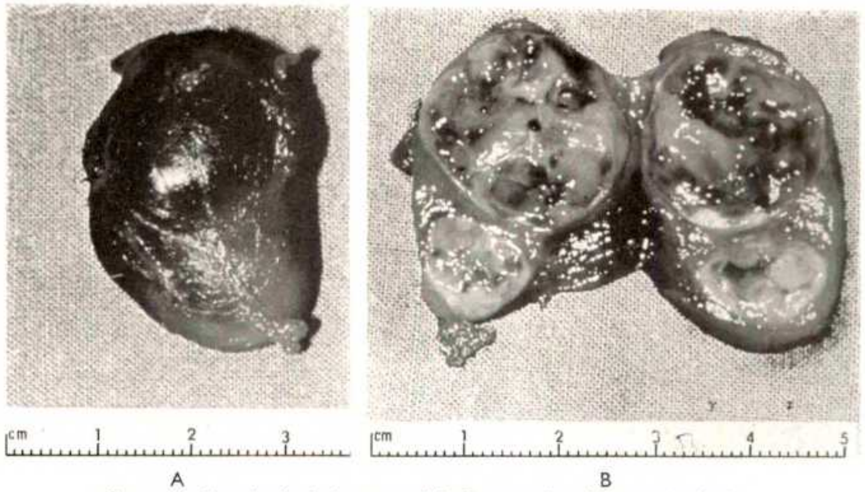

FIG. 3.—A, Ectopic gland after removal. B, Cross-section of the ectopic gland.

INVESTIGATION.—A chest radiograph and a full blood-count and erythrocyte-sedimentation rate were normal. No abnormality was found on measurement of the serum electrolytes (including calcium and phosphorus), and no antibodies to thyroid tissue were present.

A ^{131}I scan showed a single area concentrating ^{131}I which corresponded accurately with the swelling felt on examination; within the scan there was a 'cold' area superiorly (*Fig.* 1). ^{131}I uptake was not present in the normal thyroid position.

Base-line serum-thyroxine concentration was 83 nmol. per litre, T_3 uptake 113 per cent of normal, and thyroid-stimulating hormone 1·5 μU. per ml., confirming the euthyroid status. Uptake of ^{99m}Tc at 15 minutes was slightly elevated at 8 per cent. After giving thyroid-stimulating hormone, 10 U. i.m. daily for 2 consecutive days, the serum thyroxine level rose to 115 nmol. per litre and ^{99m}Tc uptake rose to 12 per cent. The neck was rescanned and no additional areas of ^{131}I uptake could be demonstrated. Tri-iodothyronine, 40 μg. t.d.s., was given orally for 7 days, at the end of which the serum-thyroxine concentration had decreased to 62 nmol. per litre and the uptake of ^{99m}Tc had been abolished.

From these results (*Table I*) it was concluded that the cervical swelling represented the patient's only functioning thyroid tissue which behaved physiologically in its responses to thyroid-stimulating hormone and T_3 suppression.

PROGRESS.—In view of the suppressibility of the ectopic thyroid gland, thyroxine, 0·3 mg. daily, was prescribed to try to reduce its size. After approximately 10 months no significant reduction in size had been achieved. Because the gland had become an embarrassment from the cosmetic point of view and also because the 'cold' area on the ^{131}I scan was viewed as possibly malignant, exploration of the neck and removal of the gland were recommended.

Table I.—RESPONSES OF SERUM T_4 AND ^{99m}Tc UPTAKE TO THYROID-STIMULATING HORMONE AND T_3 SUPPRESSION

	SERUM T_4* (nmol. per litre)	^{99m}Tc UPTAKE (Percentage at 15 min.)
Base-line	92	8
After thyroid-stimulating hormone, 10 U. 1 m. daily for 2 days	115	12
After T_3, 40 µg. t.d.s. for 7 days	62	0

* Normal serum T_4 = 60–150 nmol per litre.

At the operation the thyroid gland was laterally placed on the left wing of the thyroid cartilage (*Fig.* 2). It was supplied by a lease of blood-vessels entering inferiorly, and remnants, presumably of the lingual duct, extended up as a fibrous band behind the hyoid bone. No thyroid tissue was present in the normal position. The gland was removed *in toto*; histologically it consisted of two degenerate cysts lined externally by a narrow rim of normal thyroid tissue. This almost complete investment with normal thyroid tissue might have accounted for the relatively normal scanning appearances in such an obviously abnormal gland (*Fig.* 3).

The patient was not given immediate replacement therapy postoperatively, but approximately 6 weeks following surgery she complained of tiredness, general malaise, and weight-gain. Thyroid function tests indicated hypothyroidism (*Table II*). Thyroxine, 0·2 mg. daily, was given and she has remained euthyroid on this dose.

DISCUSSION

There are several points of interest about ectopic thyroid glands in general and the present case in particular. First, the embryological aspects should be considered. The potential thyroid gland is initially recognizable as a midline thickening on the endoderm of the floor of the pharynx at about 1 month of foetal life. From this thickening the thyroglossal duct develops; with development of the neck and descent of the heart this becomes elongated, thinned, and eventually it fragments to separate the now bilobed distal end which will form the thyroid gland proper. The primitive thyroid gland is at this stage a close relation of the third and fourth pharyngeal pouches, each of which divides into a dorsal and ventral portion. The third pouches give rise to the thymus and inferior parathyroid glands. The dorsal portions of the fourth pouches form the superior parathyroids and the ventral portions receive contributions from the rudimentary fifth pouches to form the 'ultimo-branchial bodies'. It seems that the ultimo-branchial portion, although incorporated into the thyroid gland, does not give rise to thyroxine-producing tissue but to the clear cells of the thyroid which produce calcitonin (Pearce and Carvalheira, 1967). Before this was demonstrated it had been debated whether there was any contribution to the thyroid from the fourth pouches (Boyd, 1964). The fact that removal of the lingual thyroids nearly always resulted in hypothyroidism had suggested to some workers that the fourth pouch derivatives (which presumably would be undisturbed by such surgery) made little contribution to thyroxine-producing tissue. The concept of 'lateral aberrant thyroids' had long since been discredited as such tissue could always be explained on the basis of secondary deposits from primary thyroid tumours (Dalgaard and Wetteland, 1956).

Table II.—SERIAL THYROID-FUNCTION TESTS

DATE	SERUM T_4 (nmol per litre)	T_3 UPTAKE (per cent)	THYROID-STIMULATING HORMONE (µU. per ml)
27 Jan, 1971	83	113	1 5±0 00
15 Feb, 1971	T_4 0·3 mg daily		
17 March, 1971	160	91	2 6±1 9
17 May, 1971	169	100	4 2±1·2
9 Aug., 1971	125	102	
14 Dec., 1971	Thyroidectomy		
29 Dec., 1971	54	120	1 1±0 7
17 Jan., 1972	33	131	38 7
24 Jan, 1972	28	125	91 7
	T_4 0 2 mg daily		
14 Feb., 1972	108	128	11·5±3 7
15 May, 1972	146	103	5 4±0 00

Clinically the following abnormalities of thyroid gland development are well recognized:—

Group A: Aplasia.
  1. Total.
  2. Unilateral.
  3. Isthmic.

Group B: Abnormal descent.
  1. Lingual.
  2. Sublingual.
  3. Intrathoracic.

The relative prevalence of the various abnormalities is difficult to determine with accuracy. In group A 9·5 per cent of cases of non-goitrous hypothyroidism are due to total aplasia (Niemann, Pierson, and Martin, 1961). In a series of 708 patients who had thyroid scans isthmic asplasia was judged to be present in 5·5 per cent of cases and unilateral aplasia in 0·98 per cent (Andreew, 1968). In group B thyroid tissue may be found anywhere along the line of descent of the embryonic thyroid gland. Of 46 cases of abnormal thyroid descent in hypothyroid children, 22 were lingual, 12 were between the hyoid bone and maxilla, and 12 were infrahyoid in position. Such glands were never palpable and were always situated in the midline (Niemann and others, 1961). In adults Lahey (1923) reported only 2 lingual thyroids among 8500 patients attending his goitre clinic.

In the patient described here the ectopic thyroid gland fell into group B, but was very unusual because it was laterally placed. Because it was infrahyoid in position it might have been more liable to lateral displacement in a purely mechanical fashion by the development of the laryngeal prominence of the thyroid cartilage.

The cause of maldescent of the thyroid gland is not known. It is of interest that a lingual thyroid has been reported in siblings (Orti, Castells, Qazi, and Inadar, 1971), and in view of the rarity of this abnormality (*see above*) this suggests the possibility that genetic factors may be involved in the descent of the thyroid gland.

The functional state of ectopic thyroid glands has not been adequately studied. It would seem, in paediatric practice at least, that functional underactivity of ectopically placed thyroid glands is a common cause of non-goitrous hypothyroidism. Niemann and others (1961) reviewed 74 non-goitrous hypothyroid children 62 per cent of whom had ectopic thyroid glands. Lingual thyroid glands usually present with pressure symptoms or haemorrhage; Montgomery (1936), however, reported clinical hypothyroidism in 15 per cent of cases. It is possible that many ectopic glands are symptomless and never detected clinically; if this is so the estimated prevalence of hypothyroidism in such cases is likely to be too large.

The pathology of ectopic thyroid glands has not received much attention probably because their rarity makes adequate data collection difficult. Cystic degeneration in this patient was marked, a finding which would appear to be most unusual. Hendrick (1956) reported that his cases of lingual thyroid showed no remarkable pathological changes but he gives no histological details.

The risk of malignancy developing in ectopic thyroid glands seems to be small. Akbari, Richter, and Papadakis (1967) reviewed the development of malignancy in thyroglossal duct remnants and put the risk at less than 1 per cent if neoplasms of thyroid tissue only were considered; others (Keeling and Ochsner, 1959) report similar findings. However, this does not mean that ectopic glands are not subject to the same pathological processes as normally situated glands and the presence of an apparent solitary 'cold area' on scanning was one of the indications for removal in the present case.

This case is also unusual in that the very small, histologically degenerate, thyroid gland was able to produce sufficient thyroxine to maintain a euthyroid state. After its removal the patient rapidly became hypothyroid and required replacement thyroxine therapy.

Acknowledgements.—I would like to thank Dr. R. Hoffenberg for his encouragement and helpful criticism in the preparation of this paper. I would also like to thank the Photographic Department at Northwick Park for providing the diagrams and Mrs. Nola Clark for typing the manuscript.

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REVERSED ROTATION OF THE GUT INCIDENTAL TO CHOLECYSTITIS IN A LEFT-SIDED GALL-BLADDER

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SUMMARY

A patient with reversed rotation of the midgut loop of the retro-arterial colon type is reported. She is unique in being the first case recorded in the literature with a right-sided colon and a left-sided liver without situs inversus of the abdominal viscera. An explanation of the findings is suggested, based on known embryological facts.

Previous reports indicate that patients with reversed rotation all present with obstructive symptoms secondary to the altered anatomy. This patient is unusual in that her symptoms and pathology were unrelated to the anatomical abnormality.

EXPERIENCE in treating adult patients with anomalies of intestinal rotation is limited. This is particularly true of one of the rarest abnormalities of rotation, that of reversal of the midgut loop, two variants of which are now recognized. The first is the retro-arterial colon type where the superior mesenteric vessels and duodenum cross anterior to the transverse colon. In the second type the liver and the entire colon are ipsilateral (Estrada, 1958).

The case described here is one of reversed rotation of the retro-arterial colon type but with the unique finding of a left-sided liver and right-sided descending colon. In addition the patient presented with jaundice due to gall-stones, making this the first reported case to present because of associated pathology and not with the clinical features of bowel obstruction.

CASE REPORT

The patient, a female aged 59 years, was admitted in April, 1970, complaining of severe lower retrosternal chest pain for 1 week. In the past she had been treated for angina, and a transient episode of jaundice 1 year previously was thought to be due to chlorpromazine therapy.

On examination only epigastric tenderness was noted and a provisional diagnosis of either myocardial or pulmonary infarction was made. However, subsequent chest radiographs, electrocardiograms, and enzyme studies did not confirm the diagnosis. Two days after admission the patient had a further severe attack of pain and the following day she was noticed to be jaundiced with a discrete mass in the upper abdomen and was transferred to a surgical ward. A diagnosis of acute cholecystitis with secondary pancreatitis and a possible collection in the lesser sac was made, despite a serum amylase of 84 Somogyi units. The relevant investigations confirmed an obstructive jaundice as evidenced by bile in the urine, bilirubin of 8·5 mg. per 100 ml., alkaline phosphatase of 23 K.A. units, and normal liver enzymes. On barium-meal examination the only abnormality was a widened duodenal loop, and a rounded filling defect was noted in the descending portion of the duodenum in the vicinity of the ampulla of Vater (*Fig.* 1).

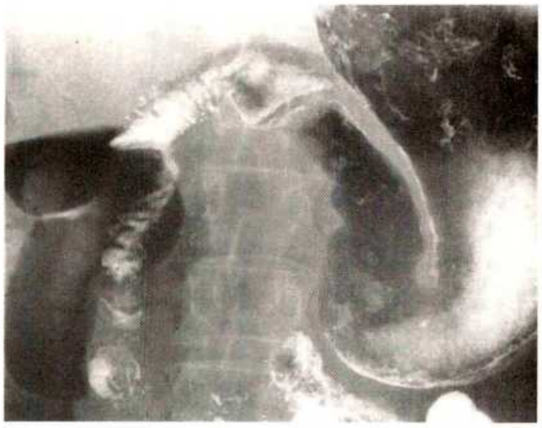

FIG. 1.—Barium-meal film, showing the widened duodenal loop. The filling defect can be seen in the second part and below this there is a duodenal diverticulum.

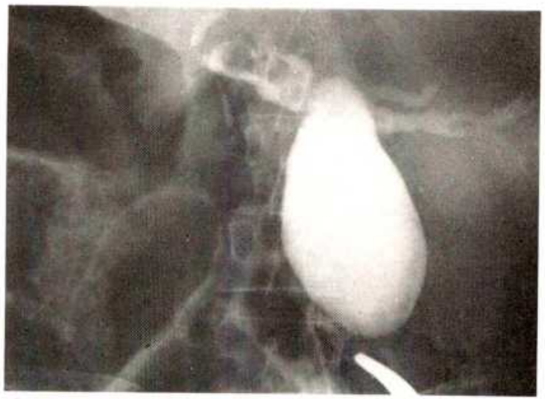

FIG. 3.—Operative choledochogram via the gall-bladder. The filling defects can be clearly seen in the duct system.

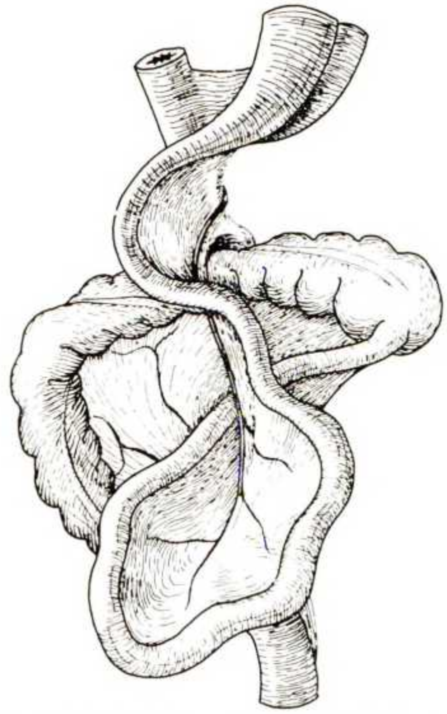

FIG. 2.—Line drawing of the anatomy described in the text.

The patient's symptoms rapidly settled within a week and prior to discharge an intravenous cholangiogram demonstrated biliary calculi. The patient remained well and was readmitted for surgery 6 weeks later.

OPERATIVE FINDINGS.—Laparotomy was performed via a right upper paramedian incision. The stomach and first and second parts of the duodenum were normal in position. The third part of the duodenum was elongated and narrowed and, together with the fourth part, took a straight course passing over the underlying transverse colon. The superior mesenteric artery was to the left of the duodenum passing across the transverse colon (*Fig.* 2). Two thin-walled diverticula were noted on the left side in the region of the duodenojejunal junction.

The gall-bladder was located in a fossa on the undersurface of a large left lobe of the liver. Later dissection revealed that the cystic duct joined the left hepatic duct by passing from left to right. The common bile-duct also passed to the right across the midline and entered the duodenum from the left. The spleen was palpable beneath the left dome of the diaphragm and the pancreas lay in its normal position across the posterior abdominal wall.

The small intestine had no mesentery, its attachment to the posterior abdominal wall being a short segment just above the region where the duodenum crossed over the transverse colon. The terminal ileum also passed through a 'tunnel'-like opening beneath the duodenum and immediately below the transverse colon to join the caecum in the left iliac fossa. The base of the appendix was situated on the right of the caecum near the entrance of the terminal ileum.

The mobile ascending colon on becoming the transverse colon under the left lobe of the liver passed to the right in the retro-arterial 'tunnel', where it was noted to be constricted. The transverse colon had no attached omentum. The descending and sigmoid colons passed down the right side of the abdomen to the rectum.

variants have been described by Estrada (1958), who 'demonstrated that both types have the same embryological basis, namely, reversal of rotation of the midgut loop during the stage of realinement' when elongation of the midgut loop occurs within the physiological hernia. In the normal embryological sequence there is a total of 270° of anticlockwise rotation (*Fig*. 4 A).

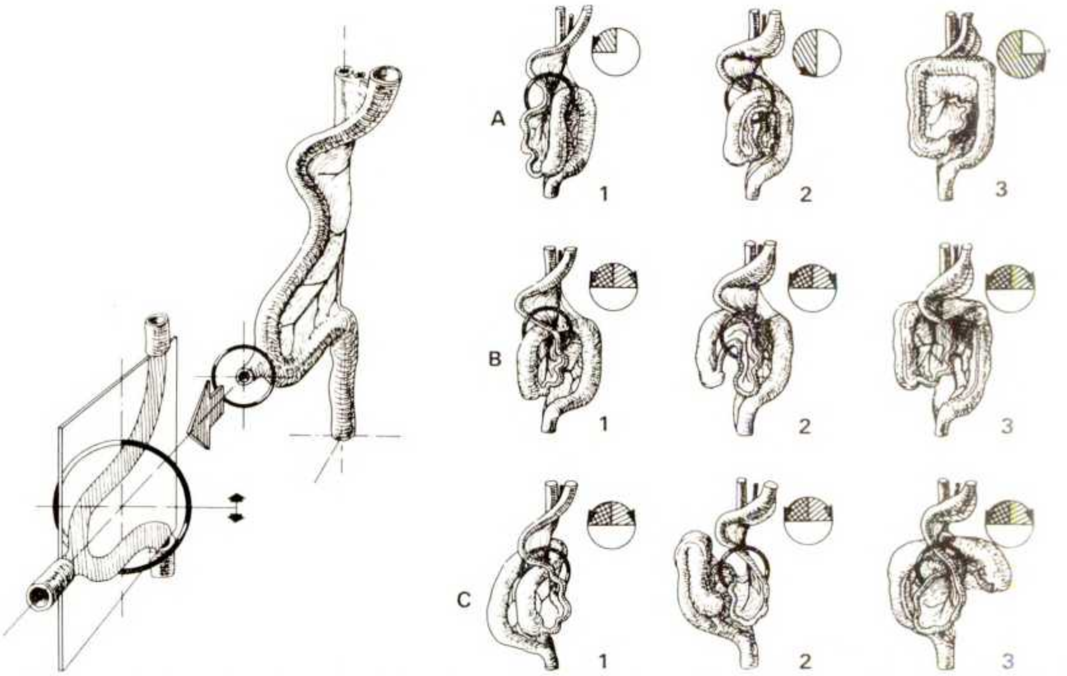

FIG. 4.—Normal and reversed rotation seen from the front. The dark ring represents the physiological hernial opening. The shaded circles represent the degree and direction of rotation at each stage. A, Normal sequence: 1, The first 90° of anticlockwise rotation has occurred. 2, Realinement of the physiological hernia with a further 90° of anticlockwise rotation. 3, Reduction and final appearance. There has been a total anticlockwise rotation of 270°. B, Reversed rotation: 1, The initial anticlockwise rotation of 90° has been reversed with a clockwise rotation of 180° following realinement in the physiological hernia. The net result is a 90° anticlockwise rotation. 2, The postarterial segment has been reduced first. No further rotation occurs. 3, Final appearance. C, Right-sided retro-arterial colon type: 1, Same stage as B1 but showing the hindgut deflected to the right. 2, Further deflexion of the hindgut as the reducing postarterial segment comes back to the left side of the dorsal mesentery. 3, The caecum has 'descended' to the left beneath the omphalomesenteric vascular axis.

In an attempt to correct the malrotation the caecum was pulled to the right from beneath the overlying duodenum and vascular pedicle but it was soon obvious that this only compounded the problem, because the terminal ileum followed the caecum through the tunnel and created a possible 'closed-loop situation' as well as a kink at its junction with the caecum. The caecum was therefore returned to the left side.

After dissection, an operative choledochogram via the gall-bladder outlined multiple filling defects in the common bile-duct as well as the anomalous anatomy (*Fig*. 3). A cholecystectomy was performed, the common duct was explored, and four calculi were removed. The duodenum was opened at the junction of the third and fourth parts and the duodenal 'tumour' was shown to be an oedematous papilla of Vater. An appendicectomy was performed and the abdomen was closed.

The patient's postoperative course was uneventful and when reviewed 3 months and 12 months later she had no complaints.

DISCUSSION

Reversed rotation is a rare anomaly, 45 cases having been reported up to 1969 (Scobie, 1969). The two

In reversed rotation 90° of anticlockwise deviation occurs normally, then during realinement a reversal of rotation of 180° in a clockwise direction occurs (*Fig*. 4 B), followed by the stage of reduction without further rotation. If the pre-arterial segment returns first the entire colon comes to be on the right side of the abdomen, producing the colon and liver ipsilateral variant. If, as is more usual, the postarterial segment returns first the retro-arterial colon variant is produced (*Fig*. 4 B). The conversion to a 'tunnel' is now believed to be a secondary phenomenon of fixation of a small intestinal mesentery which is avascular. This has been confirmed by the description of cases without the retro-arterial tunnel, and by the observation that the avascular mesentery, when present, can be divided and the anomaly totally corrected (Estrada and Gurd, 1962).

The patient described in this article is the first recorded with a left-sided liver and a right-sided colon. The explanation for these findings is difficult, but we believe that the sequence of events follows that described for the retro-arterial colon type and that the displacement of the hindgut to the right side occurred because the reducing postarterial segment returned on the left side of the hindgut dorsal mesentery, thus deflecting it into the right flank, a situation which came about because of the bulk of the developing mass of liver in the left side of the abdominal cavity (*Fig.* 4 C). Subsequently, with the enlargement of the peritoneal cavity and the 'descent' of the caecum into the left iliac fossa, the final adult disposition of the colon resulted (*Fig.* 5).

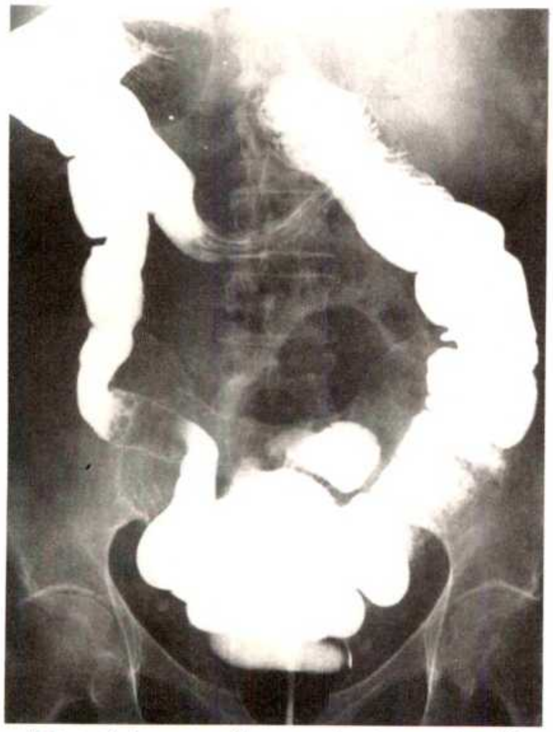

FIG. 5.—Barium-enema film 12 months after operation. The narrowed retro-arterial segment of the transverse colon is clearly seen. Note the sigmoid colon on the right side and the small bowel filling on the left.

Only 2 cases of reversed rotation in association with a left-sided liver have been reported (McIntosh and Donovan, 1939; Van Meurs, 1946), but Estrada (1958) classifies these as reversed rotation with the liver and colon ipsilateral and in which there existed situs inversus of the abdominal organs. The present patient does not have situs inversus of the abdominal organs, as evidenced by the normal positions of the spleen and stomach. Similarly this patient cannot be classified as one of non-rotation with a retro-arterial colon, a situation which Rose (1941) has suggested may easily be mistaken for reversed rotation, because of the finding that there was no attachment of omentum to the transverse colon (volvulus neonatorum excepted).

The clinical presentation of these patients is invariably with the symptoms of bowel obstruction (Estrada and Gurd, 1962). Associated pathology in the presence of reversed rotation has been reported on two occasions and these were only noted at operation (Grant, 1940; Scobie, 1969). The patient reported here is notable in that she underwent surgery for jaundice due to gall-stones and not for bowel obstruction.

At laparotomy the anatomy was not recognized and understood and no definitive repositioning procedure was done. In order to restore the anatomy in this patient a technique similar to that described by Estrada and Gurd (1962) could be employed although the descending colon would remain on the right side. In this method the avascular mesentery joining the retro-arterial tunnel is divided and the entire bowel is then rotated anticlockwise through 360° on its vascular pedicle. It remains to be seen whether further surgery will be necessary in this patient.

Acknowledgements.—We would like to thank Mr. H. Upenieks from the Medical Illustrations Department, University of Western Australia, for his care in preparing the illustrations, and Miss D. Mudie for typing the manuscript.

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REVIEWS AND NOTICES OF BOOKS

The Metabolic Basis of Surgical Care. By WILLIAM F. WALKER, Ch.M., F.R.C.S. (Edin.), F.R.C.S. (Eng.), Dundee, and IVAN D. A. JOHNSTON, M.Ch., F.R.C.S. (Eng.), Newcastle upon Tyne. 8½ × 5½ in. Pp. 251 + x. Illustrated. 1971. London: William Heinemann Medical Books Ltd. £3.

THIS book has been written to give a concise account of the composition and metabolism of the human body in health and in disease. It is both didactic and simplified in its treatment of the subject-matter and is aimed widely at clinicians who look after patients, undergraduate clinical students facing their final examinations in those schools which still adhere to this convention, postgraduates who are going to sit the primary examination for the higher diplomas, and senior members of hospital staff who are trying to care for ill patients. Both authors are well known for their original work on many of the aspects of surgical care on which they write and perhaps their own deep familiarity with their subject has made them assume a basic knowledge which some of their readers will lack; nevertheless there is a vast amount of factual information. Perhaps it is because this book attempts so much in a limited compass that it may fail to please and satisfy at least some of those for whom it was written. Yet at the price of £3 it is within the reach of many more than some current books of its kind. The index is not always accurate, for example, the four references to dextran refer to dextrose and the actual references to dextran are not indexed.

Apart from these comments this book provides a concentrated account of many aspects of a difficult area of surgical treatment and deserves to be widely read.

Essays on Future Trends in Anaesthesia. By A. BOBA, Mount Vernon, Illinois. 9 × 6 in. Pp. 93 + x. Illustrated. 1972. Berlin: Springer-Verlag. DM.28.

'PATIENTS . . . see the anaesthetist in the light of the man who puts them to sleep . . . our surgical colleagues also share this image. . . .' The phrases from the opening page of Dr. Boba's book reflect the image which he is hoping to destroy and which should be extinct in the next generation. However, he also aims to educate anaesthetists, of whom he says: 'unfortunately . . . too frequently this is also the image which he has of himself'. He does not underestimate the task since he concedes: 'The true nature of administering an anaesthetic requires a smaller number of manual skills than any equivalent procedure in medicine'.

This little book consists of four main chapters, in the first of which Dr. Boba analyses and rationalizes processes which the trained anaesthetist performs 'automatically', dealing with monitoring, messages received from the patient, and decisions taken as the result of these messages. The administration of an anaesthetic is likened to a sequential decision-taking process of the intellectual type. No doubt this applies to all of medicine, but nevertheless this is a very thought-provoking chapter. This same type of reasoning is applied to anaesthetic equipment and in Chapter 3 the author deals at length with the 'anaesthetic module' concept. Such things as an independent record of vapour concentration during anaesthesia (analogous to a flight recorder) or a more complete automatic recorder of the entire course of anaesthesia ('black box') are discussed in depth and provide much food for thought. 'Knowledge is the by-product of abstract or intellectual activity and the development of new tools leads to new knowledge.' However, he warns: 'One should avoid the pitfall of building aggregations of gadgets with functional characteristics of great white elephants.'

Next follows a section on first-hand experience which shatters all the concepts of anaesthesia being an art rather than a science and yet even the most unscientific clinician could not fail to benefit from reading this. Although the reviewer does not agree with all the views put forward in this chapter, or in the following one on the future of anaesthesia, he finds those on the value of much of our current monitoring practice challenging and are worth reading by anyone who has the future of the specialty at heart or who considers the routine administration of anaesthesia to be a boring process.

One is left with the thought that the anaesthetist–patient contact will be reduced even more if anaesthesia develops along the lines suggested by Dr. Boba. He recommends us to devote time and energy to 'programmed anaesthesia', but nowhere advises us to be 'good doctors'.

This is not an easy book to read; it is particularly difficult to get started but becomes fascinating as one proceeds. It leaves one with two big unanswered questions: Who pays for the equipment? Has the author ever heard of the millions of people who cannot get the basic necessities of medical care?

Management of Neglected Trauma. Edited by J. FRANCIS SILVA, F.R.C.S., F.R.A.C.S., F.A.C.S., Kuala Lumpur. 9¼ × 6 in. Pp. 323 + xvi. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $19.50.

THIS volume has a seductive title and amongst its nine contributors one recognizes several orthopaedic surgeons who have carried out noble work under often difficult circumstances. However, its promise is unhappily not fulfilled. With one or two exceptions, the book consists of a digest of well-known facts in everyday orthopaedic practice. Many of the techniques described can hardly be considered suitable for countries which—to use the editor's introductory words—'have hardly more than a few scattered orthopaedic centres, all with a heavy work load'. In such conditions it is difficult to understand the free use of metal prostheses for the late effects of trauma to the shoulder, elbow, knee, or hip.

In this context it is also surprising to note that time is seemingly available to follow the advice, for example, that 'small tears of the rotator cuff have to be operated upon'.

The book also suffers from some rather cursory proofreading which adds to the general impression of a lack of direction. A few examples may suffice: ulna used as ap adjective, the mis-spelling of 'Jowett' for 'Jewett', 'Nuefeld' for 'Neufeld', 'straighten' for 'strengthen' the quadriceps, and a transposition of legends to figures, e.g. 108 and 109.

Nevertheless, on more careful perusal, one finds several worth-while and occasionally highly instructive concepts. It is not surprising to find in the chapters by Professor Huckstep, with his vast experience in this field, a careful and highly informative essay on the treatment of the late traumatic dislocations of the hip which might well be read to advantage by all surgeons in metropolitan countries. 'Neglected trauma' is unfortunately not confined to any particular parts of the world! Professor P. T. Kotani of Osaka, whose treatment of brachial plexus injuries is now receiving increasing attention, gives a very interesting and modest account of his attempts to restore sensibility and occasionally some motor power to a totally paralysed upper limb. Such a challenging endeavour from one of the newer orthopaedic centres should stimulate us to re-examine many of our established (if not yet fossilized) ideas. It is very much to be hoped that serious revision of a future edition of this book will enable it to fulfil more satisfactorily the obvious need for a book on this subject.

The Anesthesiologists Handbook. By Donald G. Catron, M.D., Tennessee. 7 × 4½ in. Pp. 158. Illustrated. 1972. Baltimore: University Park Press. $7.50.

In his preface the author states that he has aimed to compile a collection of reference material in the form of a convenient handbook; he says 'few memories would fail to benefit from an occasional on the spot review of a problem situation'. Although many facts are presented in this book, explanation is scanty; Chapter 4, which is entitled 'Anaesthesia for Thoracic Surgery', is especially deficient.

The names of many of the drugs mentioned differ from the terminology used in the United Kingdom. There are very few figures, and these are very small; a mere 25 references are offered at the very end of the book and do not represent a particularly valuable selection. In the main, however, the book is to be criticized for the intense degree of condensation rather than for inaccuracy.

One is tempted to compare it with Alfred Lee's magnificent *Synopsis of Anaesthesia* which is available in the same price range; in this perspective Dr. Catron's book seems to be inadequate and cannot be recommended to British students or practitioners of anaesthesia.

Progress in Pediatric Surgery, Volume 3. Edited by P. P. Rickham, M.D., M.S., F.R.C.S., D.C.H., Liverpool, Professor W. Ch. Hecker, München, and Professor J. Prévot, Nancy. 8½ × 5½ in. Pp. 167. Illustrated. 1972. Baltimore: University Park Press. No price given.

This is the third volume of an annual review of various aspects of paediatric surgery. In this volume there are two chapters on deformities of the chest. The first by Ravitch is the Simpson-Smith Memorial Lecture of 1970, and it gives a good account, particularly, of funnel chest and advocates radical treatment. The second article discusses the aetiology and pathogenesis of funnel chest and the experimental production of it in rabbits, and suggests that the most important causal factor is probably a dysplastic anterior chest wall. Bughaigis and Emery discuss functional obstruction of the intestine in the newly born on the basis of immaturity of the nerve-supply of the bowel, and this is followed by a discussion of the effects of subvesical disturbances of urinary drainage on the upper urinary tract in childhood. There is an interesting paper on preduodenal portal vein which discusses at some length the embryology, and another section discusses the function of the cardia in childhood and reports the results of measurements of intracardial pressure in 152 children. The remainder of the book is a report of a symposium on extensive therapy in newly born babies submitted to surgical operations. It covers the administration and design of an intensive-therapy unit, the indications for intermittent positive-pressure ventilation, the features and design of ventilators, and the results of long-term positive-pressure ventilation in newly born surgical patients. It is inevitable that there should be differences of opinion about the indications for and value of positive-pressure ventilation and these two sections will well repay close study by paediatric and other surgeons and their anaesthetists who are concerned with the surgical care of the newly born.

There is much of interest in this book which really consists of a number of papers which are too long to be accepted by surgical journals and are here conveniently put together in an annual package for the specialist reader.

Scientific Basis of Surgery. Second edition. Edited by W. T. Irvine, B.Sc., M.D., Ch.M., F.R.C.S. (Eng.), F.R.C.S. (Edin.), St. Mary's Hospital, London. 9¾ × 7¼ in. Pp. 677 + x. Illustrated. 1972. Edinburgh: Churchill Livingstone. £9·50.

The merits of the scientific approach to surgery are accepted by all who take part in the training of surgeons. Craftsmanship on its own is no longer enough. Among so many distinguished Scottish academic surgeons none had a broader outlook or was more ready to contribute massively to surgical science than Professor Irvine, who in the early 1960's prepared the first edition of this accepted standard work and who has now revised and added to his material in a second edition. His modest preface could conceal the vast amount of work that he and his contributors have undertaken to maintain the leading position that this book enjoys. A perusal of the list of references (now greatly improved in interest and usefulness by the addition of titles) soon shows how much new material has been added. With the exception of the chapters on peripheral circulation (lacks ultrasound), repair process of nerves (no mention of limb replantation), urology (little on renography), hyperbaric oxygen (gas gangrene, the chief application, still eclipsed by other, less useful ones), the advances since 1965 are well covered, particularly in the sections dealing with gastric function (by the editor), shock, and surgical infection, as well as that on the biochemistry of the cancer cell. This elegant, simple, comprehensive book will clearly maintain its deservedly superior position.

Radiology in Renal Disease. Edited by Thomas Sherwood, Royal Postgraduate Medical School, London. 11 × 8½ in. Pp. 75. Illustrated. 1972. London: British Medical Bulletin. £2·25.

In no sector of clinical medicine has radiology made greater contributions in recent years than in that of urology, mainly but not exclusively because of the work of Hodson, formerly of University College Hospital, London. The tendency to think that this contribution is solely in the improved application of a diagnostic method to clinical problems is corrected in this well-produced issue which presents the whole spectrum of urological radiology. The use of newer methods is amply demonstrated in papers by Joekes and Rhys Davies on isotopes, and Barnett and Morley on ultra-sound.

Urological radiology leans heavily on the employment of contrast media which have now been elaborated to greater degrees of safety and a higher radiographic pictorial quality. The toxicity to the kidney of all types of such agents is discussed by Grainger, paying particular attention to the peculiar risks in renal and hepatic failure.

The great research potential of radiological techniques in anatomy and physiology is reflected in the work of Kelsey Fry and Cattell on nephrography, that of Lavender and Sherwood on the fine detail of circulatory patterns in hypotension which is most beautifully illustrated, and that of Sidaway using macro-angiography *in vivo* in the study of clinically common problems.

The Guy's Hospital research team record their experience with and assess the value of needle nephrostomy mainly in difficult problems of acute upper urinary-tract obstruction; this technique at once offers a means of decompressing the kidney and appraising its function. To be able to record pressure and flow recordings simultaneously and also to see the dynamic radiographic picture of the bladder by videocystography promises much in the investigation of disorders of vesical function. Whiteside has contributed an excellent and concise paper on the work done by Turner-Warwick and himself using a development of Miller's technique which is likely to lead to a much clearer appreciation of the hitherto obscure mechanisms of micturition, perhaps particularly in the neurogenic bladder.

The purely clinical aspects of urinary-tract radiology are selectively described in articles on medullary necrosis in infancy (Chrispin), tropical disease (Middlemiss), and spinal dysraphism (J. E. Williams) and in an informative contribution by Hodson on post-obstructive atrophy of the kidney which includes a correlation between the radiological picture and the pathological condition.

A high standard of illustration has been achieved in this work and is nowhere better seen than in the two articles by Doyle and his colleagues describing the patterns and pathogenesis of bone disease in renal failure.

The editor, Thomas Sherwood, in combining established findings with work in progress has produced a well-balanced issue of the *British Medical Bulletin* which will interest and inform the growing body of people in all disciplines concerned with the elucidation and treatment of urinary-tract problems.

Medicine and Public Health in the People's Republic of China. Edited by Joseph R. Quinn, Ph.D. 9 × 6 in. Pp. 305 + xii. Illustrated. 1972. United States Department of Health, Education and Welfare. No price given.

With China readmitted to the world's councils and a thaw in the long restrictions in cultural and economic exchanges the appearance of this report on one of the first medical visits to China in modern times is of certain value and interest. It is a successful outcome of much sincere goodwill on both sides and a great deal of hard work and frank discussion. In particular, the role of Chinese traditional medicine—a subject on which most Chinese are sensitive—and its special pharmacology are both faithfully reported, with a selection of English references. Although most of the book is given over to broad subjects of collective rather than individual interest (much of it in the genre of the Cultural Revolution with many faithful citations from Chairman Mao) there are other special features of great interest to Western readers; in particular, there is quite a long section on acupuncture, with many interesting examples, clinical photographs, and diagrams of puncture sites. The figures and charts that have been permitted to be reproduced are of surprising frankness and interest. This is a paperback that should not be missed by anyone with an interest in this topical subject.

Operative Anatomy of Thorax. By Edward A. Edwards, M.D., Paul D. Malone, A. B., and John J. Collins, jun., M.D., Harvard Medical School. 11 × 8¼ in. Pp. 246 + xvii, with 134 illustrations. 1972. London: Henry Kimpton. £7·90.

This is the first of a series of volumes designed to cover the 'operative anatomy' of every region of the body. By the term 'operative anatomy' the authors mean to include specific operative approaches, views seen at operation, anatomical anomalies to be expected, and operative dangers. This is a formidable list to cover in a mere 200 pages. There is a considerable amount of text, but about a third of the book consists of illustrations. Curiously, most of these are taken from classic papers on the subject, so that many are 20 or 30 years old. One has only to look at these figures to realize the enormous strides that have been made in medical illustration in the past 25 years. Many of the drawings are, therefore, quite inadequate for present-day purposes, although they may be of great historical interest.

The original illustrations (in black and white) are clear and useful. The previously published ones are often obscure. Thus, figures 3 and 9 are said to illustrate extrafascial apicolysis. There is, however, no mention of Sébileau's bands, even though they are just visible in the drawing taken from Sébileau's paper and dated 1891.

Some of the illustrations are of little value. It is difficult to see the purpose of 2 whole pages devoted to poor drawings of the standard views of the mediastinum and root of the lung which are known to every medical student. These figures are repeated on pp. 174 and 175.

The text follows the illustrations in often being of greater historical interest than practical value. Surgery would have no right to be called a profession if, indeed, all operations were still carried out exactly as described by their originators. For example, an illustration shows Blalock's operation with the original anterior thoracotomy which left an ugly scar across the front of the chest. There is no mention of Potts's or Waterston's operations. The only description of the operation for coarctation of the aorta is that of Gross (1953). The incision advised is a posterolateral T-shaped one through the fourth intercostal space, dividing the posterior ends of two ribs above and three below this level!

It is disappointing to find that the anatomy illustrated is that of the normal structures, whereas the surgeon is interested in the abnormalities and distortions caused by pathological processes. The surgeon operating on, for example, a case of Fallot's tetralogy would get little guidance in the anatomical variations within the right ventricle from the brief account given here. There are useful sections on the variations in the anatomy of the coronary arteries and on the cardiac conduction system. It is difficult to understand how the authors determined what material to include and what to exclude. This unbalanced approach is seen in a full description of the Vineberg operation but none of aorto-coronary by-pass grafting. Similarly, although there is a chapter on cardiac transplantation, there is no mention of the surgery of total anomalous pulmonary venous drainage or of transposition of the great arteries.

The book as a whole suffers from indecision, hovering between an anatomical descriptive approach and a detailed account of surgical technique. Lingulectomy is illustrated in detail as an example of segmental resection, but this would be of little help to the surgeon seeking information on how to perform a resection of the anterior segment of the right upper lobe of the lung.

The description of the antireflux mechanism at the cardia is outdated and indeed must be so, since there is no reference to oesophageal manometry. The Allison repair is described as the only transthoracic procedure and the Lucius Hill technique as the only abdominal operation, without any attempt to appraise them critically. There is no mention of the Belsey and Nissen procedures.

The book leans far too heavily on somewhat outdated published material and not at all on the authors' experience. For these reasons it will be of much less assistance to the trainee surgeon than a more personal and up-to-date approach would have been.

Atlas of Improved Surgical Procedures for Common Foot Disorders: Ingrown Toenail and Hammertoe. By George C. Wee, M.D., F.A.C.S., F.I.C.S., St. Louis. 9 × 6 in. Pp. 58 + xv. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $6.

This is an extraordinary monograph describing 'phenolic [*sic*] cauterisation . . . of ingrown toenail' (13 single line drawings including sports shoes, a beaker of phenol solution, and a tube of ointment) and 'excision of the proximal phalangeal head for . . . hammertoe' (10 single line drawings), the latter deformity being described as the most common congenital [*sic*] disorder of the foot!

There is more text in the preface and introduction than in the main body of the book. Even at $6.00 it is difficult to recommend it for serious consideration by medical students or chiropodists in training.

Spezielle Chirurgie für die Praxis. Vol. 11, Part 2, **Digestive System 11.** Edited by F. BAUMGARTLE, Augsburg, K. KREMER, Düsseldorf, and H. W. SCHREIBER, Hamburg. 10¼ × 7¼ in. Pp. 892, with 470 illustrations. 1972. Stuttgart: Georg Thieme Verlag. DM.458.

THIS major textbook of practical surgery has 22 contributors who are all actively engaged in surgery at 10 different West German clinics. The book is beautifully produced and has over 1000 diagrams, figures, and tables with clear line drawings of operative procedures. The book covers the surgery of the small and large intestines, including the appendix, and is essentially a working handbook for the operating surgeon. Each subject is fully described under the main headings of Diagnosis, Indications for Surgery (absolute and relative), Contra-indications, Operative Techniques, covering the various alternative procedures, and finally Complications. Very complete lists of references are given with the full titles of all the papers mentioned; for example, those for the jejunum and ileum number 669, including many from the English literature. The various sections are clearly and concisely written and the indexing is good.

This book is too big to allow detailed review of any special chapters but it has been well edited and must be regarded as an excellent exposition of present-day surgical practice in West Germany with the typical characteristics of German care, thoroughness, and attention to detail. It is essentially a practical book designed for the practising surgeon.

Gastrointestinal Hormones. International Symposium at Erlangen, August, 1971. Edited by Professor Dr. L. DEMLING, Erlangen. 9 × 6⅛ in. Pp. 118, with 100 illustrations. 1972. Stuttgart: Georg Thieme Verlag. DM.29.70.

OUR knowledge of gastro-intestinal hormones has notably increased during recent years and their importance has been more fully recognized both in health and disease. This book presents an excellent review of the subject, being a most expertly edited account of an international symposium held at Erlangen in August, 1971. Many of the papers are concerned with new work and the names of those contributing are sufficient guarantee of their scientific value. Professor Demling has shown great editorial skill in the way in which he has produced such a uniform pattern of reports with a clear and concise presentation by authors from seven different countries. Most of the work reported is experimental and, as would be expected, is largely concerned with the action of gastrin, secretin, cholecystokinin, and caerulein. Grossman's brilliant paper gives a fine review of much fundamental work and makes clear how it is the length of intestine exposed to hydrogen ions which ultimately controls the release of secretin and so the output of bicarbonate. There are interesting reports from the Texas school upon the way in which oral calcium raises the gastric acid without there being any increase in the serum-calcium level, and a number of other stimulating and valuable contributions. In all there are 16 papers in this small book of only 117 pages, but it is well illustrated with diagrams and tables and, in spite of its rather high price, is an important contribution to gastro-enterology. The editor and contributors are to be warmly congratulated.

Air Instrument Surgery, Vol. 2. **Orthopedics.** Edited by R. M. HALL, Santa Barbara, California. Pp. 509, with 356 illustrations. 1972. Berlin: Springer-Verlag. DM.140.

THIS is a 'textbook' or rather a technical handbook in which every conceivable operation upon almost every bone or every joint of the human body using the Hall air-driven instrument is shown. Fourteen orthopaedic surgeons and two neurosurgeons have described how their particular operation can be carried out utilizing this powered instrument. They have even managed to design an air driver for knocking in a femoral prosthesis (instead of a hammer) and an air extractor for pulling it out.

The line drawings are very well done, with the attachments of this machine being greatly in evidence. An interesting although unusual use of a rib graft is illustrated in the Addendum on Thoracic Surgery. A section of an entire rib is screwed into position across the inlet of the pelvis in the line of the superficial perineal membrane, but with no mention of the underlying pathology or of any reason for such a grafting procedure.

The most important section of this book is that entitled 'An Equipment Guide'. This describes the physical properties, the repair, and maintenance of the air drill and its attachments.

In the preface the editor quite rightly points out in describing his instrument that 'possible application and adaptations are as unlimited as the surgeon's skill and imagination'. The real limitation comes in who has DM.140 for this book.

Human Sterilization. Edited by RALPH M. RICHART, M.D., New York, and DENIS J. PRAGER, Ph.D., Seattle, 8¾ × 6 in. Pp. 402 + xx. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $21.

THIS book recording the proceedings of a conference held in October, 1969, to discuss the international problems of human sterilization contains details of the different methods of sterilization in both males and females and it provides information on the evaluation of the different techniques in different communities. The book is principally of interest to the specialist in this field for whom it provides a wealth of information, but it is of less interest to the general reader, except perhaps in selected passages, particularly the reports of the discussions.

Applied Surgical Anatomy. By CHARLES MARKS, M.D., M.B., Ch.B., M.S., F.R.C.P., F.R.C.S., F.A.C.S., New Orleans. 9 × 6 in. Pp. 598 + x. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $22.50.

A SAD feature of medical education in many schools in the United States is the downgrading of anatomy in the curriculum. The author of this book, a professor of surgery at the Louisiana State University School of Medicine, has attempted to review the fundamentals of anatomy and to relate them to clinical conditions. He has aimed this volume at both students and graduates in speciality training. Considerable space, both in the text and illustrations, is given to clinical surgery but, unfortunately for students in this country, the anatomical details are insufficient for examination requirements. Modern anatomical nomenclature is not used, many of the photographs are not of high quality and several are upside down, and a number of important structures (including the heart and coronary vessels) are not illustrated anatomically. The aim of this book is praiseworthy but it is unlikely to meet the needs of British medical schools.

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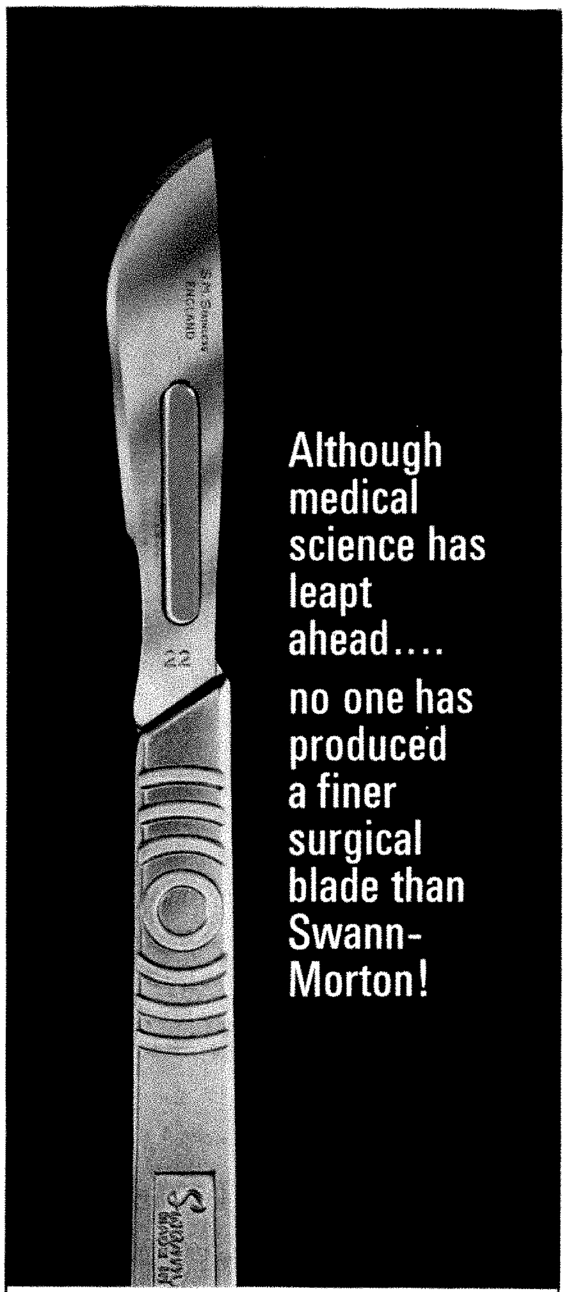
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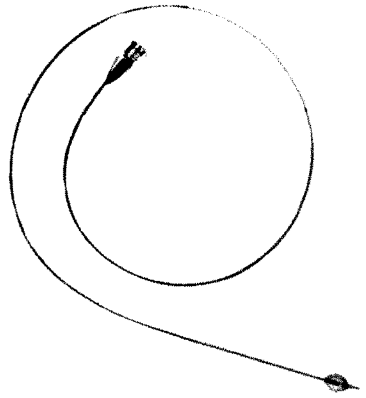

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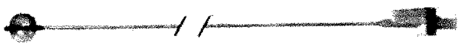

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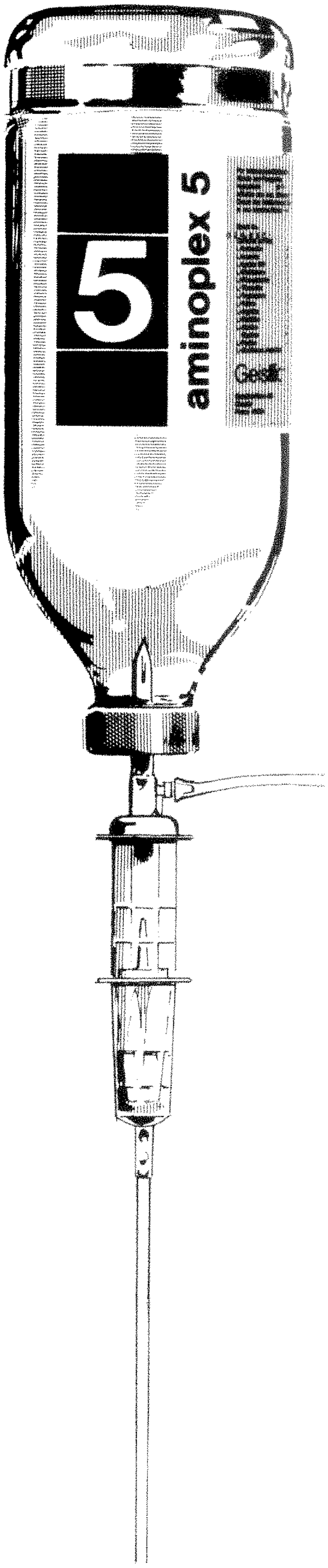

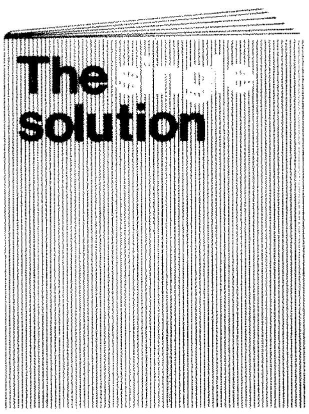

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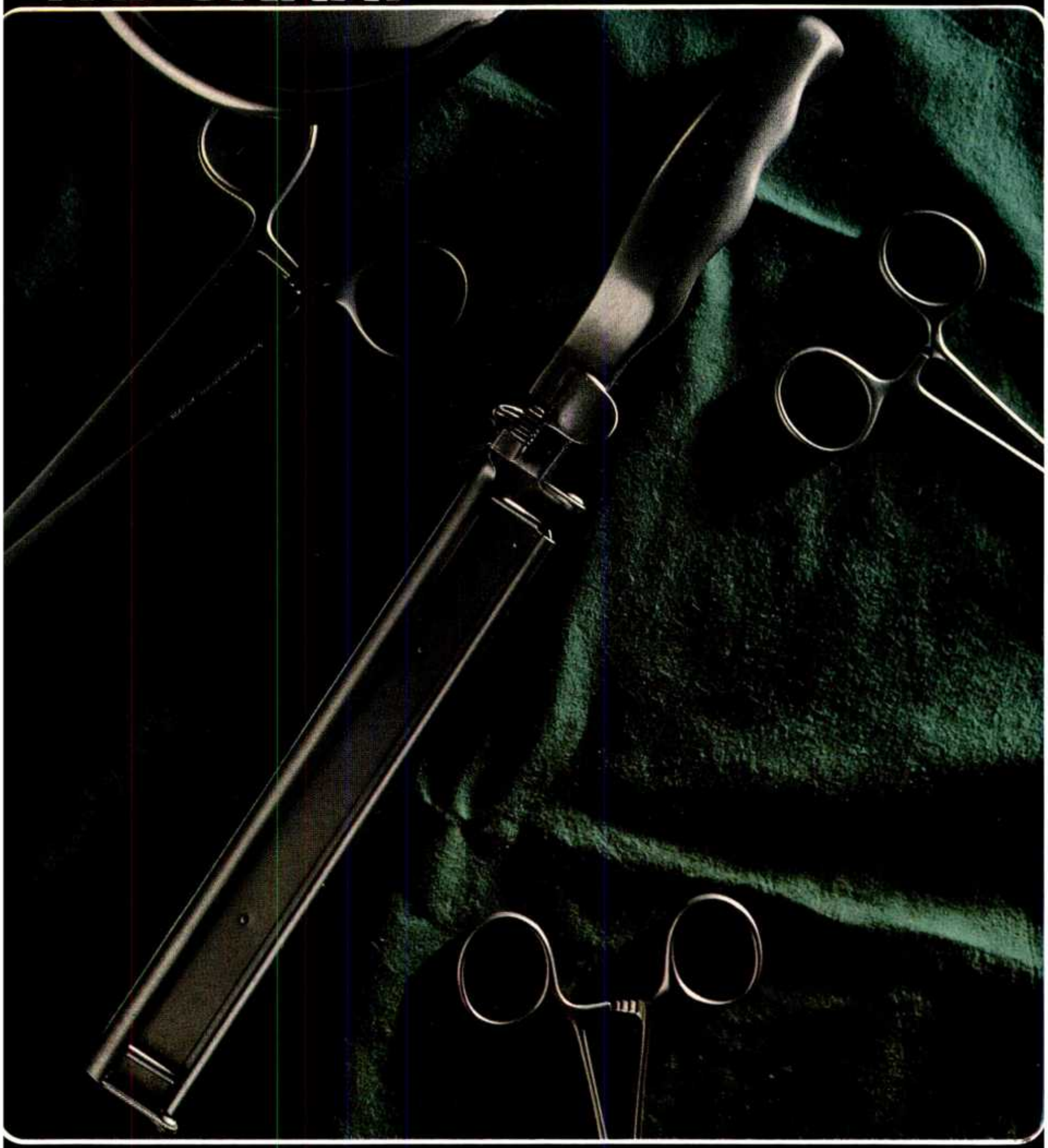

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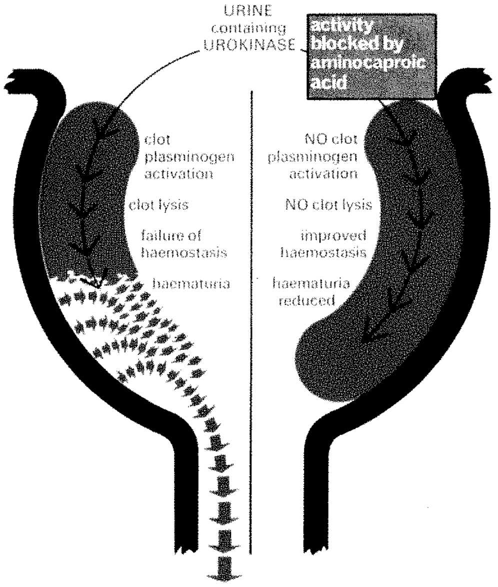

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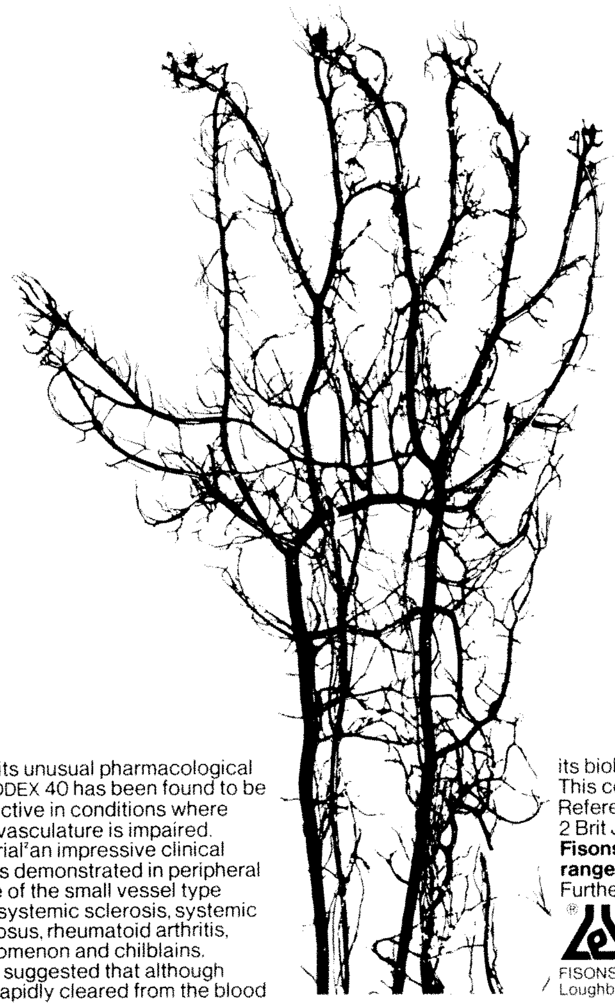

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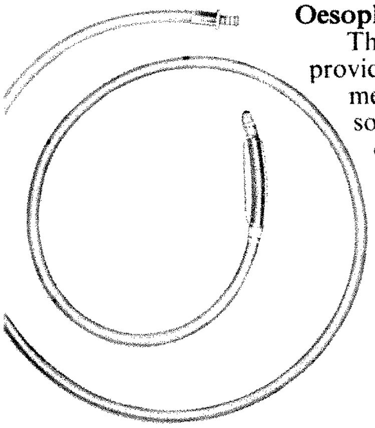

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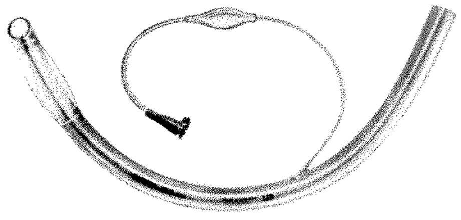

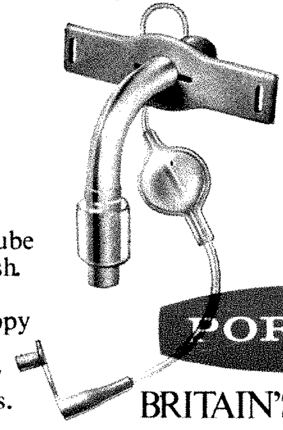

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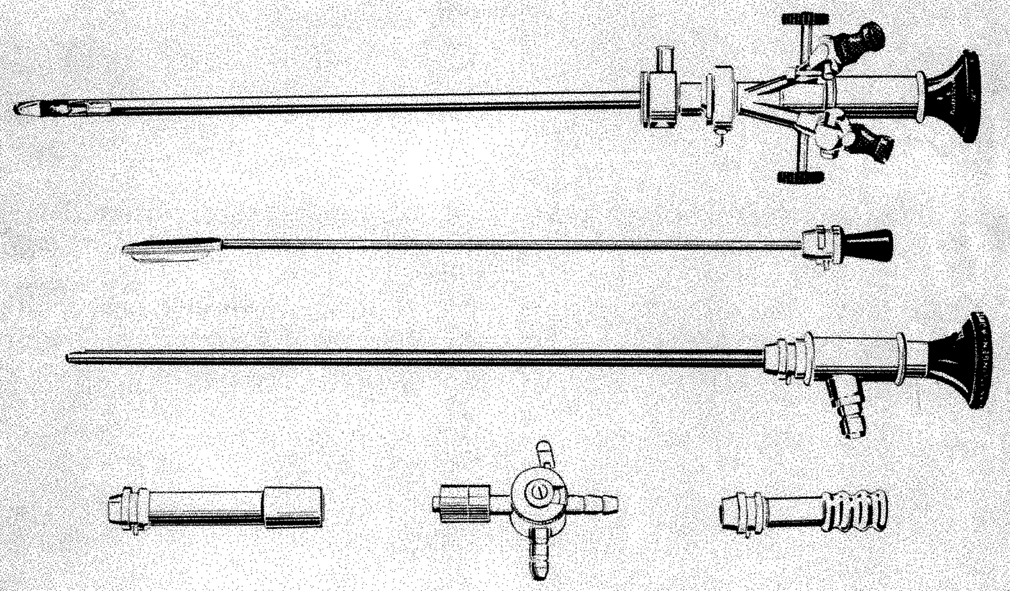

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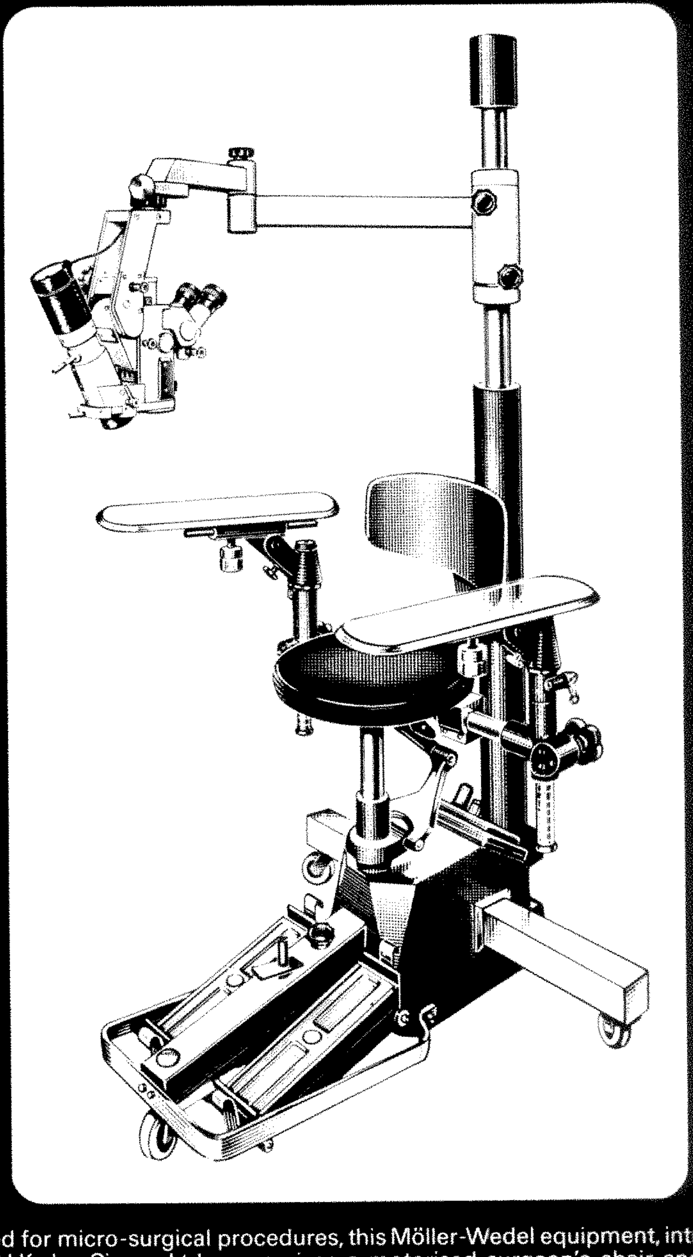

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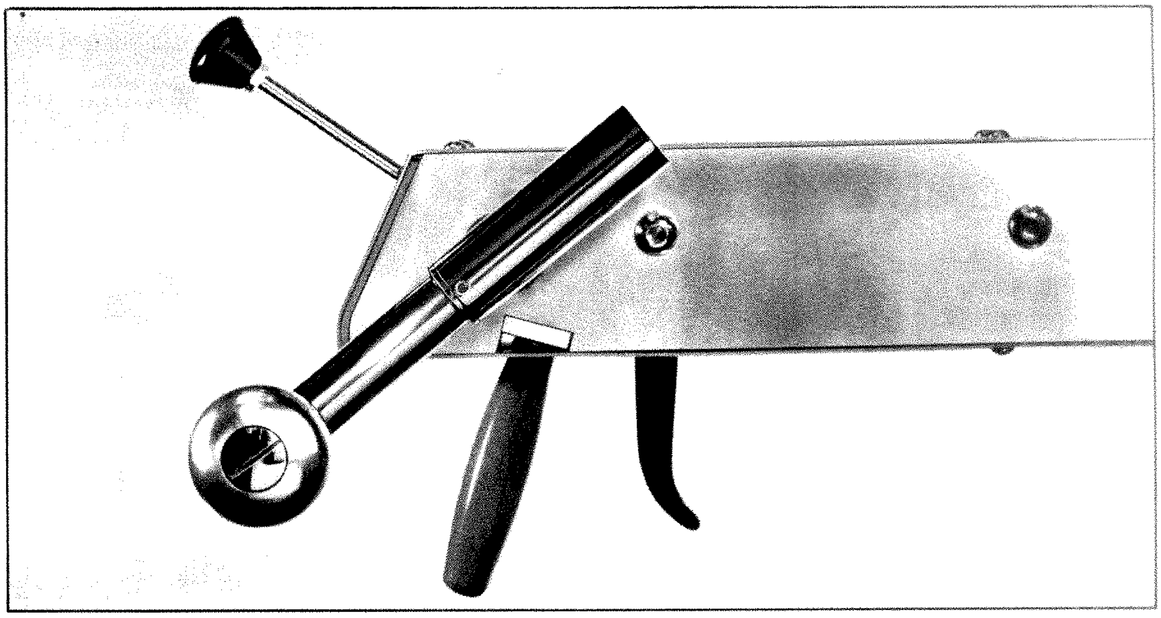

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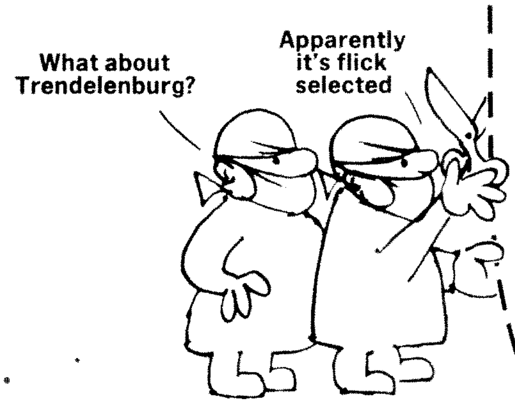

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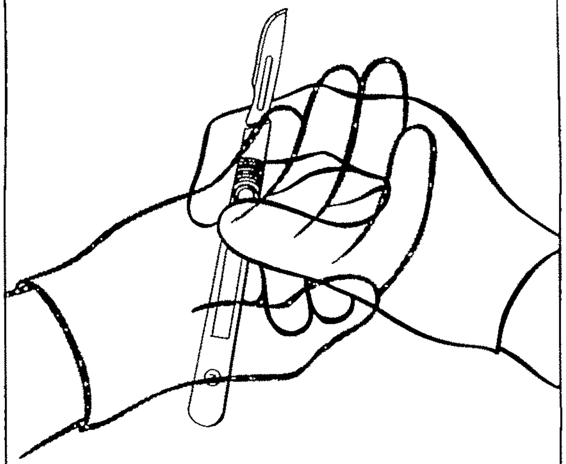

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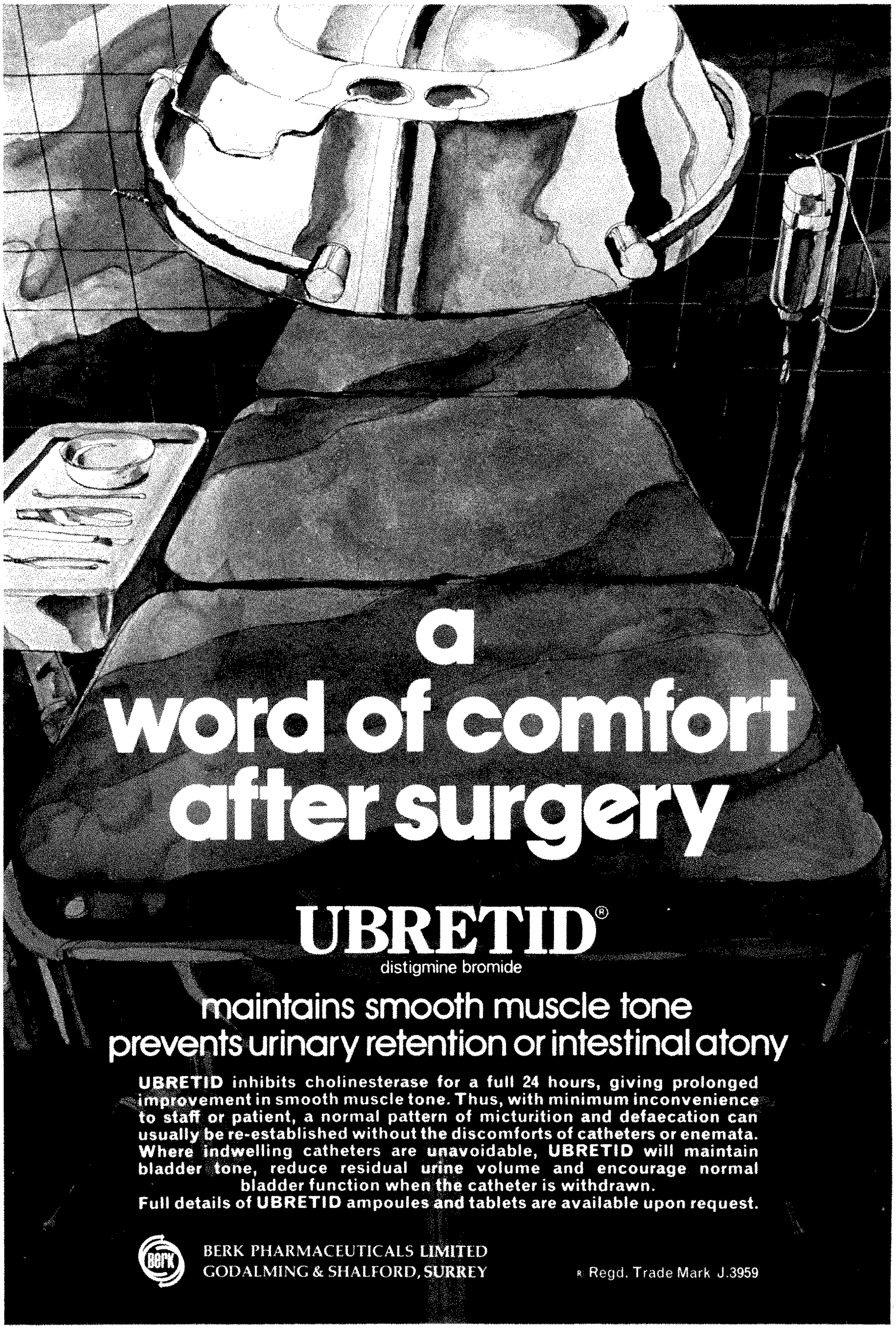

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ORIGINAL PAPERS

METABOLISM AFTER INJURY: 2. EFFECT OF A DRYISH AND WARM ENVIRONMENT ON SKIN TEMPERATURES AND ELECTROLYTE RESPONSES

By D. P. CUTHBERTSON and A. G. RAHIMI*
UNIVERSITY DEPARTMENT OF PATHOLOGICAL BIOCHEMISTRY, ROYAL INFIRMARY, GLASGOW

SUMMARY

Patients with moderate to severe fractures of the major long bones of the lower limb had generally warmer extremities if nursed in cubicles with a dryish (35–45 per cent relative humidity) and warm (29–30° C.) environment than if maintained at a normal temperature of 20–24° C. The additional heat was applied soon after the period of shock was over and was then provided for a further 10–12 days thereafter. The effect of a higher temperature in reducing the protein catabolic response to injury—which seems mainly to involve an increase in the catabolism of some muscle proteins accompanied by increased urinary excretions of potassium, creatine, and zinc—has already been described (Cuthbertson, Fell, Smith, and Tilstone, 1972). The effects of a warmer atmosphere on oral and skin temperatures over various surfaces are described in the present paper and these effects are compared with those found when extra bed coverings are applied under normal ward environmental conditions (20–22° C.). By the application of such heat the skin temperature of the extremities can be raised several degrees; that of the large toes by as much as 12° C. By the use of extra bed coverings conductive losses can undoubtedly be diminished, particularly at normal temperatures.

Oral, axillary, and frontal and mastoid process temperatures are not apparently influenced by a higher environmental temperature but appear to be mainly related to the degree of traumatic fever.

The advantage of the higher environmental temperature over extra bed coverings is presumed to be mainly in reducing total resting heat production from resting to basal values by providing thermoneutral conditions.

Apart from a significant reduction in the rise in serum potassium around the fifth day after injury and a reduction in the normal increased urinary excretion of potassium previously noted, there were no significant changes in the concentration of other serum electrolytes as a result of the higher environmental temperature, nor were the other characteristic electrolyte patterns of urinary excretion altered by the change in the ambient temperature. There were also no distinctive differences in the pattern of urinary amino-acids at the two temperatures.

THE influence of a dryish (35–45 per cent relative humidity) and warm (28–30° C.) environment on the protein, potassium, creatine, and zinc metabolic response to moderate to severe injury of the lower limbs of man has been described in a previous paper (Cuthbertson and others, 1972). The present paper provides additional data on the effect of this thermoneutral environment on smaller groups of male patients with fractures, in respect of their skin temperatures, electrolytes, and certain other metabolic responses. The skin temperatures of a few patients were studied at both temperature levels.

MATERIALS AND METHODS

Patients.—The patients were all otherwise healthy males aged 18–67 years. Two groups were studied: in the first group 11 patients were investigated intensively, some at the two temperature levels; in the second group 18 patients (9 at each temperature) were studied less intensively but with particular regard to the electrolyte responses. A few patients in the first group fitted into the second series.

The patients with long bone injury were studied for 9–12 days after injury in the same cubicles as described previously (Cuthbertson and others, 1972). The

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dietary régime was similar for the patients at the normal ward temperature (20–24° C.) and for those at 29–30° C. The total energy intake was around 2500 Cal per day and protein accounted for 13–14 per cent of the total calories. The amino-acid pattern of the intake corresponded to that of muscle protein.

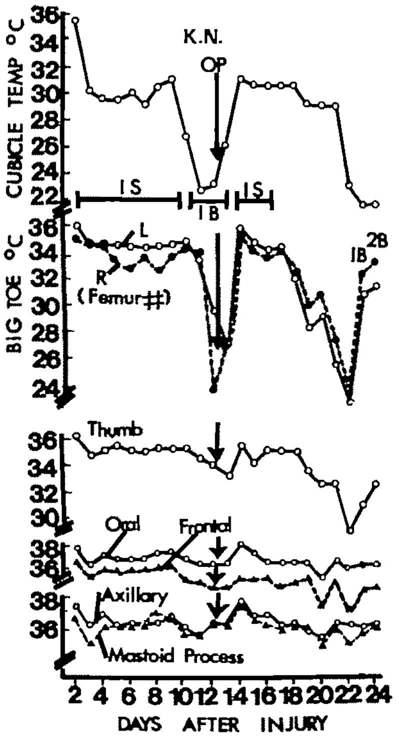

FIG. 1.—*Case* 1. The cubicle was maintained at 30° C. except for a few days at 23° C A Kunchner nail (K.N.) was inserted on the twelfth day and the temperature was raised again At the low temperature one blanket (1B) was substituted for the extra sheet (1S). L, Left. R, Right.

Urine Analysis.—Measurement of the total nitrogen in the urine and food was based on Fleck's (1967) semi-micro modification of the Kjeldahl method. Sodium and potassium were estimated by flame-emission photometry, chloride by an EEL chloride meter (Evans Electrostenum Ltd.) with coulometric titration, and calcium and magnesium by atomic absorption spectrophotometry (SP 90, Unicam Ltd.). These five electrolytes are expressed as mmol per 24 hours. The osmolality was measured by freezing-point depression (Advanced Scientific Company osmometer), glycosuria and ketonuria by the Clinstix test and the acetoacetic acid test (Ames Co.), and amino-acids by paper chromatography (Smith, 1965). Blood *p*H, base excess, and pCO_2 were determined by the Astrup method.

Skin Temperatures.—For this study a Universal Thermometer (Electrolaboratoriet, Copenhagen) with four probes was used. As it was occasionally desirable to determine skin temperatures below bed coverings, the patients were encouraged to co-operate in recording their own temperatures. The effect of the application of additional covering in contrast to the effect of the higher environmental temperature was also studied. Throughout the period of study all the patients had a basic covering of a nightgown and a half-sheet to the waist. Anterior surfaces were selected for ease of access and multiple recordings were made near the nail beds of the big toes and thumbs, and over the mid or upper thighs, the bellies of the biceps, the abdomen, the forehead, and the mastoid processes in addition to taking the oral and/or axillary temperatures. In the first group temperature recordings were made in the middle of the morning, and in the second group approximately 1 hour after lunch. There were two objectives:—

1. By daily multiple measurements to determine the effects of changing and maintaining the cubicle at normal (20–24° C.) and warm (28–30° C.) temperatures. At the latter temperature the humidity was controlled at between 35 and 45 per cent. The effects of additional bed coverings were also studied in these patients at fluctuating temperatures.

2. To determine the continuous effect of the higher ambient temperature on the skin temperature of the injured and non-injured distal extremities of the lower leg, namely, on the dorsum of the big toe proximal to the nail bed, since only injuries to the lower limbs were studied in this investigation, and to compare these areas with the respective axillary temperatures.

Having regard to Benzinger's (1969) criticism of the uselessness of rectal temperature as an index of core temperature owing to pelvic circulatory changes, and to the difficulty of access in such fracture cases, oral and/or axillary temperatures have been used in the series.

RESULTS

1. Intensively Studied Series.—Eleven patients with one or more fractures of the major long bones of the lower limbs were studied daily; some at normal temperatures, some at the higher ambient temperature of 30° C., one for 16 hours daily at the higher temperature with 8 hours at the lower temperature each night, and several at both low and high temperatures but the temperatures were imposed in differing order. The oral and/or axillary temperatures and the temperatures over several parts of the body were recorded for each patient. Details of these cases indicate the variability of individual response to injury and the warmer environment, and also the effect of extra bed coverings.

CASE REPORTS

Case 1.—A. McC., a male aged 17 years, suffered a fracture of his right femur as the result of a traffic accident. On the second day after injury he was placed in a warm cubicle which registered a temperature of 35·5° C. for the first day, and thereafter it settled at around 30° C. for 7 days when it was dropped over a period of 2–3 days to 22·5–23° C. On the third day of the reduced temperature a Küntchner nail was inserted in the femur and the temperature was again raised to around 30° C. for a further 8 days, and then it was allowed to fall to the normal ward level of around 22° C. (*Fig.* 1).

During the first 9 days the patient was covered by an extra sheet of bed clothing which was replaced by a blanket during the first period of a lower cubicle temperature. On return to the higher temperature the blanket was replaced by a sheet for 3 days. This was removed and was not replaced by a blanket until the cubicle temperature had again fallen to just below 22° C., when first one blanket and then two blankets were provided.

The temperature changes over several areas together with the oral and axillary temperature were followed.

It was evident that the degree of traumatic fever was slight after each traumatic event and was shown equally by the temperatures in the mouth, axilla, frontal, and mastoid areas.

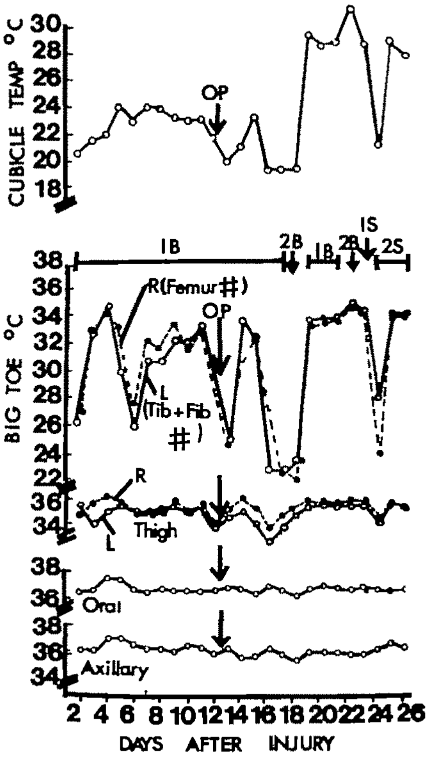

FIG. 2.—*Case* 2. The temperature was kept around 20–24° C. for 17 days, then was raised to around 29° C. for 5 days, and was intermittently low and high for 3 further days. On the thirteenth day there was exploration and resuturing of the wrist. For the first 17 days the patient was covered with one blanket in addition to his basic sheet, then intermittently with one or two blankets or sheets.

The temperatures of both big toes moved in parallel to that of the cubicle, the temperature of the right injured leg being lower by about 1–5° C. over the first 9 days but thereafter there was not much difference although the positions were marginally reversed during the last week. The big toe temperatures were very sensitive to the temperature of the cubicle and when the latter fell the provision of an extra blanket did not prevent a fall of 9–10° C. in the temperatures of the toes. The effect of operation was to cause a slight rise in the temperatures of the toes but the rise in the temperature of the cubicle induced a rapid increase to the plateau level which had been established during the earlier period of high temperature. When, however, the extra sheet was removed the temperatures of the toes could not be sustained by the remaining half-sheet and their temperatures fell by about 6° C. Reduction of the temperature of the cubicle to around 22° C. led to a fall in the temperatures of the toes to 23° C. Thus, the toes were sensitive indicators of the environmental temperature and needed some degree of insulation to maintain the changes upwards. Such insulation could raise the temperature markedly and with two extra blankets at the lower environmental temperature the temperatures of the toes were only some 2° C. less than those induced by a cubicle temperature of 30·5° C.

The skin temperatures over the thighs and biceps were relatively uninfluenced by different environmental temperatures, but the temperatures of the thumbs were much more sensitive to changes and for their maintenance the patient required at least one sheet over the basic half-sheet.

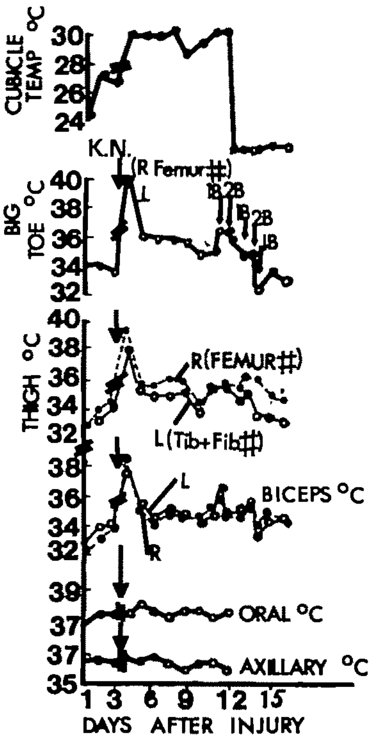

FIG. 3.—*Case* 3. The cubicle temperature was gradually raised to 30° C. On the day of his accident a Steinmann pin was inserted to fix the malleolar displacement and 4 days later a Kuntschner nail (K N) was inserted into the femur. On the twelfth day the temperature of the cubicle was reduced to 23° C. From this point onwards the patient was covered by one or two blankets.

Case 2.—J. S., a male aged 54 years, had a fracture of the right femur, compound fractures of the tibia and fibula of the left side, and lacerations of his right forearm with severance of vessels, nerves, and tendons. A Steinmann pin was inserted in the tibia for traction. The patient was studied for 17 days at 20–20° C. and then for 7 days at 30–32° C. with a drop to 21° C. on the twenty-third day (*Fig.* 2). On the thirteenth day exploration of the right wrist and resuturing were carried out. The temperatures of both big toes reflected the changes in the ambient temperature in a parallel fashion. Even the skin over the upper portion of the thighs showed comparable changes. The effects of the traumatic fever associated with injury were superimposed on the changes due to the ambient temperature, the degree of fever being reflected by the changes in the axillary and oral temperatures only. The oral temperature was about 0·5° C. higher than the axillary temperature.

The effect of increasing the ambient temperature to 30–32° C. on the seventeenth day after injury was to cause a rapid rise in the skin temperature of the big toe from 22–23° C. to 34–35° C. These temperatures were little affected by an additional blanket or sheets.

It is obvious from *Fig.* 2 that the big toe is a particularly sensitive index of both the ambient temperature change and the febrile response to injury.

Case 3.—A. J., a male aged 17 years, had sustained a fracture of the middle of the right femur, fractures of the left tibia and fibula, and a left bimalleolar fracture with diastasis in a road-traffic accident (*Fig.* 3).

The temperature of the ward cubicle was gradually raised to 30° C. by the fourth day after admission. A Steinmann pin was inserted to fix the malleolar displacement on the day of the accident and 4 days later a Küntschner nail was inserted into the femur.

It was found that the skin over different parts of the body surface responded vigorously not only to the changes in the ambient temperature but also to the effects of accidental or surgical trauma, whereas the oral and axillary temperatures were relatively little affected. This type of reaction was characteristic of patients with a rapid compensating vascular shunting and conduction.

The addition of one blanket to the one already being used at the high ambient temperature appeared to have no effect on the skin temperatures, and it was uncertain whether the use of one blanket as well as the routine half-sheet covering to the waist had any real effect at the lower ward temperature.

Case 4.—E. F., a male aged 50 years, had compound fractures of the tibia and fibula as well as fractures of the medial and lateral malleoli of the left leg. He was nursed at 28–29° C. with two extra sheets bed cover from the first day after injury.

The oral temperature remained very constant and the big toes showed first a small drop of 1·5–2° C. followed by a rise to the original levels by the fifth day. After the first day the injured side showed a rather higher temperature than the opposite side. All his other measurements remained very constant.

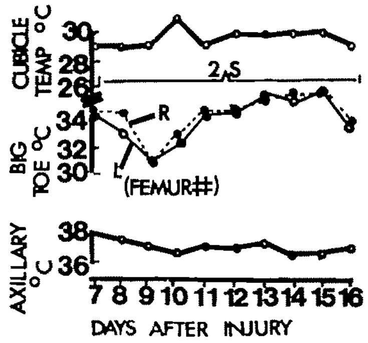

FIG 4.—*Case* 5. This patient was nursed at 29–30° C from the seventh day after injury and was covered by two extra sheets throughout.

Case 5.—R. K., a male aged 65 years, had a fracture of the left femur following a fall. He was nursed at 29–30° C. with two extra sheets bed cover (*Fig.* 4).

The patient's big toes showed the same temperature changes as *Case* 4, with first a fall in temperature of about 4° C., followed by a return to the earlier level, and subsequently a rise of 1° C. There was no sign of traumatic fever.

Case 6.—A. D., a male aged 14 years, had a fractured pelvis, right clavicle, and right tibia and fibula as the result of a road-traffic accident. He was put in a warm cubicle but on the third day after injury he complained of the heat and this was then reduced to normal levels. He was covered throughout with a half-sheet to the waist (*Fig.* 5).

There appeared to be no thermal response to the trauma and the changes in the ambient temperature resulted in corresponding fluctuations in the peripheral skin temperatures (nail beds of big toes and thumbs). The oral temperature fell slightly throughout the first 5 days and thereafter was steady. The injured side possibly showed a greater response to changes in the ambient temperature.

Case 7.—H. A., a male aged 34 years, had fractures of the right clavicle, humerus, ulna, tibia, and fibula as the result of a road-traffic accident. The patient was placed in a warm cubicle at 29° C. for the first 3 days after his accident, and then the cubicle temperature was lowered to 20–23° C.

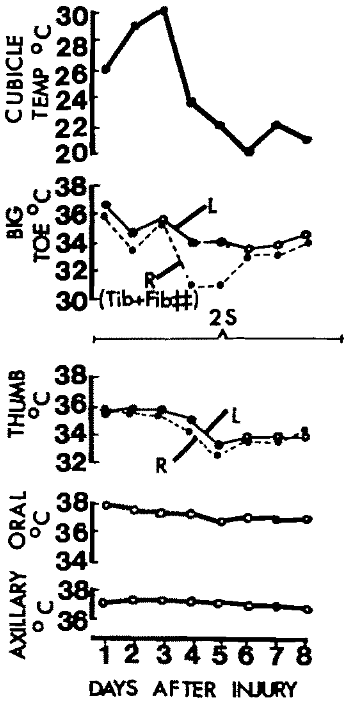

FIG. 5.—*Case* 6. This patient was nursed at high and then low cubicle temperatures He had two extra sheets throughout.

The oral and axillary temperatures and those of the skin over the forehead and mastoid processes showed parallel responses with an early small rise of 1–1·5° C. However, the temperature of the small toes seemed to be mainly influenced by the changes in the ambient temperature and the fall which appeared to follow the drop in the environmental temperature from 29 to 20–22° C. could not be arrested by the addition of two extra blankets.

Case 8.—R. S., a male aged 39 years, had fractures of the tibia and fibula. He was nursed at a temperature of 30° C. but each night the heat was switched off for 8 hours. The temperature never fell below about 25° C. The patient's oral temperature remained fairly constant throughout and the temperature of the big toes was relatively steady at 33·5–35° C.; the patient had only one extra sheet but this did not cover his big toe. He was studied from the first day after injury.

Case 9.—P. N., a male aged 59 years, had multiple fractures involving the left femur, right acetabular ring with displacement, left clavicle, first left rib, several left metacarpals, and a right Smith's fracture. He was studied without any attempt to raise the environmental temperature but the temperature of his cubicle varied between 21 and 25° C.

The temperature of the big toe of the uninjured right leg was always higher (1·5—3° C.) than that of the left leg for the first week after injury and then the difference disappeared. The same temperature trend was shown for the skin of the thighs and for a few days over the biceps also. When one blanket was applied this raised the temperature of both toes from 31·5 to 34·2° C. Two blankets did not increase the temperature of the toes further but had a slight effect on the temperature of the thighs. One blanket raised the temperature over the biceps and the abdomen slightly but a second blanket again had no additional effect. As might be expected, extra blankets did not affect the skin temperatures over the mastoid and frontal areas. The axillary temperature was about 0·6° C. below that of the mouth. There was no obvious effect of one or two blankets on these zones.

This patient felt that even an environment of 25° C. was warmer than he liked but it had not been intended to place him in the higher temperature.

It appeared that so far as the lower extremities were concerned two blankets at an environmental temperature of 25° C. and with the use of orthopaedic appliances had no greater effect than one blanket, but that in the case of the thighs two blankets raised the skin temperature slightly more than one.

Case 10.—J. F., a male aged 32 years, had a fracture of the medial and lateral malleoli with dislocation of the ankle of the left leg (*Fig.* 6). The patient was nursed at 19–20° C., but exhibited very constant oral and big-toe temperatures, the toe being maintained at 34–35° C. and the oral temperature at 36·5–37° C. He needed only one extra bed sheet to maintain these temperatures.

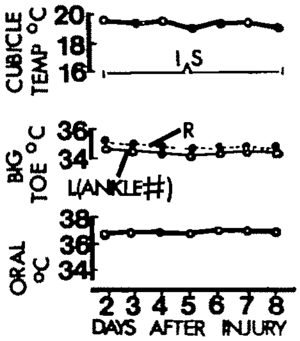

FIG. 6—*Case* 10. This patient was nursed at 20° C throughout with one extra sheet covering.

This patient can be compared with *Case* 8, who also exhibited great constancy but had a lower skin temperature under warmer conditions.

Case 11.—C. McI., a male aged 57 years, had compound fractures of the left tibia and humerus. He was kept at a normal temperature (20–23·5° C.) with two sheets. There was very little fluctuation in any of the skin temperatures or in the oral and axillary temperatures, the latter being about 0–1·0° C. lower than the oral temperature. The temperature of the big toes oscillated around 32·5° C.

Case 12.—V. N., a male aged 27 years, had a fracture of the mid-shaft of the right femur as the result of a road-traffic accident. Detailed temperature observations were made some 20 days after the accident and were concerned mainly with the effect of extra blankets when the cubicle had a temperature ranging from 23° C. up to 28° C. with a relative humidity of 60–70 per cent.

At 23–24° C. the effect of one extra blanket was to raise the temperature of the toes and thighs by about 2° C.; two blankets produced a further rise of about 1° C. in these areas. At 28° C. and without a blanket the temperature of the toes was only a little higher than that with two blankets at the lower temperature, while the temperature of the thighs was unchanged. One extra blanket plus heat produced no further change in the temperature of the toes, but two blankets produced an increase of about 2° C. and four blankets a further rise of about 2° C., i.e., the final temperature of the toes was about 9° C. higher than that with no extra blankets at 23° C. The temperature of the thighs rose only about 2·5° C. after applying four blankets. The oral temperatures were unaffected by the number of blankets.

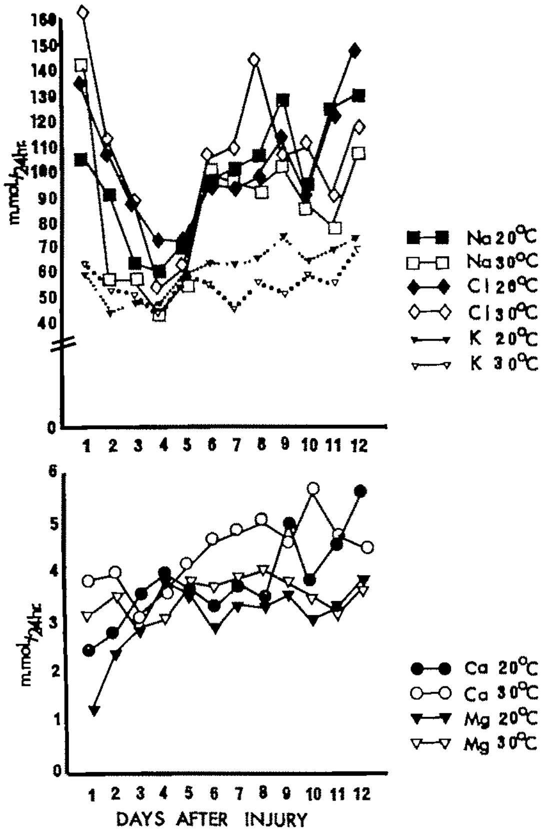

FIG. 7.—Mean daily excretion of urinary electrolytes of patients with major long bone injuries nursed at 20 or 30° C.

Whereas the oral and axillary temperatures which appeared to differ by 0·5–0·8° C., the former being higher, were apparently influenced mainly by the degree of traumatic fever, the extremities—the toes in particular—varied with the temperature of the environment and to a variable degree as the result of extra bed coverings. The fingers sometimes also showed similar rapid vasomotor responses. The other areas of the body surface do not have this capacity to shunt blood so effectively.

It was noted with interest that the temperature of the forehead and over the mastoid processes in the present cases exhibited changes similar to those in the mouth.

On occasions, despite the high ambient temperature the temperature of the toes could not be sustained without some extra bed covering. In one case it was found that when the extra sheet was taken away the temperature of the big toe dropped by 8° C. The reverse of such a change was noted in another case where a 10° C. rise in the toe temperature resulted from a 10° C. rise in the cubicle temperature, and a fall of 11° C. in the toe temperature resulted from a fall of 8° C. in the cubicle temperature. The dramatic changes in the big toe temperatures were accompanied by smaller changes in the temperatures of the skin of the thighs and biceps and even smaller ones over the abdomen. The thumbs reacted in a similar way to the toes.

In some instances relatively high distal temperatures could be achieved by the use of additional bed coverings, but such insulation obviously related to the area covered and not to the whole body.

2. Comparative Series.—The effects of the two ambient temperatures when continuously applied were also studied on the 3rd, 6th, 9th, and 12th days after injury. The influence of the high cubicle temperature (30° C.) on the skin temperature (mainly of the big toes) and the axilla temperatures was also investigated. There were 9 comparable patients at each temperature level.

Although the mean temperature of the big toes was slightly higher in the 30° C. group than in the 20° C. group on days 3, 6, and 12 of observation the differences were not statistically significantly different. On the ninth day, however, the differences reached significance. There was no significant difference in the axillary temperatures between the two groups.

The application of one blanket as an extra bed covering normally raised the skin temperature of the big toes by 3–5° C. in patients who were at the normal ambient temperature. The addition of a second blanket had a slight extra effect.

Urinary Electrolytes (*Fig.* 7).—

Sodium and chloride: As was to be expected there was a very close parallelism between the urinary excretions of sodium and chloride at the two temperatures. There was first a progressive fall lasting approximately 4 days or more, indicating the normal retention effect which has been described by Wilkinson, Billing, Nagy, and Stewart (1949) and Moore and Ball (1952). This was followed by a rise to earlier values. There was no sign of a reduced urinary excretion of chloride at the higher temperature but there was some evidence of a lower excretion of sodium at 30° C. but this was not significant ($P > 0{\cdot}05$).

Potassium: There was a tendency for this ion to fall very slightly over the first few days but this was then followed by a slight rise to a level above that found earlier and this was most marked during the second period of 6 days. The behaviour was according to the pattern described by Wilkinson and others (1950) and Moore and Ball (1952). Although when viewed in terms of 3-day groups there was no significant difference in excretion at the two temperatures, nevertheless calculations based on the total data revealed a significant overall difference ($0{\cdot}05 > P > 0{\cdot}02$). This was a more definite reduction at the higher temperature than that reported in the previous paper (Cuthbertson and others, 1972).

Calcium and magnesium: The courses of excretion of calcium and magnesium moved in parallel at the two temperatures but with slow small rises—more obvious at 20° C.—which did not decline during the period of observation, presumably arising from disruption of muscle and bone and from atrophy. Walker, Fleming, and Stewart (1968) have drawn attention to the rise in magnesium following soft-tissue surgery. The excretions were not statistically significantly different at the two ambient temperatures ($P > 0{\cdot}05$ for each element). The excretions of calcium and magnesium at 30° C. and also at 20° C. were more nearly in parallel as expressed in mmol per 24 hours than were the excretions of these two ions when considered individually at the two temperatures; more particularly at 20° C. (*Fig.* 7).

Osmolality: There was high urine osmolality in the first few days following injury and this was associated with oliguria. A few cases subsequently showed polyuria.

Glycosuria and ketonuria: Glycosuria occurred in some cases and was an early manifestation. One case continued to show these two associated metabolic disturbances in traces for 6 days after injury.

Table I.—SERUM ELECTROLYTES (mmol per litre)

SERUM ELECTROLYTE	DAY AFTER INJURY					
	3		5		10	
	20° C.	30° C.	20° C.	30° C.	20° C.	30° C
Na	137	138	137	138	139	139
Cl	99	100	101	100	99	102
K	4·4	4·2	5·4	4·8	4·2	4·4
Ca	2·4	2·5	2·4	2·4	2·5	2·5
Mg	1·2	1·3	1·2	1·2	1·2	1·3
Osmolality (mosmol per kg)	284	288	286	290	286	289

Serum Electrolytes (*Table I*).—Blood samples were collected on days 3, 5, and 10 after injury and analysed for electrolytes and osmolality. There were no changes from normality with time after injury or with ambient temperature except in the case of potassium, where the values at 30° C. were slightly less than those at 20° C. especially at the time of maximum metabolic response, i.e., around the fifth day after injury, and this was to a significant degree.

Urinary Amino-acids.—In a small series of 4 patients (2 at each of the two ambient temperatures) who were examined in respect of the excretion of α-amino-acids in the urine there appeared to be no group difference in respect of both non-essential and essential amino-acids, although there were differences within each group in respect of the excretion of histidine and lysine in particular. Such differences were not referable to the transfusions administered to 1 patient in each group. The injuries were severe to moderate in each group, the patients with severe injuries receiving multiple transfusions.

The essential amino-acids, threonine, valine, leucine, isoleucine, and methionine, which are not normally detected in the urine, were found and this confirmed Nardi's (1954) observations made, however, in cases with burns.

DISCUSSION

In a previous paper the effect of a dryish and warm (29–30° C.) environment in reducing the catabolic response to moderate to severe injury, mainly of the lower limbs, has been described together with the reduction in the loss of nitrogen, potassium, creatine, and zinc in the urine (Cuthbertson and others, 1972). So far as albumin is concerned the fall which occurs at the higher temperature seems to be due to reduced synthesis in the liver rather than to increased catabolism (Tilstone, Ballantyne, Kahn, and Fleck, 1972). Since 'acute phase reactants' such as C-reactive protein and fibrinogen are almost certainly synthesized at an increased rate after injury it is clear that the metabolic response to trauma, producing increased urinary nitrogen, is not due to an increase in catabolism of all proteins or to a decrease in the synthesis of all proteins. Thus the view that there is increased breakdown of muscle protein is still further emphasized (Tilstone and others, 1972).

In the patients whom we have studied the situation is made complex since coinciding with the greater exposure of the limbs because of the remedial means employed there is also variable degree of cover by plaster, bandages, etc. Furthermore, the normal behavioural responses to facilitate core-temperature maintenance are restricted by the patient's position in bed and the maintenance of muscle tone itself may be painful.

Owing to the greater exposure of an injured lower limb to the prevailing ward temperatures (20–22° C.) there is frequently a degree of cold exposure which will result in an increased firing rate of the peripheral cold receptors, and the changes in temperature gradient induced between the core and the surface will result in increased heat conduction and, if continued, might result in a fall in the core temperature or a contraction in the core of higher temperature. There is also compensating contraction of the peripheral vascular system by shunting. A diminished rate of warm-receptor firing and reduction of the anterior warm inhibition of the posterior hypothalamic centre presumably follow, leaving the posterior centre to mediate heat production (Benzinger, 1969).

Cold-receptor firing is apparently considerable at 20° C. but there is no increase in oxygen consumption if the core temperature remains at 37° C., i.e., the warm inhibition of chemical thermoregulation is still in force (Benzinger, 1969). It has been established that if the core temperature falls by 0·5° C. by core-to-surface conduction losses, then a brisk metabolic response occurs. It is now well established that following injuries of the type that we have studied there is an increase in oxygen consumption and heat production (Cuthbertson, 1932; Cairnie, Campbell, Cuthbertson, and Pullar, 1957) and this constitutes the flow phase with an accompanying increase in protein catabolism, and that at an ambient temperature of 30° C. this increment in heat production is largely if not entirely abolished (Caldwell, 1962; Campbell and Cuthbertson, 1966, 1967) in experimental animals, and diminished in man (Barr, Birke, Liljedahl, and Plantin, 1968). In experimental animals healing of superficial wounds is accelerated (Erici, 1954; Cuthbertson and Tilstone, 1967).

The advantage of a higher ambient temperature in conserving heat compared with the effect of one or two extra sheets or blankets is that while the latter undoubtedly act in respect of their insulating capacity and in reducing the rate of heat flow to the environment the provision of an ambient temperature within the zone of thermoneutrality tends to reduce the resting metabolic rate to basal level as the surface area as a whole is affected. Even a slight increase in surface temperature at the edge of a wound accelerates skin healing in experimental animals (Cuthbertson and Tilstone, 1967). Erici (1954) and Caldwell (1962) have also noted the beneficial effects of a higher ambient temperature on wound healing in rats and rabbits.

Although common experience demonstrates the rapidity and extent of the vascular shunting mechanisms involved in heat conservation we were somewhat surprised on the extent of this lability of skin temperature, particularly in the nail bed of the big toes, though the observations of Gibbon and Landis (1932) and the vascular surgeons who have used the reflex vasodilatation test for testing circulation in the limb should have warned us to expect such findings. It is of interest that the former found no appreciable increase in toe temperatures following the use of blankets at normal ward temperatures in the 2 subjects whom they studied under such conditions.

The temperature of the warm water used by Gibbon and Landis (1932), namely 43–45° C., was based on the temperature of the hot chamber which Lewis and Pickering (1931) had used earlier which was 46° C. It is interesting that we obtained similar increments in toe temperature at the higher environmental temperature as we did at the lower temperature. Reid (1973) found little effect of the higher temperature on thigh temperature. He has also noted that the degree of response of the toes of his patients to warming the hands and forearms is dependent on the ambient temperature, a few degrees making a considerable difference, except where there is vascular occlusion of the lower limb.

Apart from a reduction in the rise in serum potassium to a significant degree around the fifth day after injury and in the increased urinary excretion of potassium already described (Cuthbertson and others, 1972) there were no significant changes in the concentrations of the other serum electrolytes studied as a result of the higher temperature imposed (*Table I*), nor were the characteristic patterns of urinary excretion altered by changes in the ambient temperature except that potassium excretion was significantly less at 30° C. The excretions of calcium and magnesium showed slow small rises at 20° C. There were also no obvious distinctive differences in the pattern of urinary amino-acids at the two cubicle temperatures in the small group investigated.

Acknowledgements.—The senior author (D. P. C.) wishes to express his sincere thanks to the Medical Research Council for a grant for this research. The junior author (A. G. R.) is greatly indebted to the World Health Organization for a travel grant. The authors are grateful for the facilities provided in the Department of Pathological Biochemistry, Glasgow Royal Infirmary, by Professor H. G. Morgan, and the Board of Management of the hospital. They also wish to acknowledge their indebtedness to Professor W. A. Mackey and his nursing staff and also to Mr. John White, Chairman of the Department of Orthopaedic Surgery and Accident Unit, and his surgical colleagues and University staff for their great co-operation, and for making available space for the erection of the special air-conditioned cubicles. Skilled technical assistance has been provided by Miss Christine Hall.

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THE SURGICAL MANAGEMENT OF ACUTE RENAL PAPILLARY NECROSIS

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SUMMARY

Analgesic nephropathy can present as an obstructive uropathy by ureteric impaction of a sloughed renal papilla. Five out of 12 patients admitted with analgesic nephropathy presented with obstructive renal failure. Endoscopic surgery to deal with the obstruction was successful in every case. Removal of the necrotic renal papilla with a Dormia ureteric stone basket was performed six times whilst ureteric catheterization was sufficient to restore urine flow on two occasions. Two of the 5 patients had had a previous nephrectomy for obstructive pyelonephritis. These results suggest that endoscopic surgery is safe and effective in the treatment of acute obstructive renal papillary necrosis.

THE association of analgesic abuse and chronic renal disease is well known. A leading article in the *British Medical Journal* (1970) noted that patients presented with various symptoms and that occasionally separated renal papillae may produce acute renal failure by ureteric obstruction. The prognosis in acute renal papillary necrosis is poor, it being a major cause of death in Edmondson, Reynolds, and Jacobson's (1966) series; 20 out of 105 alcoholics with pyelonephritis had papillary necrosis in their post-mortem study. As healed lesions at autopsy were rare Edmondson and others believed that most patients died in the acute phase. Immediate nephrectomy has been recommended (Harrow, 1967) but most of these cases are in poor condition and may have a solitary kidney. A more conservative approach is advocated here and an account is given of experience with endoscopic methods to relieve obstruction.

PATIENTS AND METHODS

In the past 2 years 12 patients were admitted to the Liverpool Regional Urological Centre with renal papillary necrosis. Approximately double this number are seen annually in out-patients' clinics. Five of the 12 patients presented with acute obstruction; their history and management are summarized in *Table I*. *Case* 2 is of particular interest and is described fully.

A detailed history was taken from each patient to determine the cause of the renal condition. Urine culture and microscopy, measurement of the haemoglobin, blood-urea and electrolytes, and serum creatinine, and infusion pyelography were done routinely. A urethral antiseptic was introduced before any catheterization or instrumentation and most of the endoscopic procedures were done with the aid of the image intensifier. The papilla was demonstrated as a filling defect by passing a Dormia basket alongside the ureteric catheter and injecting contrast medium. The Dormia stone basket was passed no higher than the pelvic ureter, although in every case the necrotic renal papilla was never more than 10 cm. from the ureteric orifice. The tissue that was retrieved was sent for histological examination and proved in every case to be a renal papilla. The ureteric catheter was maintained in position by strapping it to a Foley balloon catheter which drains the bladder. Each catheter was connected to a closed drainage system. As the urine is frequently infected antibiotics were given and continued in reduced dosage for a long period.

Once the patient had recovered from the acute obstruction as shown by absence of fever, loin tenderness, and an improvement in renal function the draining catheters were removed. Prevention of further episodes was attempted by stopping analgesics, insisting upon a high fluid intake, and giving long-term antibiotic therapy—a régime similar to that used in the treatment of chronic pyelonephritis. Subsequently 2 men required resection of the prostate gland.

CASE REPORT

Case 2.—A woman aged 43 years had had a right nephrectomy for pyonephrosis in 1959. She had remained well until 2 weeks before her present admission when she had had left ureteric colic. A pyelogram demonstrated a dilated

Table I.—SUMMARY OF 5 CASES WITH ACUTE RENAL PAPILLARY NECROSIS WHO PRESENTED WITH ACUTE OBSTRUCTION

CASE No.	AGE AND SEX		PREDISPOSING CONDITION	DURATION OF ANALGESIC INGESTION (yr)	BLOOD-UREA AT ADMISSION (mg. per cent)	OPERATION	CLINICAL COURSE
1	68	M	Osteoarthritis	5	280	Dormia extractions (2 operations)	Improved
2	43	F.	Addiction	6	103	Dormia extractions (3 operations)	Defaulted
3	48	M.	Rheumatoid arthritis	16	160	Retrograde ureteric catheter	Improved
4	55	M.	Addiction	20	200	Retrograde ureteric catheter; transurethral resection 1 year later	Improved
5	60	M.	Addiction	7	140	Dormia extraction; transurethral resection 1 year 4 months later	Improved

left kidney and ureter down to the level of the intramural ureter. She was tender over the solitary kidney and became anuric. She was immediately transferred from the local hospital to the Regional Urological Centre, Liverpool.

On admission her blood-urea was 103 mg. per cent and serum potassium 5·3 mEq. She did not respond to diuretics, and cystoscopy was performed within 24 hours of admission. The bladder was normal apart from a bulge over the left intramural ureter and some blood-clot protruded from the left ureteric orifice. A No. 5 catheter was passed easily to the renal pelvis. A Dormia stone basket was manipulated alongside the catheter and a 2-cm. piece of tissue was removed from the intramural ureter. This was later proved to be a renal papilla. The ureteric catheter was left in situ and strapped to a urethral Foley catheter to hold it in position. Both catheters were connected to sterile closed-drainage systems. During the next 24 hours the patient passed 8 litres of urine and her temperature which had previously been 38° C. fell to normal. As her general condition improved with a fall in the blood-urea to normal the catheters were removed on the second postoperative day. That evening she wished to be discharged but was persuaded to stay in hospital. Thirty hours later she became anuric, had left loin pain, and a fever (39° C.). A blood culture grew *Bacillus proteus*. She was treated with intramuscular gentamicin and frusemide. The blood-urea rose and she did not respond to the diuretic. At cystoscopy a No. 5 ureteric catheter was passed to the renal pelvis, a slight obstruction being noted 6 cm. from the left ureteric orifice. There was an immediate copious flow of urine. Two passages of the Dormia stone basket in the lower ureter failed to produce tissue. A urethral catheter was passed as before and the urinary tract was drained. Four days later the patient was afebrile with a normal blood-urea and the catheters were removed. Five days after the second cystoscopy she became anuric for the third time and again at cystoscopy Dormia extraction of a sloughed renal papilla was performed. At operation retrograde pyelography using an image intensifier showed no further upper urinary-tract obstruction. A week later the catheters were removed. The patient repeatedly wished to be discharged and she finally signed herself out the day that the catheters were removed. Her demeanour was odd even allowing for the original toxicity and she denied habitual self-medication with analgesics. Long-term antibiotics with a high fluid intake were recommended but the patient has persistently defaulted from review.

RESULTS

Every endoscopic operation for acute obstructive renal papillary necrosis was rewarded by an immediate and profuse diuresis. Simple retrograde ureteric catheterization was sufficient on two occasions. A whistle-tip catheter is preferred. Manipulation of a Dormia ureteric stone basket was used to retrieve an impacted renal papilla six times. If a ureteric renal papilla was shown radiologically it could always be removed as it impacted in the lower ureter. Large papillae offer little resistance to the passage of a Dormia ureteric catheter compared with ureteric calculi of a similar size, and their size should not discourage attempted extraction.

We stress that combined medical and surgical management is essential. The obstruction having been relieved and the fluid and electrolyte disturbances corrected, the patient must stop all analgesics and maintain a high urinary output, and long-term antibiotics must be given to prevent urinary infection. Because outflow obstruction hinders renal recovery this must be dealt with, as illustrated by *Cases* 4 and 5. Both cases had proved analgesic nephropathy, one having passed a necrotic renal papilla 2 years previously. Having stopped analgesics the renal function of these patients slowly improved. Subsequent pyelography showed residual urine in the bladder after micturition with some thickening of the bladder wall. The urine was found to contain white cells on microscopy and repeated culture failed to reveal a significant bacteriuria. Each of these patients had minimal prostatic symptoms, but the serum creatinine which was raised above 3 mg. per cent only fell to normal after resection of the small obstructing prostate glands.

Although 1 patient has persistently defaulted from review (*Case* 2) all the other cases have improved as shown by an absence of symptoms, freedom from pyuria and infection, and a fall in the serum-creatinine levels to normal. The period of review has been for a minimum of 6 months.

DISCUSSION

Analgesic damage to the kidney results from papillary necrosis following interruption of the blood-supply in the vasa recta (Kincaid-Smith, 1968). Some patients take analgesics for the relief of chronic pain (e.g., in arthritis as *Cases* 1 and 3), but the majority take them for ill-defined reasons such as general fatigue or chronic headache (Prescott, 1966). In one series an addiction to phenacetin was noted and two-thirds of the patients had psychiatric abnormalities (Dawborn, Fairley, Kincaid-Smith, and Kings, 1966). In the present series the majority of the patients are 'odd' and habitually take analgesics. Retrospective study of the records in all our cases confirms the finding of a sterile pyuria antedating the acute symptoms by many years. Direct questioning about analgesic intake is helpful as a screening test. Where the patient denies self-medication with analgesics the relatives may confirm that tablets have been regularly taken for years (*Case* 2). Whilst few of our patients were as advanced as those in the series of Bell, Kerr, Swinney, and Yeates (1969), in which 3 out of 14 patients died of acute pyelonephritis, there was improvement after the withdrawal of analgesics. The combination of obstruction with infection can be lethal and major surgery carries some risk. Emergency nephrectomy has been recommended for acute papillary necrosis (Harrow, 1967) and this had been performed in 3 cases subsequently referred to the Regional Centre. One of the patients needed nephrectomy for pyonephrosis with suspected carcinoma of the renal pelvis, which may occur in conjunction with analgesic nephropathy. Another patient had carcinoma of the lower ureter. Patients with analgesic nephropathy do not withstand surgery well (Koutsaimanis and de Wardener, 1970) and endoscopic surgery is safer. Retrograde ureteric catheterization has been used to by-pass the obstruction (Rutner and Smith, 1961; Bonnin, 1964; Hellebusch, 1969), and recently this has been used with the addition of proteolytic enzyme instillation into the ureter (Jones and Morrow, 1971). We have found the renal papillae impact in the lower ureter and removal using the Dormia stone basket is safe and successful. If subsequent improvement is slow and residual urine is present, endoscopic treatment of the bladder-neck obstruction will produce a further improvement. Sloughing of a renal papilla may still occur after analgesics have been discontinued for many months.

Prompt endoscopic surgery in patients with acute papillary necrosis is recommended. This conservative approach removes the obstructing tissue and ensures prompt drainage of the affected kidney. Unlike immediate nephrectomy it can be applied in patients with a solitary kidney. Retrieval of the tissue with the Dormia stone basket enables histological confirmation and preserves renal tissue in a potentially bilateral disease.

Acknowledgements.—We thank our colleagues in the Liverpool region who have promptly referred the cases, and Mr. N. O. K. Gibbon, Dr. Goldsmith, and Dr. Finn for permitting us to include some of their cases from the Regional Urological Centre in this series.

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DIAPHRAGMATIC RUPTURE DUE TO BLUNT TRAUMA

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SUMMARY

With the increasing number of abdominal, pelvic, and thoracic injuries due to trauma as a result of road-traffic accidents rupture of the diaphragm is becoming more frequent. Two personal cases are presented and the literature as regards symptomatology, mechanism of rupture, site of rupture, and treatment is reviewed. Early operative treatment is recommended.

RUPTURE of the diaphragm is a serious condition because although the lesion itself may not threaten life the function of the heart and lungs may be seriously impaired owing to herniation of intraperitoneal viscera into the chest. Furthermore, it may cause gastro-intestinal symptoms and signs unless treated. Indeed, the herniated viscera may strangulate and produce an emergency situation.

This paper reports 2 cases which were personally seen and treated by the author and reviews the literature on the various aspects of the subject.

CASE REPORTS

Case 1.—A 22-year-old man was admitted to the General Hospital, Johore Bahru, Malaysia, in August, 1967, having been knocked down by a motor-car. On examination the patient was in a state of shock but was conscious. There was a haematoma on the left and right subcostal margins in the midaxillary line. The abdomen was tender and rigid in the left upper quadrant. Radiological investigation revealed no abnormality in the chest. A diagnosis of rupture of the spleen was made and he was immediately subjected to laparotomy. The spleen and other intraperitoneal organs were found to be normal. There was no blood in the peritoneal cavity.

On the second postoperative day the patient began to develop dyspnoea. Radiological examination of the chest showed the presence of air in the lower part of the left hemithorax. A diagnosis of pneumothorax was made. The chest was drained by needle suction and this produced 50 ml. of brownish fluid. However, the dyspnoea became worse and further radiological examination of the chest 4 days later showed that the amount of air had greatly

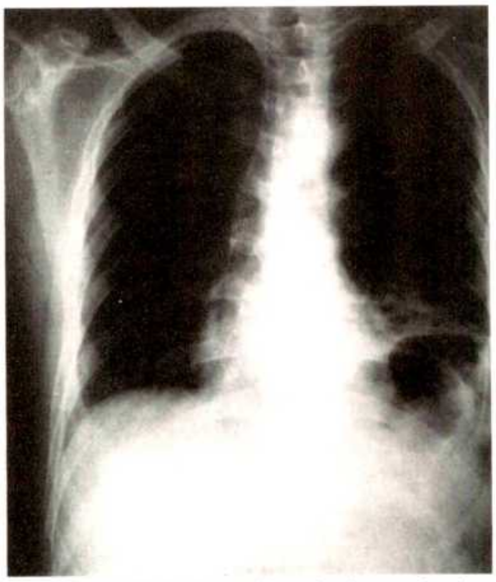

FIG. 1.—*Case* 2. Plain chest radiograph taken on the day of admission. Gas is present in the lower part of left hemithorax.

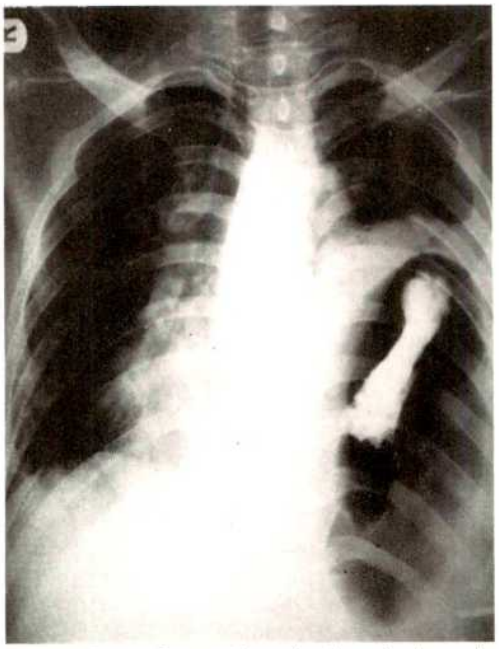

FIG. 3.—*Case* 2. Gastrografin-meal radiograph taken 3 days after admission, showing the presence of dye in an intrathoracic stomach.

increased. At this stage diaphragmatic rupture with herniation of the stomach was suspected. A Gastrografin-meal radiological examination on the same day confirmed this finding. The patient was immediately subjected to an operation. A thoracotomy incision was made through the left ninth intercostal space. The upper half of the stomach was found to have herniated through a 5-cm. anteroposterior tear in the dome of the left hemidiaphragm. The fundus of the stomach was gangrenous. This portion was excised and the defect in the stomach was repaired in two

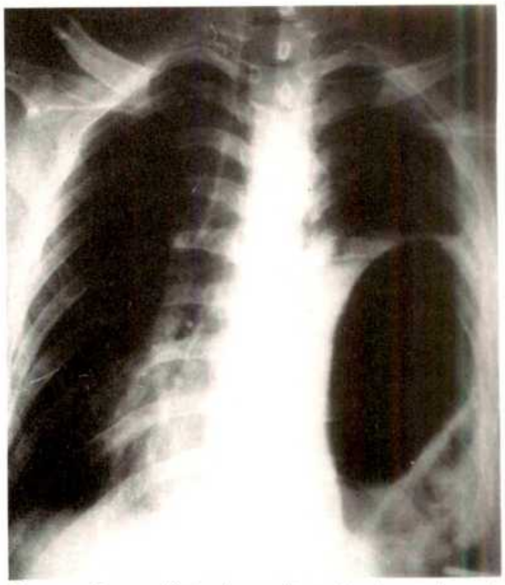

FIG. 2.—*Case* 2. Plain chest radiograph taken 3 days after admission. The amount of gas in the left hemithorax is much increased and is obviously in the stomach.

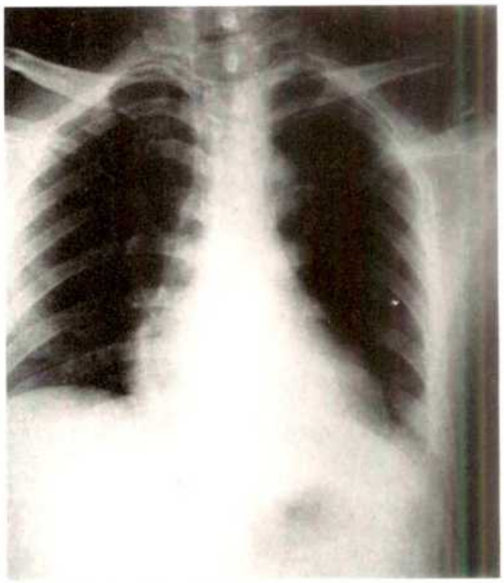

FIG. 4.—*Case* 2. Plain chest radiograph the day after operation, showing a return to normal.

layers using catgut. The stomach was reduced into the peritoneal cavity and the tear in the diaphragm was repaired in two layers with interrupted silk and continuous catgut. An underwater-seal drain was inserted into the left chest. The patient subsequently made an uneventful recovery.

Case 2.—A 27-year-old man was admitted to the General Hospital, Kuala Lumpur, Malaysia, in March, 1972, after a road-traffic accident. On examination his condition was good. He was not in shock and the abdomen was soft. He had multiple abrasions all over the body including one over the left subcostal margin anteriorly. Radiological examination of the chest revealed the presence of air in the lower zone of the left chest (*Fig.* 1) and drainage of this yielded some blood-stained fluid. Two days later his respiration became laboured and this was made worse by lying down. A diagnosis of a ruptured left diaphragm with herniation of the intraperitoneal contents was made. This was confirmed by a further radiological examination of the chest and a Gastrografin-meal radiograph (*Figs.* 2, 3). A laparotomy through a left upper paramedian incision was performed on the same day. There was a 7·5-cm. tear running anteroposteriorly in the dome of the left hemidiaphragm and through this the upper half of the stomach and the spleen had herniated. These organs were brought down into the peritoneal cavity. The splenic hilum was found to be slightly lacerated and there was some oozing of blood. Splenectomy was carried out. The tear in the diaphragm was repaired in two layers using interrupted silk and continuous catgut. An underwater-seal drain was inserted into the left chest cavity. A repeat radiological examination of the chest on the following day showed a normal picture (*Fig.* 4). The patient subsequently made a good postoperative recovery.

DISCUSSION

Bowditch (1853) reviewed 68 cases of diaphragmatic hernia which had all been diagnosed at autopsy. He recognized the following signs:—

1. Absence of respiratory sounds in the affected hemithorax.
2. A change in the position of the heart, with its displacement to the right or left of the midline depending on whether the rupture is in the left or right hemidiaphragm respectively.
3. Abnormal gurgling sounds in the affected hemithorax.
4. A tympanitic note on percussion of the lower part of the affected hemithorax.
5. Prominence and reduced movement of the affected hemithorax.

In 1886 Riolfi (quoted by Hedblom, 1925) successfully operated on a diaphragmatic stab wound. Walker in 1899 successfully repaired a torn left diaphragm caused by a tree falling on a patient (Walker, 1900).

The diagnosis of diaphragmatic rupture may be made fairly easily soon after the injury from the history, examination, and usual radiological investigations of the chest. This is shown in *Case* 2, where the diagnosis was made within 72 hours of the injury. The Gastrografin-meal radiograph was used merely to confirm a confident diagnosis. Contrast radiological studies are needed in difficult cases, such as the present *Case* 1, where there is a long delay in diagnosis. In right hemidiaphragmatic rupture diagnosis is often difficult as the herniated liver may easily be mistaken for an elevated intact right hemidiaphragm. Air may be introduced into the peritoneal cavity and if this leads to a right pneumothorax, then the right hemidiaphragm is ruptured (Lavender and Potts, 1959; Noon, Beall, and DeBakey, 1966).

The mechanism of disruption of the diaphragm due to blunt trauma is unknown. Magee (1935) postulated that the diaphragm was a membrane stretched tightly over a hoop. If the hoop is distorted by pressure, the membrane tears. Desforges, Strieder, Lynch, and Madoff (1957) thought that the diaphragm ruptured as a result of the force transmitted to it through the abdominal viscera. Probert and Havard (1961) considered that diaphragmatic rupture was due to respiratory effort acting on a diaphragm fixed by a crushing force. Ebert, Gaertner, and Zuidema (1967) suggested that diaphragmatic rupture occurred after thoracic rather than after abdominal trauma. In fact, when the chest has suffered severe blunt trauma there may be associated diaphragmatic rupture (Bassett, Gibson, and Wilson, 1968). In any patient with an abdominal or pelvic injury it should be considered that the diaphragm may rupture (Evans and Simpson, 1950; Levine and Crampton, 1963; Peltier, 1965). This is illustrated in *Case* 1 where no attempt was made at the original operation to inspect the diaphragm.

Herniation of the peritoneal contents into the chest does not always occur when the diaphragm is ruptured (Wren, Texada, and Krementz, 1962). This is shown in *Case* 1 where a diaphragmatic rupture was not diagnosed at the first operation although it was present at the time. Abdominal viscera tend to herniate into the thorax through a rupture in the diaphragm as there is normally a pressure differential between the peritoneal and thoracic cavities, the abdominal pressure being higher. There is disagreement about the level of intra-abdominal pressure (Keddie and Neill, 1967). Marchand (1957) stated that the difference in pressures ranged from 7 to 20 cm. of water during quiet respiration. This may increase to 100 cm. of water with deep breathing. Any increase of intra-abdominal pressure, such as in ileus, vomiting, or pregnancy, causes herniation when the diaphragm is ruptured. Bernhardt and Lawton (1966) reported delayed herniation associated with increased intra-abdominal pressure in pregnancy. Herniation may occur while the patient is straining under anaesthesia (Hamdi and Sturdy, 1955).

The common sites of rupture in the left hemidiaphragm are the dome and posterior half of the left leaf (Harrington, 1950), the posterocentral part extending towards the pericardial attachment (Ebert and others, 1967), and the anterolateral or pericardial part (Sutton, Carlisle, and Stephenson, 1967; Pomerantz, Rodgers, and Sabiston, 1968). Childress and Grimes (1961) believed that there was no particular site of localization. The pericardium protects the diaphragm immediately beneath it. Rupture of the diaphragm in this area is rare and may result in cardiac compression due to herniation of intraperitoneal viscera into the pericardial space (Moore, 1959). Owing to the protective effect of the liver, rupture of the right hemidiaphragm is rare compared with the left side. Hughes, Kay, Meade, Hudson, and Johnson (1948) recorded 5 ruptures on the right side and 23 on the left. Hedblom (1925) stated that 95 per cent of diaphragmatic ruptures were left-sided. Diagnosis of a right hemidiaphragmatic tear is usually made late (Epstein and Lempke, 1968).

TREATMENT

The tear in the diaphragm should be repaired as soon as possible, the ideal time being when the diaphragm is found to be ruptured at laparotomy for a suspected intraperitoneal injury. For a diaphragmatic tear which is diagnosed preoperatively the urgency of the operation is dictated by the general condition of the patient. In the presence of cardiorespiratory embarrassment with such effects as cyanosis, respiratory distress, and shock the enlarging hernia should immediately be repaired. Another reason why early surgery is advisable is the ever present possibility of early strangulation of the herniated peritoneal contents, as occurred in *Case* 1. Grage, Maclean, and Campbell (1959) recorded the death of a patient within 3 days of injury as a result of gangrene of a stomach strangulated by a traumatic diaphragmatic hernia. Hedblom (1925) described 126 patients with diaphragmatic hernia and reported that the death-rate doubled after the patient developed intestinal obstruction due to the hernia. D'Arcy Sutherland (1958), in describing 10 cases of ruptured diaphragm, reported 3 deaths which were all due to delay in diagnosis or failing to undertake immediate surgical treatment. It can thus be seen that it is better to repair the hernia as soon as possible after the injury.

An operative approach through an abdominal incision is the most suitable as it is possible to inspect the intraperitoneal organs at the same time. However, the thoracic approach is better for rupture of the right hemidiaphragm as access to the right hemidiaphragm would be hindered by the liver if the abdominal approach were used. In a long-standing chronic traumatic diaphragmatic hernia a thoracic approach would also be better as it is then easier to free the dense intrathoracic adhesions which are present and reduce the hernia into the peritoneal cavity. Either incision may be extended for increased exposure so that an abdominal incision becomes abdominothoracic and a thoracic incision becomes thoraco-abdominal.

The actual tear in the diaphragm is best repaired in two layers, using interrupted silk reinforced by continuous catgut. Each silk suture should pass through the pleura, diaphragm, and peritoneum bounding the tear in the diaphragm (Allison, 1962). To repair a very large tear or an old-standing tear it may be necessary to use a supporting piece of pericardium or synthetic material (Waldhausen, Kilman, Helman, and Battersby, 1966). At the end of the operation the pleural cavity on the affected side should be drained and the drain connected to an underwater seal.

Acknowledgements.—My thanks are due to the Director-General, Ministry of Health, Malaysia, Dato (Dr.) Abdul Majid Ismail, for permission to publish this article, and to Dato (Dr.) Omar Din, Senior Consultant Radiologist, General Hospital, Kuala Lumpur, for the radiological reports in *Case* 2. I am indebted to Professor M. Balasegaram, Senior Consultant Surgeon, General Hospital, Kuala Lumpur, for advice in preparing this paper. The help of the medical officers, house doctors, and nursing staff in managing the 2 cases is gratefully acknowledged.

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THE REDUCTION OF SURGICAL WOUND INFECTIONS BY PROPHYLACTIC PARENTERAL CEPHALORIDINE

A CONTROLLED CLINICAL TRIAL

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SUMMARY

In a series of 762 general surgical wounds 376 were selected at random to receive three parenteral doses of cephaloridine and 386 remained as untreated controls. In all types of operation, with the exception of wounds in the lower extremities associated with arterial surgery, the rate of wound infection was lowered by the prophylactic use of cephaloridine. The results were statistically significant for total wounds, clean wounds, total contaminated wounds, and contaminated wounds other than in colorectal surgery. We therefore recommend the routine use of three doses of cephaloridine.

DESPITE the high standard of sterility of surgical instruments, dressings, and ligatures, improved operating-theatre design, and strict aseptic technique, many patients whose wounds are expected to heal by first intention suffer the discomfort, inconvenience, and, sometimes, actual danger of a wound infection.

The incidence of wound infection in the Scarborough Hospital (Jackson, Pollock, and Tindal, 1971a, b; Pollock and Tindal, 1972) is comparable with that in most other hospitals. In the three trials reported the infection rates were 12·7, 12·7, and 13·5 per cent, whereas the Public Health Laboratory Service (1960) reported an incidence of clinical infection in 14 per cent of 2746 wounds in 21 hospitals. In these trials three different methods were tested to try to reduce the wound-infection rate. They were the use of a plastic adhesive drape, a prophylactic antibiotic spray, and a prophylactic, single, parenteral dose of ampicillin preoperatively. None of these was effective.

Davidson, Clark, and Smith (1971) have produced a valuable computer analysis of some of the factors responsible for wound infections in 1000 operations and found only 5 out of 14 which strongly influenced the infection rate. These were a potentially dirty operation, the presence of bacteria in the wound at the end of the operation, old age, a long operation, and the nursing of patients in large, multi-bed, open wards as opposed to wards consisting of single beds and small groups. The factors which were of less significance were glove punctures, the presence of *Staphylococcus pyogenes* in patients' noses, emergency operations, skin towelling, and differences in technique. They found no significance in wound drainage, the presence of pathogens on the patients' skin, or different methods of, or even poor, skin disinfection. Perhaps the most important factors are endogenous contamination of wounds (Altemeier, Culbertson, and Hummell, 1968) and large, open wards.

Davidson and others (1971) did not analyse certain other predisposing causes of wound infection including obesity (Welch, 1891), a long preoperative stay in hospital (Todd, 1968), and the site of operation. Clean operations on the head and neck, for instance, rarely become infected.

Unfortunately the principal causes of wound infection cannot, as yet, be controlled and we have therefore turned our attention to the prophylactic role of another antibiotic, cephaloridine. Various authors have reported conflicting results with prophylactic antibiotics. Fekety, Chiff, Sabiston, Seidl, Smith, and Thorburn (1969) reported a trial of penicillin and methicillin against controls in 213 cases of cardiac surgery, and found no reduction in the wound-infection rate with either antibiotic. Altemeier and others (1968) came to the conclusion that 'the incidence of wound infection following the use of preoperative or prophylactic antibiotics was greater than the infection rate of wounds in patients not treated with them'.

There has been one favourable, adequately controlled, prospective study of a prophylactic parenteral antibiotic. This was by Polk and Lopez-Mayor (1969), who studied 172 gastroduodenal and colorectal operations and found a spectacular reduction in the wound-infection rate with the intramuscular use of three 1-g. doses of cephaloridine, the first given immediately preoperatively and the second 5 hours and the third 12 hours later.

METHODS

In the present trial cephaloridine has been used in the same dosage as given by Polk and Lopez-Mayor (1969) in randomly selected cases, the remainder of the cases being given no antibiotic. The preoperative dose was, however, administered intravenously during induction of anaesthesia, the other two doses being given intramuscularly. The method of random selection has been, as before, by the toss of a coin, and the definition of a wound infection has remained the standard one adopted in previous surveys from this hospital, namely the presence of pus which either discharged or needed to be released from the wound (*see also* Ljungqvist, 1964; Stoker and Ellis, 1972). If the operation entailed two incisions these wounds were counted separately. The results refer to the number of wounds, which is greater than the number of patients.

The wounds have been divided into 'clean' and 'contaminated'. The degree of contamination is likely to be much less in a cholecystectomy, for example, than in a large-bowel operation. The contaminated operations, therefore, have been subdivided into those with a low expectation of infection (gastro-duodenal, intestinal, biliary, urological, and appendicectomy apart from perforated appendices) and those with a high expectation of infection (perforated appendices and colorectal surgery). We previously named these groups 'potentially contaminated' and 'contaminated' (Jackson and others, 1971a, b; Pollock and Tindal, 1972).

Table I.—WOUND-INFECTION RATE WITH AND WITHOUT CEPHALORIDINE

TYPE OF WOUND	CEPHALORIDINE			NO CEPHALORIDINE			χ^2	*P*
	No. of Wounds	No Infected	Per cent	No. of Wounds	No Infected	Per cent		
Clean								
Arterial surgery	27	6	22·2	46	7	15 2		N S
Other surgery	164	3	1 8	171	11	6·4	4·43	<0·05
Contaminated								
Colorectal	41	14	34 1	46	20	43 5	0·79	N S
Other surgery	144	11	7 6	123	19	15·4	4·05	<0 05
Total contaminated wounds	185	25	13·5	169	39	23 1	5·45	<0·02
Total all types of wound	376	34	9·1	386	57	14·7	5·25	<0·05

N.S. = not significant.

Table II.—CLEAN WOUNDS: TYPES OF OPERATION

TYPE OF OPERATION	CEPHALORIDINE		NO CEPHALORIDINE	
	No. of Wounds	No. Infected	No. of Wounds	No. Infected
Arterial (lower limb)	27	6	46	7
Non-arterial				
Head and neck	11	0	9	0
Breast and axilla	18	0	21	1
Hand	1	1	0	0
Laparotomy	29	1	29	1
Lumbar incisions	8	0	14	1
Scrotal incisions	6	0	4	0
Groin hernias	48	1	49	2
Varicose veins	20	0	25	1
Other groin incisions	14	0	12	4
Amputations	9	0	8	1
Total	164	3	171	11

Patients under the age of 16 years were excluded because we do not favour injections in children if they can be avoided. Thirty-two patients who died within 2 weeks of operation in whom the presence or absence of infection was uncertain have been excluded from the study, leaving 762 wounds for analysis out of a total of 794. All patients were seen by one of us for at least 4 weeks. When the infection developed in hospital the pus was cultured and the sensitivity to cephaloridine tested by the Multidisc method. Five late wound infections escaped bacteriological study and 7 pus swabs were sterile. No restriction was placed on the use of therapeutic antibiotics, but no other prophylactic antibiotic was allowed except for the usual oral preparations for colonic surgery.

To avoid bias the details were entered not in the patients' case notes but on punch cards which were kept separately and analysed manually.

RESULTS

Seven hundred and sixty-two wounds were studied, 91 of which became infected (11·9 per cent). There were 376 wounds in patients who were given cephaloridine and 386 in patients who were not. Thirty-four wounds in the former group became infected (9·1 per cent) and 57 in the latter (14·7 per cent). The difference is statistically significant ($\chi^2 = 5{\cdot}25$, $P < 0{\cdot}05$) (*Table I*).

Table III.—CONTAMINATED WOUNDS: TYPES OF OPERATION

TYPE OF OPERATION	CEPHALORIDINE		NO CEPHALORIDINE	
	No. of Wounds	No. Infected	No. of Wounds	No. Infected
Perforated appendices	7	4	11	5
Colorectal	34	10	35	15
Total	41	14	46	20
Stomach				
Vagotomy and pyloroplasty	9	1	9	2
Vagotomy and pyloroplasty, and appendicectomy	12	0	10	2
Gastrotomy	1	0	3	1
Gastrectomy	11	0	8	1
Gall-bladder and ducts				
Cholecystectomy	12	1	15	3
Cholecystectomy and appendicectomy	19	1	13	3
Intestinal resection	4	2	5	0
Appendix				
Acute	18	0	11	0
Normal	15	2	9	0
Cystotomy and prostatectomy	30	2	26	4
Renal pelvis and ureter	5	0	4	0
Hysterectomy	1	0	3	0
Excision of infected lesions	7	2	7	3
Total	144	11	123	19

Clean Wounds.—Clean wounds are not uniform in their infection rate. There were no infections after head and neck surgery, and only one in any wound above the abdomen (*Table II*). On the other hand, incisions for arterial reconstruction in the lower limbs were much more likely to become infected. Most of these infections were probably acquired in the ward postoperatively on the basis of discharging haematomas. Long operating times and the presence of drains in these wounds may also have contributed.

There were 73 clean wounds for arterial disease of the lower extremities; 27 in patients given cephaloridine and 46 in patients who were not. There were 6 infections in the first group (22·2 per cent) and 7 in the second (15·2 per cent). This was the only area in the entire series which showed poorer results using prophylactic cephaloridine and the difference is not significant.

There were 335 clean wounds apart from those for arterial disease in the lower limbs, with 14 infections (4·2 per cent); 164 in patients given cephaloridine and 171 in patients who were not. In the former there were 3 infections (1·8 per cent) and in the latter 11 infections (6·4 per cent). The difference is significant ($\chi^2 = 4{\cdot}43$, $P < 0{\cdot}05$).

Table IV.—THE INCIDENCE OF WOUND INFECTIONS IN OBESE AND NON-OBESE PATIENTS: CONTAMINATED OPERATIONS

	NO OF WOUNDS	NO OF INFECTIONS	PER CENT	χ^2	P
Obese	77	20	26·0	4·14	<0·05
Non-obese	277	44	15·8		

Contaminated Wounds.—There were 354 contaminated wounds with 64 infections (18·0 per cent) (*Tables I* and *III*). Of 185 wounds in patients protected by cephaloridine, there were 25 infections (13·5 per cent), whereas in 169 wounds not so protected there were 39 infections (23·1 per cent). The difference is significant ($\chi^2 = 5{\cdot}45$, $P < 0{\cdot}02$).

In the contaminated group with a low expectation of infection (30 infections in 267 wounds, 11·2 per cent) there were 144 wounds in patients given prophylactic cephaloridine and 123 in patients who were not. Of the former, 11 wounds became infected (7·6 per cent) and of the latter, 19 (15·4 per cent). The difference is significant ($\chi^2 = 4{\cdot}05$, $P < 0{\cdot}05$).

In the smaller group of colorectal surgery and perforated appendices (87 wounds with 34 infections, 39·1 per cent) 14 out of 41 wounds became infected in patients protected by cephaloridine (34·1 per cent) and 20 out of 46 wounds in patients not so protected (43·5 per cent). These figures are not significant ($\chi^2 = 0{\cdot}79$).

As in previous surveys, we have found that obese patients are more liable to wound infections than non-obese ones. This is shown in the contaminated group, in which 20 out of 77 wounds in obese patients became infected (26·0 per cent) compared with 44 out of 277 wounds in non-obese patients (15·8 per cent) ($\chi^2 = 4{\cdot}14$, $P < 0{\cdot}05$) (*Table IV*). Clean wounds have not been tabulated for obesity because the numbers were small.

As in other series (Davidson and others, 1971) we found that on the whole older patients were more liable to wound infections than younger ones, and this difference was statistically significant for all wounds except in the arterial group and for contaminated wounds other than those for colorectal operations. Nine contaminated wounds out of 145 (6·2 per cent) became infected in the under-60 age-group, compared with 21 wounds out of 122 (17·4 per cent) in patients over 60 ($\chi^2 = 8{\cdot}05$, $P < 0{\cdot}01$). The difference between the infection rate in young and old patients is not significant in clean wounds or in wounds associated with colorectal surgery (*Table V*).

Table V.—THE INCIDENCE OF WOUND INFECTIONS IN PATIENTS UNDER 60 YEARS ('YOUNG') AND OVER 60 YEARS ('OLD')

TYPE OF WOUND	TREATMENT	YOUNG			OLD			χ^2	P
		No. of Wounds	No. Infected	Per cent	No. of Wounds	No. Infected	Per cent		
Clean (non-arterial)	Cephaloridine	83	1	1·2	81	2	2·5	0·36	N.S.
	No cephaloridine	92	4	4·3	79	7	8·9	1·43	N.S.
	Total	175	5	2·8	160	9	5·6	1·59	N.S.
Contaminated (colorectal)	Cephaloridine	8	5	62·5	33	9	27·2	3·55	N.S.
	No cephaloridine	10	5	50·0	36	15	41·7	0·22	N.S.
	Total	18	10	55·5	69	24	34·8	2·58	N.S.
Contaminated (other)	Cephaloridine	79	2	2·5	65	9	13·8	6·46	<0·02
	No cephaloridine	66	7	10·6	57	12	21·1	2·55	N.S.
	Total	145	9	6·2	122	21	17·4	8·04	<0·01
All wounds (except arterial)	Cephaloridine	170	8	4·7	179	20	11·2	4·94	<0·05
	No cephaloridine	168	16	9·5	172	34	19·7	7·10	<0·01
	Total	338	24	7·1	351	54	15·4	11·77	<0·01

N.S. = not significant.

Table VI lists the organisms cultured from infected wounds. Five infected wounds were not submitted to bacteriological examination, pus swabs were sterile in 7 cases, and organisms were frequently multiple. The figures, therefore, do not tally with the number of infected wounds. The majority of the infections were due to staphylococci in clean wounds and to intestinal organisms in the contaminated group. Most of the organisms were sensitive to cephaloridine whether or not the patient had received it prophylactically.

DISCUSSION

Cephaloridine has been shown to exert a significantly favourable influence on the wound-infection rate. In total wounds, in clean wounds other than those for arterial diseases of the lower extremities, in total contaminated wounds, and in contaminated wounds other than those for colorectal surgery, the improvement with cephaloridine was statistically significant.

The results of the present trial are not as startling as those of Polk and Lopez-Mayor (1969), who studied both wound and intra-abdominal infections. In 32 patients with gastroduodenal operations given cephaloridine prophylactically they found no infections, whereas in 36 patients given a placebo 11 infections occurred. In 54 colorectal operations protected by cephaloridine there were 4 infections and in 50 without cephaloridine there were 15 infections.

Cephaloridine is a bactericidal antibiotic active against *Staphylococcus pyogenes* and other Gram-positive cocci (but only some strains of *Streptococcus faecalis*). The Gram-negative organisms which are sensitive to cephaloridine include *Proteus mirabilis* (but not other species of *Proteus*), *Escherichia coli*, and most strains of *Klebsiella pneumoniae*. It has no activity against *Pseudomonas aeruginosa*. In the present series wound infections were mainly due to staphylococci and intestinal organisms. The administration of cephaloridine did not result in any change in the type of organism or, curiously enough, in the emergence of cephaloridine-resistant organisms.

Table VI.—ORGANISMS ISOLATED FROM INFECTED WOUNDS

ORGANISMS	CEPHALORIDINE				NO CEPHALORIDINE			
	Clean Wounds		Contaminated Wounds		Clean Wounds		Contaminated Wounds	
	+	−	+	−	+	−	+	−
Staphylococcus pyogenes (coagulase positive)	5	1	3	0	13	0	12	0
Staphylococcus epidermidis (coagulase negative)	0	0	2	1	3	0	3	1
Intestinal organisms	1	3	15	4	3	2	32	12
Proteus sp.	0	2	4	0	1	0	10	1
Escherichia coli	1	1	8	0	0	1	13	4
Pseudomonas aeruginosa	0	0	0	2	0	1	0	4
Streptococcus faecalis	0	0	1	1	2	0	2	3
Klebsiella aerogenes	0	0	1	0	0	0	4	0
Clostridium welchii	0	0	1	0	0	0	0	0
Salmonella sp.	0	0	0	0	0	0	1	0
Enterobacter aerogenes	0	0	0	0	0	0	1	0
Acinetobacter anitratus	0	0	0	1	0	0	0	0
Micrococcus tetragenes	0	0	0	0	0	0	1	0
Total organisms	6	4	20	5	19	2	47	13

+, Organism sensitive to cephaloridine. −, Organism not sensitive to cephaloridine.

Against the achievement of this drug must be set the inconvenience to the patient of intramuscular injections in the immediate postoperative period, the slight increase in nurses' work, and the cost of the drug. However, assuming a daily cost for in-patient treatment in a non-teaching hospital of approximately £10 per day and keeping in mind the discomfort of any wound infection, the saving due to the use of cephaloridine more than outweighs these disadvantages.

There have been several favourable reports on the topical use of antibiotics in the prevention of wound infection. Local ampicillin reduced the wound-infection rate after grid-iron appendicectomy (Mountain and Seal, 1970) and after biliary and gastro-intestinal surgery (Stoker and Ellis, 1972). Longland, Gray, Lees, and Garrett (1971) reported benefit from the application of a solution of tetracycline to appendicectomy wounds, while Moylan and Brockenbrough (1968) reported improvement with 1 per cent kanamycin irrigation. On the other hand, Jackson and others (1971b) failed to show a significant reduction in the wound-infection rate by the use of a bacitracin–polymixin–neomycin spray.

We think it may be more acceptable to staff and patients to instil cephaloridine into the wound before closure rather than to use it parenterally. If its topical use can be shown to have equally satisfactory results we will be prepared to change to this method. This is at present under investigation.

Acknowledgements.—We gratefully acknowledge the assistance of Dr. R. D. Foord of Glaxo Laboratories Ltd., who also supplied the cephaloridine (Ceporin).

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THE EFFECT OF INSULIN HYPOGLYCAEMIA ON SERUM GASTRIN AND GASTRIC ACID IN NORMAL SUBJECTS AND PATIENTS WITH DUODENAL ULCER

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SUMMARY

Serum gastrin was measured by radio-immunoassay in normal subjects and in patients with duodenal ulcer during insulin hypoglycaemia with and without concomitant aspiration of gastric acid. Insulin hypoglycaemia alone caused a rise in serum gastrin from 8·0 to 45·0 pg. per ml. in patients with duodenal ulcer, which was significantly greater than the rise from 13·0 to 29·0 pg. per ml. in normal subjects. During gastric aspiration serum-gastrin levels remained elevated for longer periods. The maximum increase of serum gastrin after insulin during gastric aspiration provided an almost complete discrimination between patients with duodenal ulcer and normal subjects. This discrimination between the groups was complete when serum gastrin was measured during insulin hypoglycaemia combined with intragastric neutralization of acid. The timing of the peak serum gastrin and the lowest blood-glucose coincided, but the peak acid output occurred 15–30 minutes later. Serum gastrin was inversely correlated with blood-glucose. Blood-glucose decreased to significantly lower levels in unaspirated than in aspirated subjects.

These studies suggest that patients with duodenal ulcer produce more gastrin than normal subjects in response to insulin hypoglycaemia (and, by inference, to vagal stimulation). The results support the concept of an increased functional G-cell mass in duodenal ulcer patients, and indicate the physiological roles of vagally released gastrin and of the acid inhibitory mechanism. Discriminant functions observed in the study could form the basis of tests for the presence of the duodenal ulcer diathesis.

GASTRIN release in response to both food stimulation and insulin hypoglycaemia has been extensively studied in normal subjects (Korman, Soveny, and Hansky, 1971a, b) and in patients with duodenal ulcer (Hansky, Korman, Cowley, and Baron, 1971; Korman, Soveny, and Hansky, 1971c). It has been shown that concomitant acid secretion modifies the gastrin response to insulin hypoglycaemia (Hansky and others, 1971). However, the relationship between the stimulatory effects on acid secretion of direct vagal impulses, on the one hand, and of gastrin, on the other, is unknown.

In an attempt to resolve this question and to study further the effect of acid inhibition on gastrin release, the serum-gastrin response to insulin hypoglycaemia has been investigated, with and without simultaneous aspiration of gastric juice, both in normal subjects and in patients with duodenal ulcer.

MATERIALS AND METHODS

Seventeen patients, comprising 15 men and 2 women of mean age 39 years, with radiologically proven duodenal ulcer were studied. These were compared with 11 normal subjects: 10 men and 1 woman of mean age 34 years. All the investigations were performed after an overnight fast. Venous blood was collected for gastrin and glucose estimation 30 minutes before and at 15-minute intervals for 2 hours after the rapid intravenous injection of soluble insulin (Insulin B.P., Boots), 0·2 U. per kg. body-weight.

1. Insulin Hypoglycaemia with No Gastric Aspiration.—Eight patients with duodenal ulcer and 8 normal subjects were studied.

2. Insulin Hypoglycaemia with Gastric Aspiration.—Thirteen patients with duodenal ulcer and 7 normal subjects were investigated. Two of the patients with duodenal ulcer and 4 normal subjects had previously been studied without gastric aspiration.

Gastric juice was aspirated continuously via a nasogastric tube which had been positioned fluoroscopically so that the tip lay in the gastric antrum. Collections were made in 15-minute fractions for 1 hour in the basal state and for 2 hours after insulin. An intramuscular injection of pentagastrin, 6 μg. per kg., was then given and four further 15-minute collections of gastric juice were obtained. The volume of gastric aspirate was measured and the acidity determined by electrometric titration with 0·1 *N* sodium hydroxide to *p*H 7·0. Acid output (mEq. per 15 minutes) was obtained by the product of volume and acidity.

Blood-glucose was estimated using a glucose oxidase AutoAnalyzer method (Wincey and Marks, 1961). The serum was separated by centrifugation and the gastrin was estimated in duplicate by radioimmunoassay (Hansky and Cain, 1969; Hansky and others, 1971). The sensitivity of this assay is 5 pg. per ml. and it should be noted that the levels obtained in our laboratory are lower than in previous reported studies.

Conventional statistical methods were employed. The significance of the difference of means and of mean differences was calculated from unpaired and paired *t* tests. Linear regression lines were calculated from the correlation coefficient, *r*. The significances of differences between regression lines were derived from the standard deviations of the slopes (difference of slopes) and the standard deviations of the intercepts (separation of slopes).

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RESULTS

Gastrin Response to Insulin Hypoglycaemia with No Gastric Aspiration.—*Fig.* 1 shows the serum-gastrin response to insulin in 8 patients with duodenal ulcer and in 8 normal subjects. The mean basal gastrin level was insignificantly lower in the patients with duodenal ulcer ($P = 0{\cdot}2$). After insulin the serum-gastrin level of the patients with duodenal ulcer increased significantly, from a mean basal level of 8·5 pg. per ml. to a peak of 45·1 pg. per ml. 45 minutes after the injection ($P = 0{\cdot}00006$). In normal subjects there was a smaller, significant increase in serum gastrin from 13·4 to 29·2 pg. per ml. 45 minutes after the injection of insulin ($P = 0{\cdot}00003$). The mean increase of serum gastrin was significantly greater in patients with duodenal ulcer than in normal subjects ($P = 0{\cdot}003$).

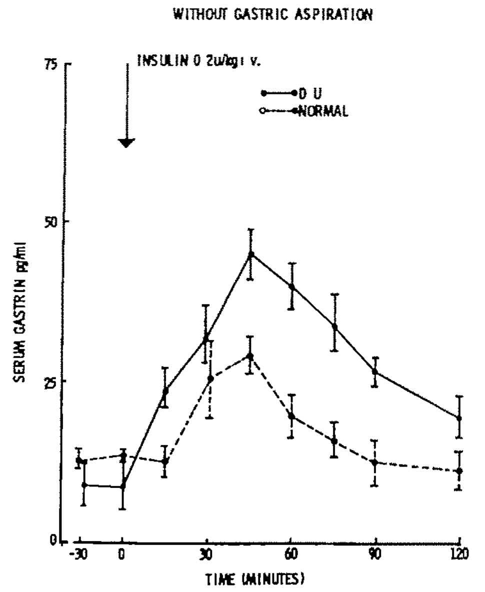

FIG. 1.—Serum-gastrin responses to intravenous insulin, 0·2 U. per kg., in 8 patients with duodenal ulcer and in 8 normal subjects studied without gastric aspiration.

As the peak rise in gastrin level occurred at varying times after the injection of insulin in each subject the peak gastrin level has been compared with the corresponding basal gastrin for each individual (*Fig.* 2). Although the mean peak gastrin level after insulin was still significantly higher in patients with duodenal ulcer than in normal subjects ($P = 0{\cdot}03$), there was no discrimination between the two groups, as every value of the ulcer group falls within the range found in the normal subjects. A clearer separation of the two groups can be obtained by plotting the absolute rise in serum gastrin of individual subjects (*Fig.* 3), and when treated in this way the values in the majority of patients with duodenal ulcer are above those in the normal group.

Gastrin Response to Insulin Hypoglycaemia with Concomitant Gastric Aspiration.—*Fig.* 4 shows the mean serum-gastrin response to insulin with concomitant gastric aspiration in 13 patients with duodenal ulcer and in 7 normal subjects. The mean basal gastrin levels were almost identical in the two groups ($P = 0{\cdot}8$). The mean basal gastrin level in duodenal ulcer patients was lower with gastric

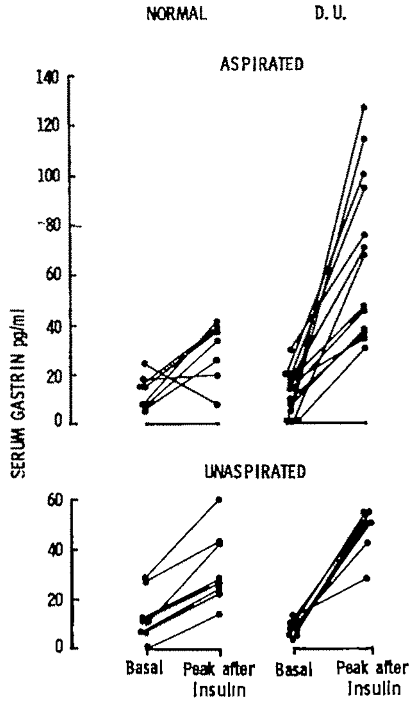

FIG. 2.—Basal serum-gastrin and peak serum-gastrin levels after intravenous insulin, 0·2 U. per kg., in patients with duodenal ulcer and in normal subjects, with and without gastric aspiration.

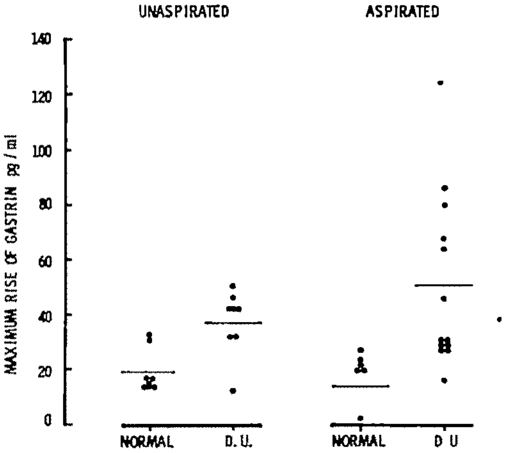

FIG. 3.—Maximum rise in the serum-gastrin level after intravenous insulin, 0·2 U. per kg., in patients with duodenal ulcer and in normal subjects, with and without gastric aspiration.

aspiration than without but the difference was not significant (*Fig.* 1). After insulin the serum-gastrin level of the patients with duodenal ulcer increased significantly from a basal level of 12·5 pg. per ml. to a peak of 51·4 pg. per ml. 75 minutes after the injection ($P = 0·003$). In normal subjects there was a smaller increase in the mean serum gastrin from 13·7 to 24·4 pg. per ml. 60 minutes after the injection of insulin but this increase was not significant ($P = 0·16$). The failure to elicit a significant rise in the normal group is due to the variation in the timing of the peak gastrin level between individuals.

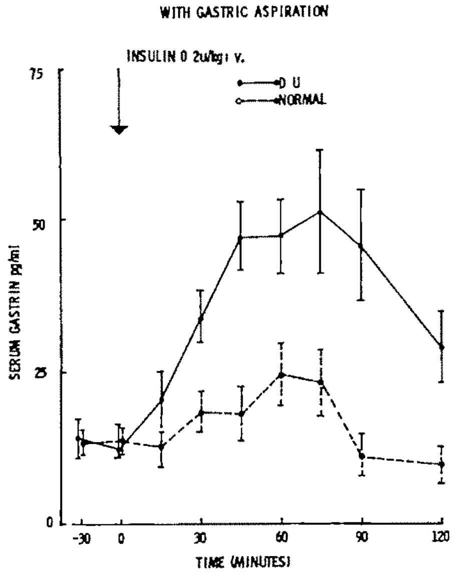

FIG. 4.—Serum-gastrin responses to intravenous insulin, 0·2 U per kg., in 13 patients with duodenal ulcer and in 7 normal subjects studied with concomitant gastric aspiration.

Table I.—COMPARISON OF BASAL SERUM-GASTRIN LEVELS OF PATIENTS WITH DUODENAL ULCER AND NORMAL SUBJECTS, SHOWING THE EFFECT OF CONCOMITANT GASTRIC ASPIRATION

GROUP	BASAL SERUM GASTRIN (pg per ml)		*P*
	Duodenal Ulcer Patients	Normal Subjects	
Aspirated	12·5±2·60	13·7±2·48	0·76
Not aspirated	8·5±0·82	13·4±3·56	0·20
P	0·26	0·89	

Fig. 2 shows the basal and peak gastrin levels of the individual subjects, and the mean peak gastrin level is significantly higher than the basal level in the normal subjects ($P = 0·045$). It can also be seen that the majority of the ulcer patients had peak levels above the range found in the normal group.

Comparing the aspirated and unaspirated series (*Fig.* 2), there was no significant difference between the mean peak levels of the normal subjects with aspiration and those with no aspiration ($P = 0·1$). However, half the patients with duodenal ulcer in the aspirated group attained serum-gastrin levels which were considerably higher than the highest level in the unaspirated group.

Fig. 3 shows that the mean absolute rise in serum gastrin was significantly greater in the patients with duodenal ulcer than in the normal subjects ($P = 0·01$) and 12 of the 13 ulcer patients had values above those achieved in the normal group.

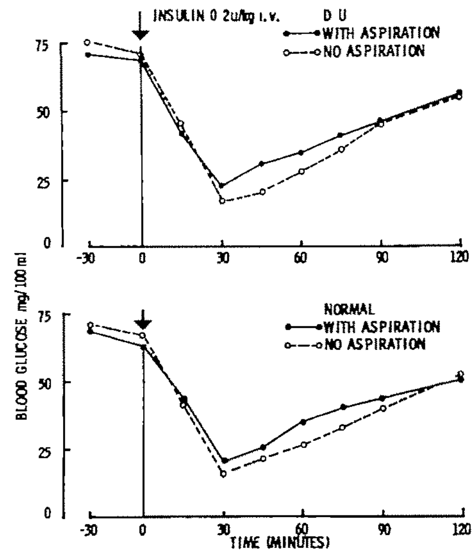

FIG. 5.—Mean changes in the blood-glucose after intravenous insulin, 0·2 U. per kg, in patients with duodenal ulcer and in normal subjects, with and without gastric aspiration.

Table II.—COMPARISON OF ACID OUTPUTS OF PATIENTS WITH DUODENAL ULCER AND NORMAL SUBJECTS

ACID OUTPUT	HCl (mEq. per hr.)		*P*
	Duodenal Ulcer Patients	Normal Subjects	
Basal acid output	4·06±0·76	1·62±0·33	0·037
Peak acid output to insulin	27·68±3·50	20·43±4·36	0·22
Peak acid output to pentagastrin	36·30±3·15	33·70±6·37	0·68

Comparing *Figs.* 1 and 4, it can be seen that the serum-gastrin response in the duodenal ulcer patients persisted for a longer time in the aspirated group than in the unaspirated group and 2 hours after the injection of insulin it remained significantly higher than basal levels ($P = 0·01$).

Blood-glucose Response to Insulin Hypoglycaemia.—*Fig.* 5 shows the mean blood-glucose levels after the injection of insulin in normal subjects and in patients with duodenal ulcer, both with and without concomitant gastric aspiration. The blood-glucose decreased to a nadir 30 minutes after the injection and then recovered progressively towards basal levels. Gastric aspiration appeared to influence the degree of hypoglycaemia after insulin. Thirty and 45 minutes after intravenous insulin the blood-glucose decreased to lower levels in subjects who had no gastric aspiration than in those with aspiration. These differences were significant in patients with duodenal ulcer ($P = 0{\cdot}01$) but not in normal subjects ($P = 0{\cdot}1$). However, when both these groups were combined the differences at 30 and 45 minutes were highly significant ($P = 0{\cdot}003$).

Gastric Acid Secretion by the Two Groups.—In *Table II* the gastric acid secretion of the patients with duodenal ulcer has been compared with that of normal subjects. The mean basal acid output of the patients with duodenal ulcer was significantly greater than that of the normal subjects. On the other hand, in this small series there was no significant difference between the mean peak acid outputs (in response to insulin or to pentagastrin) of the two groups.

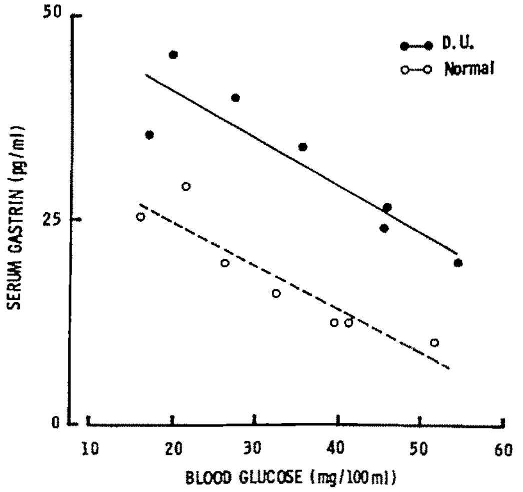

FIG. 6.—Relationship between blood-glucose and serum-gastrin levels at the end of each 15-minute period after intravenous insulin. Mean values of 8 patients with duodenal ulcer and of 8 normal subjects without gastric aspiration. For duodenal ulcer patients $y = -0{\cdot}568x + 52{\cdot}1$; $r = -0{\cdot}90$, $P = 0{\cdot}003$. For normal subjects $y = -0{\cdot}526x + 35{\cdot}1$; $r = -0{\cdot}92$; $P = 0{\cdot}001$. Difference between the slopes, $P = 0{\cdot}2$; separation of the slopes, $P = 0{\cdot}001$.

Temporal Relationships of the Changes in Blood-glucose, Serum Gastrin, and Gastric Acid Secretion.—After insulin the blood-glucose level falls while serum-gastrin and gastric acid output increase. Each measured function is changing rapidly, reflecting a highly unsteady state; their interrelationships have been studied by finding meaningful significant correlations between the separate measurements.

a. Blood-glucose and Serum Gastrin.—Changes in the serum gastrin paralleled changes in the blood-glucose. *Fig.* 6 shows that in subjects who did not have gastric aspiration there was a highly significant inverse correlation between the blood-glucose level at the end of each 15-minute period and the corresponding serum-gastrin level. It can be seen further from this graph that there was a clear, significant separation of the two groups ($P < 0{\cdot}05$) and that at any level of blood-glucose after insulin, gastrin levels were approximately 50 per cent greater in the patients with duodenal ulcer than in the normal subjects. This temporal relationship was not found in subjects who had concomitant gastric aspiration; aspiration appeared to prolong the serum-gastrin response but it did not prolong the blood-glucose response to insulin.

b. Blood-glucose and Gastric Acid Secretion.—Changes in the gastric acid secretion lagged approximately 30 minutes behind changes in the blood-glucose. This can be seen from *Fig.* 7, in which the mean blood-glucose level at the end of each 15-minute period has been plotted against the mean gastric acid output 15–30 minutes later. A highly significant inverse correlation between these two groups of values was found both in patients with duodenal ulcer and in normal subjects, with significant separation of the two regression lines ($P < 0{\cdot}05$). This correlation was not found if the blood-glucose level at the end of each 15-minute period was plotted against the acid output for the same 15-minute period or for that 0–15 minutes later.

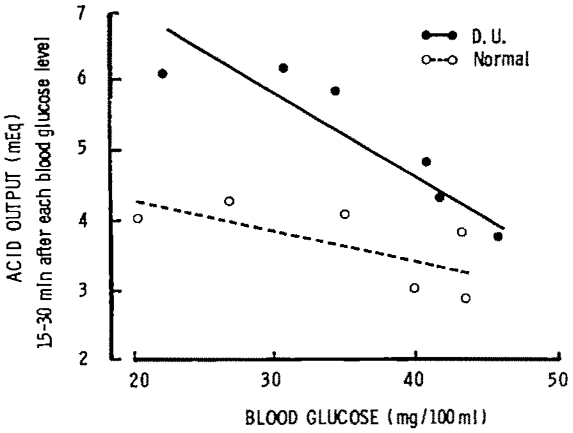

FIG. 7.—Temporal relationship between blood-glucose in each 15-minute period after intravenous insulin and gastric acid output 30 minutes later. Mean values of 13 patients with duodenal ulcer and of 7 normal subjects. For duodenal ulcer patients $y = -0{\cdot}121x + 9{\cdot}45$, $r = -0{\cdot}89$; $P = 0{\cdot}009$. For normal subjects $y = -0{\cdot}045x + 5{\cdot}20$; $r = -0{\cdot}69$; $P = 0{\cdot}06$. Difference between the slopes, $0{\cdot}05 < P < 0{\cdot}1$, separation of the slopes, $P < 0{\cdot}001$.

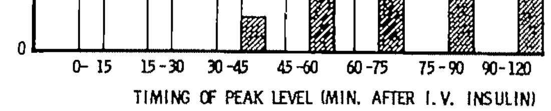

FIG 8.—Time intervals during which the peak gastrin levels and peak acid outputs occurred after insulin in 20 individuals (13 patients with duodenal ulcer and 7 normal subjects). Serum gastrin was measured at the end of each 15-minute period, whereas gastric juice was collected continuously during each 15-minute period.

c. Serum Gastrin and Gastric Acid Secretion.—*Fig.* 8 shows the timing of the peak gastrin level and of the peak acid output in 20 individual subjects (including all the ulcer patients and normal subjects). Serum gastrin was measured at 15-minute intervals at a precise instant in time. Gastric juice was collected over a period of 15 minutes and measurements of gastric acid are therefore not timed so precisely. However, it is clear that changes in the serum gastrin preceded changes in gastric acid secretion; peak gastrin levels occurred at any time from 0 to 75 minutes, whilst the peak acid output lagged 15–30 minutes behind, over the range of 30–120 minutes. The individual relationships which are not shown in the figure were as follows: in 15 subjects the peak gastrin level occurred 15–30 minutes before the peak acid output, in 4 subjects the peaks coincided, and in 1 subject the peak gastrin level followed the peak acid output by 15 minutes.

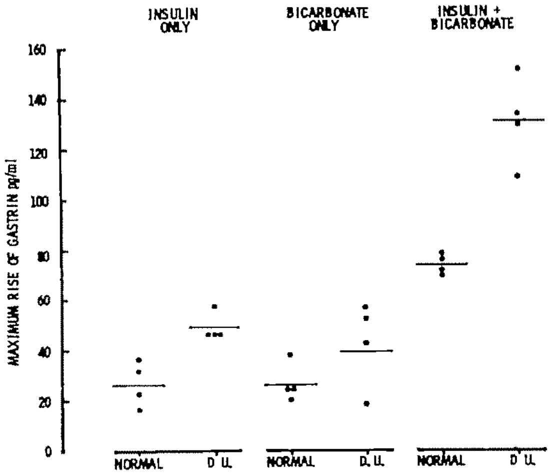

FIG. 9.—Maximum rise in serum-gastrin level in 4 normal subjects and 4 patients with duodenal ulcer after insulin, 0·2 U. per kg, during intragastric $NaHCO_3$ instillation, and in response to intravenous insulin and intragastric $NaHCO_3$ given simultaneously.

Relationships between Blood-glucose, Serum Gastrin, and Gastric Acid Output.—

a. Basal Levels.—Fasting blood-glucose was not related to basal gastrin or to the basal gastric acid output in either patients with duodenal ulcer or in normal subjects. No relationship was found between basal gastrin levels and the basal acid output in patients with duodenal ulcer ($r = -0·04$, $P = 0·45$), but there was a significant correlation between them in normal subjects ($r = 0·73$, $P = 0·03$).

b. Peak Serum-gastrin and Peak Acid Output.—Peak serum-gastrin and peak acid output after insulin were not related in patients with duodenal ulcer ($r = 0·01$, $P = 0·5$) but in normal subjects there was a relationship of doubtful significance ($r = 0·6$, $P = 0·08$).

DISCUSSION

Insulin hypoglycaemia consistently produced a greater increase in serum gastrin in patients with duodenal ulcer than in normal subjects. In the present study not only was the mean rise in serum gastrin significantly higher in patients with duodenal ulcer, but the absolute peak serum-gastrin levels were also significantly higher. This difference had not been found in our previous study of a smaller group of subjects (Korman and others, 1971b). In another study (Hansky and others, 1971) we suggested that patients with duodenal ulcer have an increased G-cell mass as well as an increased parietal-cell mass. In the present study, in which a group of patients with duodenal ulcer had insignificantly higher peak acid outputs than normal, the peak serum gastrin in the patients with duodenal ulcer was about 50 per cent greater than normal. This increased functional G-cell mass could be due either to an increased number of G cells (hyperplasia) or to a higher than normal rate of release of gastrin from each G cell in response to cholinergic stimuli. This point cannot be resolved until the number of G cells in the stomachs of patients with duodenal ulcer and of normal control subjects has been compared. However, the fact that the two regression lines in *Fig.* 6 are parallel but separate is compatible with the hypothesis that patients with duodenal ulcer do have increased numbers of G cells, and that for any degree of vagal stimulation produced by hypoglycaemia the rate of release of gastrin per G cell is the same as normal. Extrapolation of the lines of *Fig.* 6 might suggest that patients with duodenal ulcer should have higher serum-gastrin levels at normal fasting glucose levels, whereas the opposite is the case (Hansky and others, 1971). However, the data used in *Fig.* 6 are confined to measurements after insulin, so that such extrapolation is not appropriate. If measurements in the fasting state are included, then the lines do converge towards normal levels of blood-glucose.

In a previous study (Hansky and others, 1971) attempts were made to counteract the mechanism of acid inhibition of the release of antral gastrin by neutralizing gastric acid *in vivo* with sodium bicarbonate, and in the present study by aspirating gastric juice as it was secreted. With gastric aspiration the effect of insulin hypoglycaemia in increasing serum-gastrin levels was prolonged but the peak level attained was not significantly different from that of the unaspirated groups. The results of intragastric neutralization from our previous study are summarized in *Fig.* 9. Intragastric neutralization greatly increased the serum-gastrin response to insulin hypoglycaemia and in this small group there was complete discrimination between the serum-gastrin responses of normal subjects and of patients with duodenal ulcer. Presumably the neutralization of gastric acid raised the *p*H of the gastric contents and suppressed the mechanism for inhibition of the release of antral gastrin from the G cells. Gastric aspiration, while removing most of the acid as it was secreted, still allowed some juice of a low *p*H to remain in contact with the G cells. These results support the suggestion made by Woodward, Lyon, Landor, and Dragstedt (1954) that an increasing hydrogen-ion concentration in the pyloric antrum inhibits the release of gastrin. Measurement of the serum gastrin after insulin hypoglycaemia and intragastric neutralization in the non-intubated subject is a relatively simple procedure. If the excellent discrimination between patients with duodenal ulcer and normal subjects is confirmed when larger numbers are tested, this procedure might form the basis of a simple test for the duodenal ulcer diathesis.

The role of the vagus nerves in stimulating acid secretion by the stomach is complex. Vagal stimulation can cause the parietal cells to release acid even if all the antral gastrin-producing tissue has been extirpated (Pevsner and Grossman, 1955). However, in this animal study it was impossible to be certain that all the non-antral G cells had been removed. Antral gastrin is released by stimulation of the vagi electrically (Fyro, 1967) or by insulin hypoglycaemia (Korman and others, 1971b). The relationships between this gastrin release and the acid secretion during vagal stimulation by insulin hypoglycaemia have been examined in the present study. After the injection of insulin serum-gastrin levels increased as blood-glucose levels decreased and there was a highly significant inverse correlation between these two concentrations. On the other hand, the peak serum-gastrin level was attained about 15–30 minutes before the peak acid output, suggesting that the vagally released gastrin could play some part in stimulating acid secretion. The size of this contribution is uncertain. We found no correlation between the peak serum-gastrin level and the peak acid output. Furthermore, in some normal subjects, relatively low peak gastrin levels were associated with peak acid outputs which lay in the upper half of the range in duodenal ulcer patients. Thus, gastrin released by vagal stimulation may indirectly (by a chemical stimulus) 'prime' the parietal cells to respond to direct cholinergic vagal stimulation.

In this study gastric aspiration appeared to influence the degree of hypoglycaemia achieved after insulin injection. The mean blood-glucose levels at 30 and 45 minutes after the injection of insulin were significantly lower in the unaspirated group in spite of having fallen from a slightly higher basal level than in the aspirated group. The finding may well be due to chance, but it is interesting to speculate that acid passing into the duodenum initiated the release of a hormone which increased the hypoglycaemia by release of endogenous insulin.

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THE SIGNIFICANCE OF HUMORAL ANTIBODIES IN THE LOCALIZATION OF HUMAN MALIGNANT MELANOMA

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SUMMARY

A study of patients with malignant melanoma, in various stages of the disease, by means of regular repeated examination of sera for the presence of tumour antibodies is presented.

These antibodies were mostly seen in patients with early or localized tumours and were not related to the total mass or volume of the tumour present. Sequential testing in individual patients showed not only the disappearance of antibodies as the disease progressed from localized to disseminated, but also that the disappearance preceded the appearance of disseminated tumour by several months. It is, therefore, suggested that circulating tumour antibodies are important in preventing or delaying blood-borne metastases.

THE existence of some form of host immune response to human malignant melanoma is now beyond reasonable doubt and has been established by means of several types of investigation, indicating the presence of both humoral antibodies and cellular immunity (Lewis, 1967; Morton, Malmgren, Homes, and Ketcham, 1968; Lewis, Ikonopisov, Nairn, Phillips, Hamilton-Fairley, Bodenham, and Alexander, 1969; Muna, Marcus, and Smart, 1969; Zeigler, Lewis, Luyombya, and Kiryabwire, 1969; Fass, Herberman, Zeigler, and Kiryabwire, 1970; Currie, Lejeune, and Hamilton-Fairley, 1971; Hellstrom, Hellstrom, Sjogren, and Warner, 1971; Nagel, Piessens, Stilmant, and Lejeune, 1971). These investigations were originally stimulated by clinical observations on the natural history of malignant melanoma, exemplified by such phenomena as the variable natural history (Bodenham, 1968; Lewis and Kiryabwire, 1968), spontaneous regression (Smithers, 1964; Everson and Cole, 1966), the apparent presentation of tumours in regional lymph-nodes (Das Gupta, Bowden, and Berg, 1963), and the appearance of metastases many years after removal of the primary tumour (Eve, 1903; Allen and Spitz, 1953; Pack and Miller, 1961). The more sophisticated methods of detecting immune responses in patients with variable types of tumour have now made it possible for more detailed examination of the original clinical factors which first stimulated these studies. It is the purpose of this paper to present data illustrating relationships between circulating humoral antibodies and particular aspects of the natural history of malignant melanoma, namely, the length of time of the phase of localization and the possible influence on dissemination.

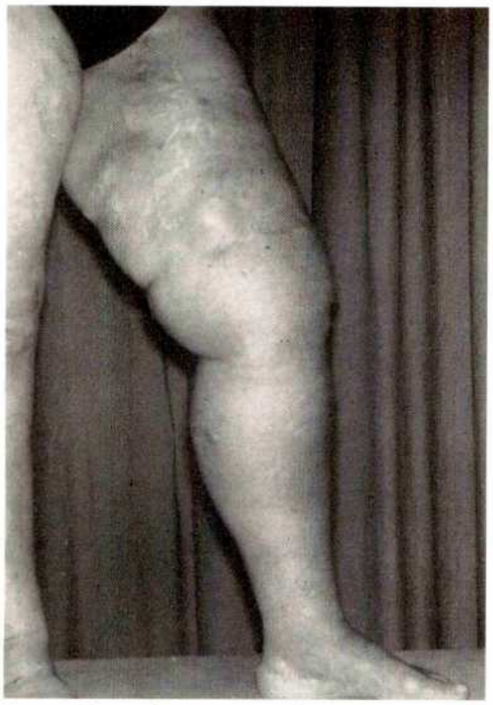

FIG. 1.—*Case* 1. Large amounts of subcutaneous melanoma deposits confined to one leg with no extension beyond the groin. (Antibody studies were positive at this time.)

MATERIALS AND METHODS

All the patients with malignant melanoma attending the Westminster Hospital are examined regularly at the follow-up clinic, where 10 ml. of venous blood are taken. The serum is then coded and stored in vapour-phase liquid nitrogen. Tumours removed by operation from any of these patients are prepared in cell suspension by a method which has previously been described (Pulvertaft, 1965; Lewis, 1967) and stored with dimethyl sulphoxide (DMSO) in liquid nitrogen. In addition, cytological smears are made from the tumour cells on glass slides and snap-frozen in liquid nitrogen and isopentane (Nairn, 1969; Phillips and Lewis, 1970). These are stored in plastic bags in the vapour phase of liquid nitrogen (− 136° C.).

This study so far comprises over 70 patients who have been subjected to regular follow-up, and their blood samples have been tested on each visit by means of immunofluorescence (Lewis and others, 1969; Phillips and Lewis, 1970) against their own stored tumour cells, fresh tumour cells or smears, and on some occasions by means of complement-dependent cytotoxicity (Lewis, 1967; Lewis and others, 1969).

RESULTS

The investigations carried out have continued to support previous work in this area indicating that in the majority of cases the early or localized melanomas have positive antibodies in their sera but that the disseminated cases showed no antibodies detectable by any of the test systems used (Lewis and others, 1969). It has now been possible by means of these sequential testings to show in individual patients the progression from localized to disseminating disease accompanied by the loss of antibodies. Of particular note during this study were several examples showing a clear relationship between the degree of localization of the tumour and the presence of antibodies, independent of the mass of tumour, with the drop in the antibody titre preceding the appearance of more disseminated tumour sometimes by several months. Some typical cases are presented to illustrate the phenomena.

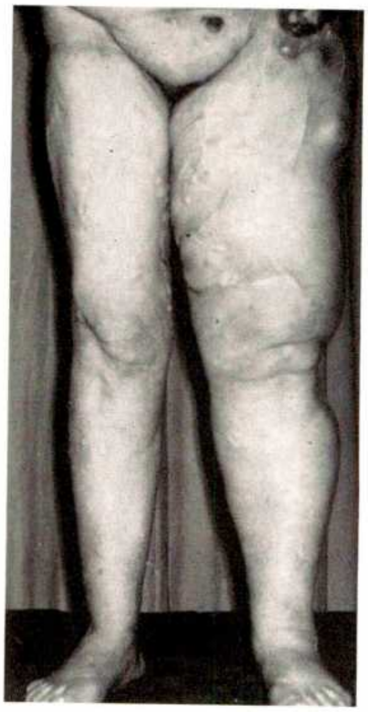

FIG. 2.—*Case* 1. Extension of the tumour, beyond the groin, including early deposits on the anterior abdominal wall. (Antibody studies were negative at this time.)

CASE REPORTS

Case 1.—A 51-year-old woman presented with a primary malignant melanoma of the thigh in 1963, and following excision she remained free of the disease until 1968. She then developed multiple subcutaneous deposits, including deposits in the regional groin lymph-nodes. Numerous attempts at local excision resulted in a gradually increasing mass of tumour, largely replacing most of her leg (*Fig.* 1). The first antibody studies carried out on this patient were in 1969 and showed a positive serum against her own melanoma cells and against fixed melanoma cells of other patients in high titres. Between 1969 and May, 1971, repeated serum samples showed a persistence in the positivity of her serum and there was still no sign of the tumour spreading beyond the groin. Extensive clinical examination revealed no sign of metastases elsewhere. In May, 1971, her serum was shown to be completely negative against autologous and homologous melanoma cells for the first time. In June, 1971, the first evidence of spread beyond the groin, namely to the anterior abdominal wall, was demonstrated (*Fig.* 2). Following this, over a period of 3 months, further metastases appeared at various sites. Throughout this time she remained completely antibody-negative. These results are summarized in *Fig.* 3.

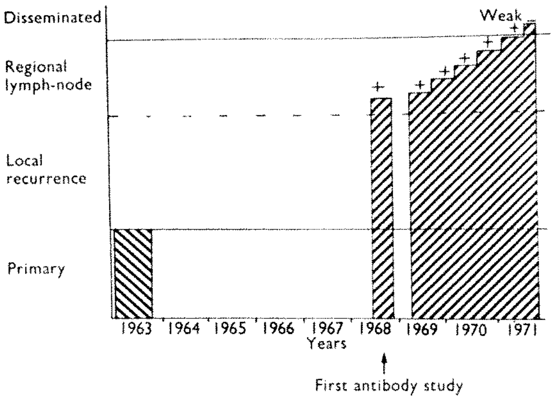

FIG. 3.—*Case* 1. Schematic representation on the slow progression of the natural history of malignant melanoma with a positive (+) antibody titre obtained on several occasions when the tumour remained localized.

Case 2.—A 37-year-old woman presented with a primary malignant melanoma of the left buttock in February, 1967. This was excised, and in July, 1969, further excision of a lump in the left groin was shown to be a lymph-node metastasis. She remained well with no further signs of recurrence of the tumour until December, 1970, when a new lump appeared in the left groin. Serum antibodies were shown to be strongly positive to malignant melanoma cells at this time. The groin nodule was excised in January, 1971, and on routine follow-up 1 month later her serum-antibody levels were found to be unrecordable. Three months following this she developed hepatomegaly and a mass in the right iliac fossa, and pulmonary metastases were seen on a radiograph. The course of the disease is summarized in *Fig.* 4.

Case 3.—A 36-year-old female was first diagnosed as having primary malignant melanoma of the left thigh in 1966. Several local recurrences were treated by excision until January, 1971, when a removal of regional groin lymph-nodes revealed metastatic tumour. At this time serum-antibody studies gave positive results Three months later a routine check of the serum showed no detectable antibodies, and within 3 months dissemination of tumour beyond the limb was noticed, when again no antibodies were detected in the serum (*Fig.* 5).

Case 4.—A 27-year-old male had a small primary malignant melanoma on the left calf. This was excised and was shown histologically to be an invasive malignant melanoma but serum antibodies were persistently negative. On very careful investigation no clinical metastases could be found but examination of the sternal bone-marrow revealed pigmented malignant melanoma cells.

Case 5.—A 20-year-old female presented with a primary malignant melanoma on the back, followed 6 months later by an isolated lymph-node containing tumour cells in the right axilla. This was excised and 3 months later a solitary nodule removed from the breast also revealed metastatic malignant melanoma. Very careful clinical examination revealed no further metastatic disease. This has been reconfirmed 7 months later. During this time serum samples showed no antibody activity.

DISCUSSION

The main findings in this study are that the presence of circulating humoral antibodies is not related to the volume or mass of tumour present, since several cases with massive amounts of tumour localized within the area of the draining lymph-nodes showed persistently positive antibodies, whereas patients with dissemination beyond the regional draining lymph-nodes, however small the deposits were, showed a loss of antibody detection. The next important feature is the apparent drop in antibody detection preceding metastatic disease in several cases. In view of the considerable amount of work reported in the recent literature on the importance of cellular immunity in malignant disease and particularly the impression gained that antibodies appear to be of no value but rather may even be a disadvantage to the patient, it seemed necessary to present the results of this study. It would appear from this investigation and from previously reported results in malignant melanoma from Africa (Lewis and Kiryabwire, 1968; Zeigler and others, 1969), Europe (Nagel and others, 1971), and America (Jehn, Nathanson, Schwartz, and Skinner, 1970; Morton, Eilber, Malmgren, and Wood, 1970) that the presence of

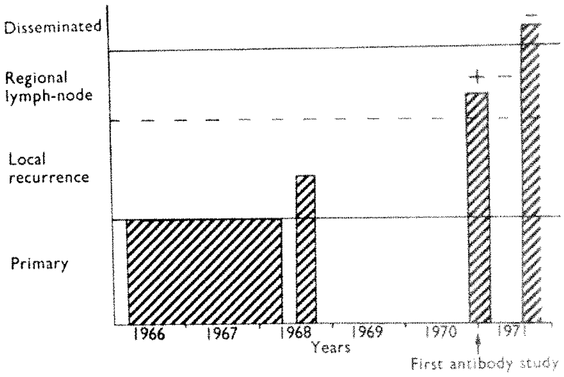

FIG. 4.—*Case* 2. Schematic representation, showing a positive (+) antibody titre changing to a negative (—) one prior to dissemination of the tumour.

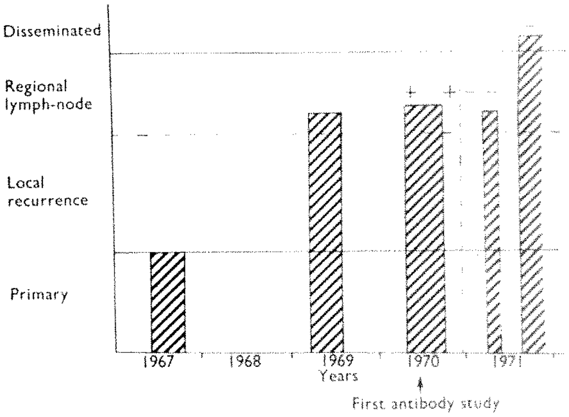

FIG. 5.—*Case* 3. Schematic representation, showing progression of the tumour over a period of years with a long phase of localization and a positive (+) antibody titre, followed by a negative (—) antibody titre and subsequent rapid dissemination of the disease.

humoral circulating antibodies in the course of the natural history of this disease is of considerable significance and has a direct relationship with the process of dissemination. We would like to suggest, on the basis of these results, that the role of circulating humoral antibodies in this disease is important in protecting the blood-stream from blood-borne metastatic tumour. The demonstration of the cytotoxic action of such antibodies (Lewis, 1967) and the close correlation between cytotoxicity and immunofluorescence in previous investigations of the tumour support this theory (Lewis and others, 1969; Ikonopisov, Lewis, Hunter-Craig, Bodenham, Phillips, Cooling, Proctor, Hamilton-Fairley, and Alexander, 1970). The importance of cellular immunity in the early phase of this tumour and its involvement in solid tumour deposits are beyond any reasonable doubt, though in most cases of established cancer the mechanism appears to have failed, but surely the most critical stage in the natural history of this disease, as in all forms of malignancy, is the change from localized to disseminated. It is, after all, the metastasis that is the important process in malignant disease. We would like to emphasize, therefore, the importance of continuing with such studies, particularly the sequential testing of patients' immunity, both humoral and cellular, during and related to the natural history of the disease. Since it was the natural history and the clinical manifestations of this particular tumour which first led to immunological studies it does seem very appropriate at this time that we should return time and time again to such observations and relate our laboratory data to them if we are to understand further the complexities involved in this relationship.

The immediate questions raised, of course, are: if the circulating antibodies are so important in preventing dissemination, why, in certain individuals, do these disappear early in the course of the disease and why, even in patients with long histories of localization, does the mechanism eventually become ineffective?

The suggestion that the antibody levels falling are merely a reflection of the mass in disseminated tumour is to some extent challenged by these results, and in other studies we have indicated the presence of what appears to be a blocking substance in the antibody-negative serum directed against the antibody positive in the same patient (Lewis, Phillips, Cook, and Blake, 1971). The nature of the blocking substance, which appears to be acting at a different site from that described by others in preventing cellular immunity from being effective, is at present under investigation (Hellstrom and Hellstrom, 1970; Bansal and Sjogren, 1971).

Acknowledgements.—This work was supported by grants from the Cancer Research Campaign and the Westminster Hospital Research Fund.

We would like to thank Mr. G. Westbury, Dr. K. A. Newton, and Mr. G. Stanley Lee for support and Mr. P. Elliot and Mr. T. M. Phillips for technical assistance.

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DEEP-VEIN THROMBOSIS IN PATIENTS WITH FRACTURE OF THE UPPER PART OF THE FEMUR

A PHLEBOGRAPHIC STUDY

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SUMMARY

Deep-vein thrombosis was found by phlebography in 60·3 per cent of 58 patients with fracture of the upper end of the femur. The incidence was higher on the left side. Thrombus was detected in the uninjured leg in many cases, and therefore the need for bilateral investigation is emphasized.

The convenience of the radioactive fibrinogen test and ultrasound technique for detecting thrombosis in patients has been widely accepted, but we also consider that phlebography, using a portable radiograph machine, is a valuable and easy method for the detection of deep-vein thrombosis in seriously ill patients.

THE most common cause of death in patients with a fractured femur is pulmonary embolism (Sevitt and Gallagher, 1959). A large number of these patients develop thrombosis in the deep veins of the leg (Hamilton, Crawford, Gardiner, and Wiley, 1970; Field, Nicolaides, Kakkar, and Crellin, 1972) which is inadequately diagnosed by clinical methods (McLachlin and Paterson, 1951; Coon and Coller, 1959). Many patients show no signs of thrombosis and yet die from a fatal embolus (Sevitt, 1962).

It is well known that the early treatment of thrombosis gives the best immediate results and helps to prevent permanent damage to the valves and the post-thrombotic syndrome (Kakkar, 1969). It is therefore obvious that there is a need for methods other than clinical to be used in the detection of this condition.

Recent studies have clearly demonstrated that it is possible to detect thrombi using radioactive-labelled fibrinogen (Hobbs and Davies, 1960; Atkins and Hawkins, 1965, 1968; Flanc, Kakkar, and Clarke, 1968; Negus, Pinto, LeQuesne, Brown, and Chapman, 1968). The ultrasound technique is another new diagnostic method for venous thrombosis (Evans, 1971; McIlroy, 1972), but phlebography has undoubtedly been established because of its high degree of accuracy in detecting the presence and extension of a thrombotic lesion (Kakkar and Flanc, 1968; Negus and others, 1968).

The initial clinical impression was that the incidence of thrombo-embolic episodes in patients with a fracture of the femur admitted to the Third Surgical Unit of the Evangelismos Hospital, Athens, was small. However, many of these injured patients developed the late sequelae of deep-vein thrombosis: swelling and pain of the leg, varicose veins, and other changes. Because these findings indicated inadequate diagnosis and treatment of thrombosis at the time of the fracture we considered that it would be interesting to investigate this subject using phlebography.

MATERIAL AND METHODS

The patients studied were admitted to the hospital between September, 1970, and September, 1971, with a fracture of the upper part of the femur. All had been fully ambulant before the injury and were operated on within 6 days of admission. Fifty-eight patients were included in this investigation. Patients with other serious injuries or neoplastic disease, as well as those with clinical evidence of a previous thrombosis, were excluded from the study.

There were 25 males and 33 females. The mean age of the males was 58 years and for the females 69·5 years (youngest 19, oldest 91).

Thirty-six patients had a fracture on the right side and the remaining 32 on the left side. In 24 cases the fracture was subcapital and in 34 pertrochanteric.

All except 3 patients were managed surgically. Two of the fractures which were treated conservatively were in patients who were admitted to hospital 3 weeks after injury, and 1 patient was not operated on because of severe cardiopulmonary failure.

The phlebographic study was carried out within 10 days of admission but never more than 6 days after the operation. Although no special criterion was used to determine the timing of this radiography, in the event of a venous thrombosis being suspected clinically or signs of pulmonary embolism being present a phlebogram was done. It must be noted that the patients were examined only during regular ward rounds, unless some urgent complaint arose. Otherwise no clinical examination was done for the detection of a possible thrombosis in the legs.

Phlebography.—During the present investigation phlebography was done using a portable radiograph machine with the patient staying in his bed. The patient was placed in the supine position and the head of the bed was elevated 20 cm. so that the patient's legs were placed in a position which permitted a better mixing of the contrast medium with his blood.

A needle was inserted into a vein in the dorsum of each foot. Sometimes percutaneous puncture was difficult, but a cut-down was only necessary in 6 cases. A single tourniquet was placed just above each ankle to exclude the superficial blood-flow. The needle was connected to a set of rubber tubing and a syringe containing 50 ml. of 60 per cent Urografin. Then 20 ml. of the contrast medium were slowly injected simultaneously bilaterally, at the completion of which the first radiograph was taken on a 30 × 40-cm. film placed behind the lower part of the limbs.

Following this, a radiograph cassette was placed behind the thigh and lower pelvic regions. The bed was lowered to the horizontal position and the tourniquet was removed from the ankle and placed just below the knee. Immediately after the injection of about 30 ml. of contrast medium the second exposure was taken, resulting in visualization of the popliteal and femoral veins. This technique frequently filled the iliac veins but the demonstration was not always of diagnostic value.

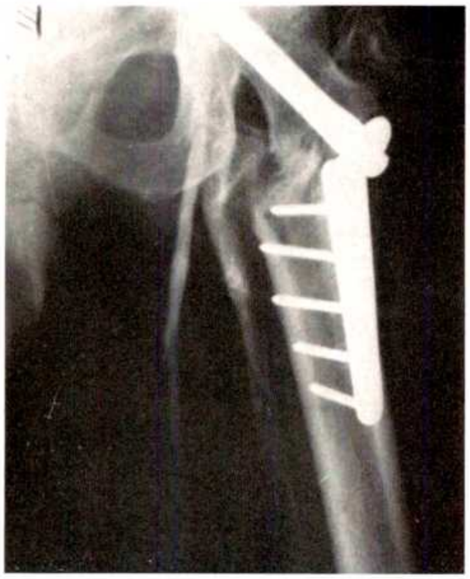

FIG. 1.—Phlebogram showing thrombosis in the veins of the fractured limb.

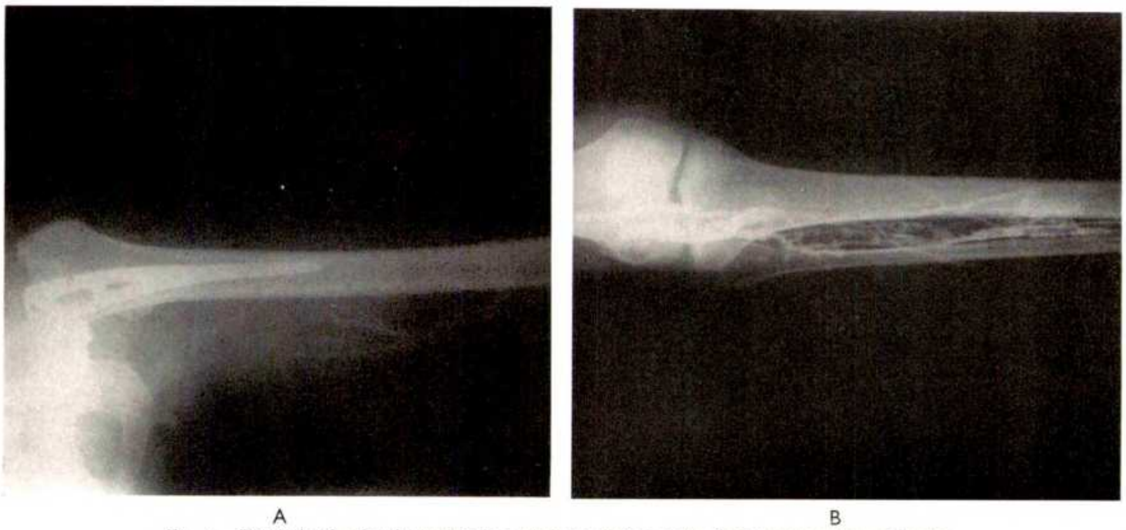
A B

FIG. 2.—The lesion is often located in more than one region of the deep venous system of the leg.

This was the standard method used, but in some cases the contrast medium was injected, when it was possible, into a vein just below the knee for better visualization of the femoral and iliac veins. In 12 patients the new technique described by Nicolaides, Kakkar, and Renney (1970) was used for detecting thrombus in the soleal sinuses. Cotton and Clark (1965) have shown that the vast network of these sites is quite impossible to fill completely by the common phlebographic methods.

The amount of contrast medium usually required was 50 ml. for each side, but more was used if repeated injections were given when necessary for re-examining doubtful areas in the films. No complications have been experienced using this technique of phlebography.

RESULTS

Table I shows that deep-vein thrombosis was detected phlebographically in 35 (60·3 per cent) of the 58 patients studied. In 20 patients thrombosis was found in the veins of the fractured limb (*Fig.* 1), in 9 cases on the opposite side, and in 6 patients the thrombotic process was detected bilaterally.

The sites of the thrombi are shown in *Table II*. It is clear that in almost half of the cases the lesion was located in more than one region of the deep venous system of the leg (*Fig.* 2). In 3 out of the 10 patients in whom we used the method described by Nicolaides and others (1970) a defect was outlined within the soleal sinuses, but in all 10 there was additional thrombosis elsewhere.

Table III shows the higher incidence of thrombus found on the left side, although the overall number of patients with a fracture of the left side was lower than those with a right-sided injury. Thirty-six patients had a fracture of the right femur and of these, 7 developed thrombosis in the unfractured left limb (*Fig.* 3). Only 2 out of the 22 patients with a fracture of the left side had thrombosis in the veins of the opposite limb. One of the 3 patients who did not have an operation developed femoral thrombosis. The phlebogram (*Fig.* 4) of this patient shows numerous collateral veins, indicating that the thrombotic process had existed for some weeks.

Pulmonary embolism was confirmed by a radiograph of the chest in 6 patients. Two of these presented with symptoms suggesting this condition before deep-vein thrombosis was diagnosed. Furthermore, phlebography was done in 4 other patients because of clinical signs of thrombosis, but in 1 of these cases no thrombus was found.

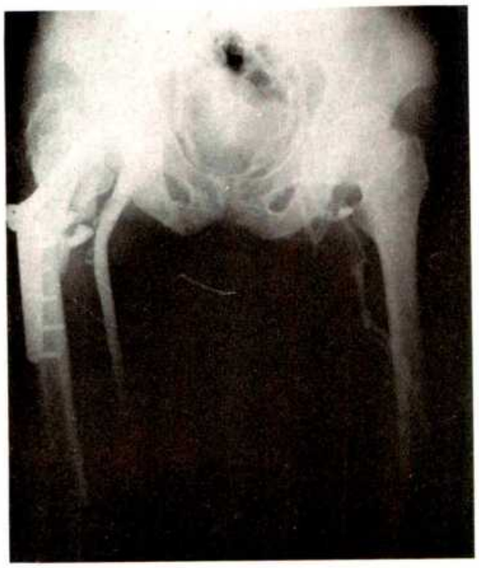

FIG. 3.—A patient who had a fracture of the right femur and developed thrombosis in the unfractured left limb.

Table I.—INCIDENCE OF DEEP-VEIN THROMBOSIS COMPARED WITH AGE IN 58 PATIENTS

AGE-GROUP	NO. OF PATIENTS	INCIDENCE OF THROMBOSIS (60·3 per cent)			
		Fractured Leg	Un-fractured Leg	Both Legs	Total No. of Cases
10–19	4	—	—	—	—
20–29	2	1	—	—	1
30–39	4	2	1	—	3
40–49	1	—	1	—	1
50–59	7	1	2	1	4
60–69	12	5	4	—	9
70–79	16	7	1	3	11
80–89	11	4	—	2	6
90 +	1	—	—	—	—
Total	58	20	9	6	35

Two patients died in this series. One of these died from a massive haematemesis and the other, who had a multiple thrombosis, from renal failure. In both cases no post-mortem examination was done.

DISCUSSION

On the basis of clinical criteria deep-vein thrombosis seemed to be rare in patients with a fractured femur. However, using phlebography a positive diagnosis of thrombosis was made in 35 (60·3 per cent) of the 58 patients investigated. These results, together with those of Hamilton and others (1970) and Field and others (1972), clearly show the high incidence of this condition in such cases.

In the series of Hamilton and others (1970) in which thrombosis was detected phlebographically in 75 per cent of patients with fractured limbs, 26 per cent of the thromboses were in the uninjured limb. Field and others (1972), using a radioactive fibrinogen technique, found an incidence of thrombosis of 54 per cent in the fractured limb and of 34 per cent in the opposite side. These findings show that the presence of thrombi in the veins of the uninjured leg must never be overlooked and indicate the importance of bilateral investigation. The present study confirms this. In 20 of our cases the thrombosis was located in the injured leg and in 9 cases the thrombosis was found in the uninjured leg.

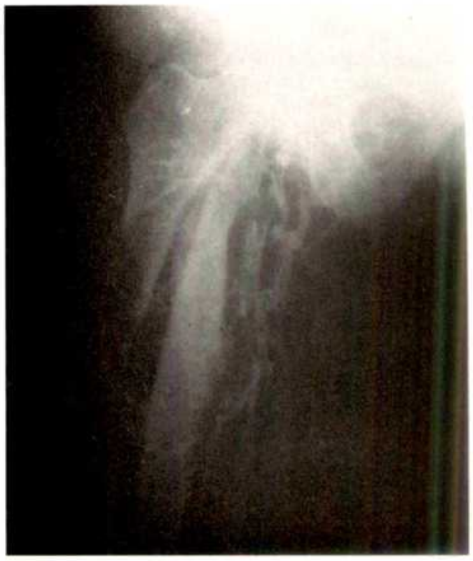

FIG. 4.—Phlebogram showing numerous collateral veins which indicate that the thrombotic process had existed for some weeks.

Table II.—LOCATION OF THROMBI

Location	*No. of Legs*
Deep veins of the calf	7
Popliteal	6
Femoral and iliac veins	9
More than one region	19
Total	41

Table III.—SIDE OF DEEP-VEIN THROMBOSIS COMPARED WITH SIDE OF FRACTURE

SIDE OF FRACTURE	NO. OF PATIENTS	SIDE OF THROMBOSIS		
		Right	Left	Both Legs
Right	36	11	7	4
Left	22	2	9	2
Total	58	13	16	6

Analysis of our data showed that thrombosis developed at a particularly high rate in the left leg. More than half of the 35 patients with thrombosis had the lesion in the left side, though only 37 per cent of these had a fracture of this side. Probably the higher incidence of thrombosis in the left leg is due to the left common iliac vein being compressed at a point where it is crossed by the right common iliac artery (Cockett, 1967).

Although over half of the cases of deep-vein thrombosis could be accurately diagnosed by taking a combination of two or more of the clinical signs—pain, tenderness, and oedema (Hall and Clark, 1971)—many are overlooked in routine practice so that treatment is often late or not given at all. Kakkar (1969) emphasized the fact that early detection of venous thrombosis of the leg is of the utmost importance if the treatment of this condition is to be improved.

Using the radioactive fibrinogen technique it is possible to detect thrombi early and with greater certainty than by the clinical method alone (Atkins and Hawkins, 1965, 1968; Flanc and others, 1968; Negus and others, 1968; Field and others, 1972). The ultrasound technique is also a promising diagnostic method and there are no contra-indications even in seriously ill patients with venous thrombosis (Evans, 1971; McIlroy, 1972). However, the value of phlebography is without doubt. This method is used to correlate the accuracy of ultrasonic findings and to check all the positive results obtained with the radio-isotope technique.

Many phlebographic methods have been described. We have tried to make the procedure as simple as possible for the convenience of patients with fractures. We feel that phlebograms taken with a portable radiograph machine give sufficient information to make an accurate diagnosis of deep-vein thrombosis.

Acknowledgements.—We wish to thank the Director of the Radiology Department, Associate Professor L. Stergiou, and also Dr. G. Vrachlio and the technicians of this department for the invaluable help in this investigation.

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AN OPERATION FOR LARGE SCROTAL HYDROCELE

BY J. L. WILKINSON*
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SUMMARY

A relatively minor operation of partial eversion in which some residual sac is left in situ has been performed in over 500 cases of large tropical hydrocele. The method is applicable to smaller hydroceles, and also provides a method of treating recurrent testicular torsion.

THE desirability of relatively bloodless surgery in the radical cure of hydrocele was recognized in the operations described by Andrews (1907), Solomon (1955), Özdilek (1957), and Lord (1964), and the method of the last author has been widely accepted with excellent results, as reported by Efron and Sharkey (1967) and Doyle and Rush (1968).

In many tropical countries scrotal hydrocele is of more frequent occurrence than in temperate climates. Such hydroceles are often very large, sometimes bilaterally so, as noted by Burkitt (1951), Burkitt and Williams (1964), and Davey (1968).

A reappraisal of surgical technique for large scrotal hydrocele was carried out, and later a historical review of the principles involved. During the yea 1955 to 1971, 889 scrotal hydroceles were operat on at the Nixon Memorial Hospital, Sierra Leon West Africa, mostly by the author. Inherent con plications in many patients included gonococc epididymo-orchitis, filarial lymphangitis, schist somal funiculitis, or previous unskilled tappin Occasionally there were gross abnormalities such filarial elephantiasis, greatly thickened and ev calcified tunica vaginalis, or a sac filled with sem solid debris associated with testicular degeneratio The majority of hydroceles were similar to tho seen in Europe, though larger, and for these t following operation was designed.

OPERATIVE TECHNIQUE

In a large hydrocele the testicle is situated on t upper part of the posteromedial aspect of the sa The operation consists of preparing a pouch betwe the parietal layer of the tunica vaginalis and t internal spermatic fascia, into which the testis implanted. In a big hydrocele much of the origin sac which is emptied is left in situ.

Following induction of anaesthesia, the skin havi been cleansed with chlorhexidine, the scrotum is he so that the skin is tense. For a unilateral hydroce a 3–4-cm. oblique anterolateral incision is made in the line of and between the skin vessels of the upper scrotum (*Fig.* 1). For a bilateral case a single transverse incision is placed at right angles to the median skin raphe, about 4 cm. below the penoscrotal junction. A low-power cutting diathermy with a fine needle, preferably angled, is used to divide the dartos and the layer made up of external spermatic fascia, cremasteric fascia, and internal spermatic fascia. Any tiny bleeding points are sealed off. When the tunica vaginalis is exposed it is separated digitally from the internal spermatic fascia to form a pouch below the incision large enough to accommodate the testis (*Fig.* 2). This is a natural plane of cleavage and there should be no bleeding at all. The two layers of the tunica, though individually distinguishable, are closely adherent to one another and are picked up together. Through a small incision the contained fluid is aspirated, or a trocar and cannula may be used. In a small hydrocele the testis may then be extruded through the incision, but in a large sac Babcock's forceps are used to deliver it to the surface. When the testicle is drawn outwards through the skin the naturally mobile tunica becomes everted until the edges of the sac incision come to lie alongside the spermatic cord. (With a small hydrocele the effect is to turn the sac inside out almost entirely, ensheathing the cord.) The cut edges of the sac opening are then sutured together on the upper aspect of the cord, catching in the coverings of the cord (*Fig.* 3). This has the dual effect of narrowing the sac incision sufficiently to prevent prolapse of the testis into the original sac, yet by leaving the latter in continuity with the extruded serosal tunica a natural conduit is established.

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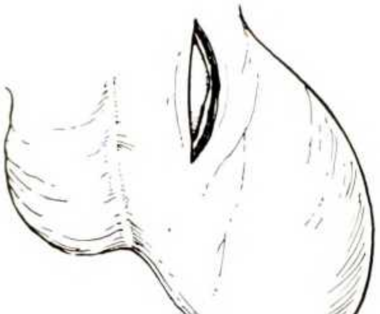

FIG. 1.—The skin incision in the upper scrotum.

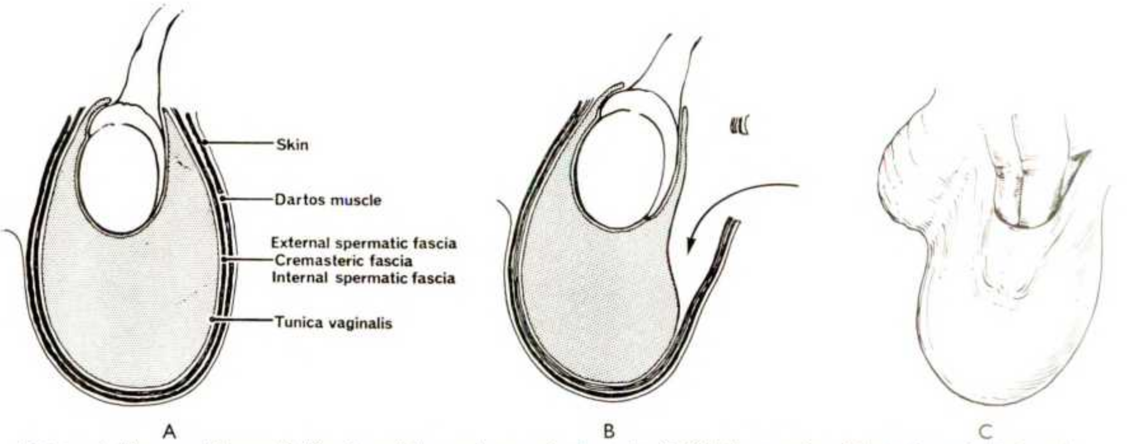

FIG. 2.—A, The normal layers. B, The plane of the pouch to receive the testis. C, Digital separation of the tunica vaginalis from the internal spermatic fasia, developing a pouch into which the testis may be transferred.

Lane's forceps are used to hold up the skin, dartos, and fasciae as the testicle is tucked into the prepared pouch. The fasciae and dartos are approximated with interrupted 00 chromic catgut. Initially 16 mm. Michel skin-clips were used for closure, but recently a continuous intradermal 00 Dexon suture has been found more satisfactory in terms of comfort, healing, and postoperative care. The scrotum is gently compressed to expel any air or fluid, the skin is wiped with ether, and nobecutane spray is applied to the wound and ribbon gauze applied. With large hydroceles a scrotal compression bandage is used, but in Europe an appropriate scrotal support over gamgee is all that is required, the patient being discharged from hospital on the following day.

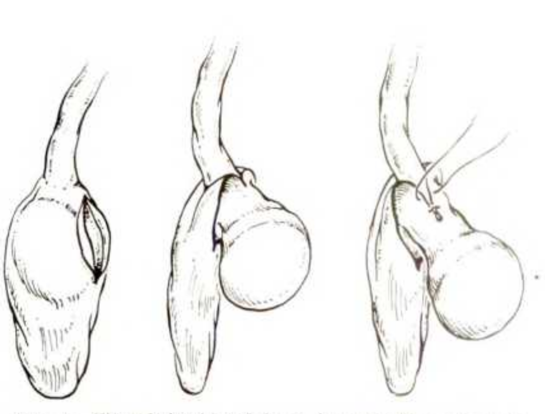

FIG. 3.—The relationship of the tunica vaginalis to the testis and spermatic cord as the latter are withdrawn through an incision in the sac.

RESULTS

The operation described here has been carried out in over 500 cases since 1959, and no redevelopment of a hydrocele has been reported. Complete routine follow-up is not feasible where patients often travel over 100 miles to a surgical centre, as in many tropical areas.

The everted epithelium of the tunica vaginalis quickly loses its secretory nature, and becomes, together with the testis, adherent to the internal spermatic fascia. In large hydroceles the fluid which for a time continues to be formed in the residual sac passes alongside the ensheathed cord to be absorbed by lymphatics. When the sac walls are no longer separated by fluid, adherence and atrophy take place. Subsequent to operation on truly massive hydroceles there may be some transient oedema of the lax scrotal tissues. If there is redundant scrotal skin it is best left for 3 months, by which time some contraction has taken place and it is rarely necessary to remove it.

DISCUSSION

Operative procedures for hydrocele have been a source of debate for hundreds of years. Recently an extrusion operation without sac excision or plication was described by Solomon (1955) and McGowan and Howley (1969), suturing the sac edge to the epididymis, with satisfactory results, and Andrews's (1907) 'bottle operation' has been well tried since the first decade of this century. Jaboulay's eversion operation is frequently referred to in standard texts, but the source of the original account was surprisingly difficult to ascertain (Bèrard, 1895; Jaboulay, 1902). The technique was also recorded by Vautrin (1893, 1913) and Barral (1896). Doyen (1895) performed an eversion operation through a 2·5-cm. incision which in some respects is comparable to that described here. The basic concept of these operations that sac eversion *per se* by exposing the secretory layer of the tunica to the parietes inhibits fluid formation has withstood the test of over 80 years of surgical practice. The operation described here indicates that even in large hydroceles a form of partial eversion is an adequate and effective procedure.

This method of eversion has been used by the author as a simple means of fixing the congenitally mobile testis in which the tunica commonly sheathes the cord to some extent and the gubernaculum may be absent. Displaced operatively into a pouch under the spermatic fascia, the testicle quickly becomes adherent and unable to rotate. Symptoms such as deep iliac fossa discomfort which may have been present for months rapidly subside after operation.

Acknowledgements.—I am indebted to Mr. J. Hartshorn, of the Department of Medical Illustration, Manchester Royal Infirmary, for the illustrations. I wish to thank Mr. Thomas Moore, Consultant Urologist, for his encouragement to write this paper, and Professor I. E. Gillespie for his helpful and constructive criticism.

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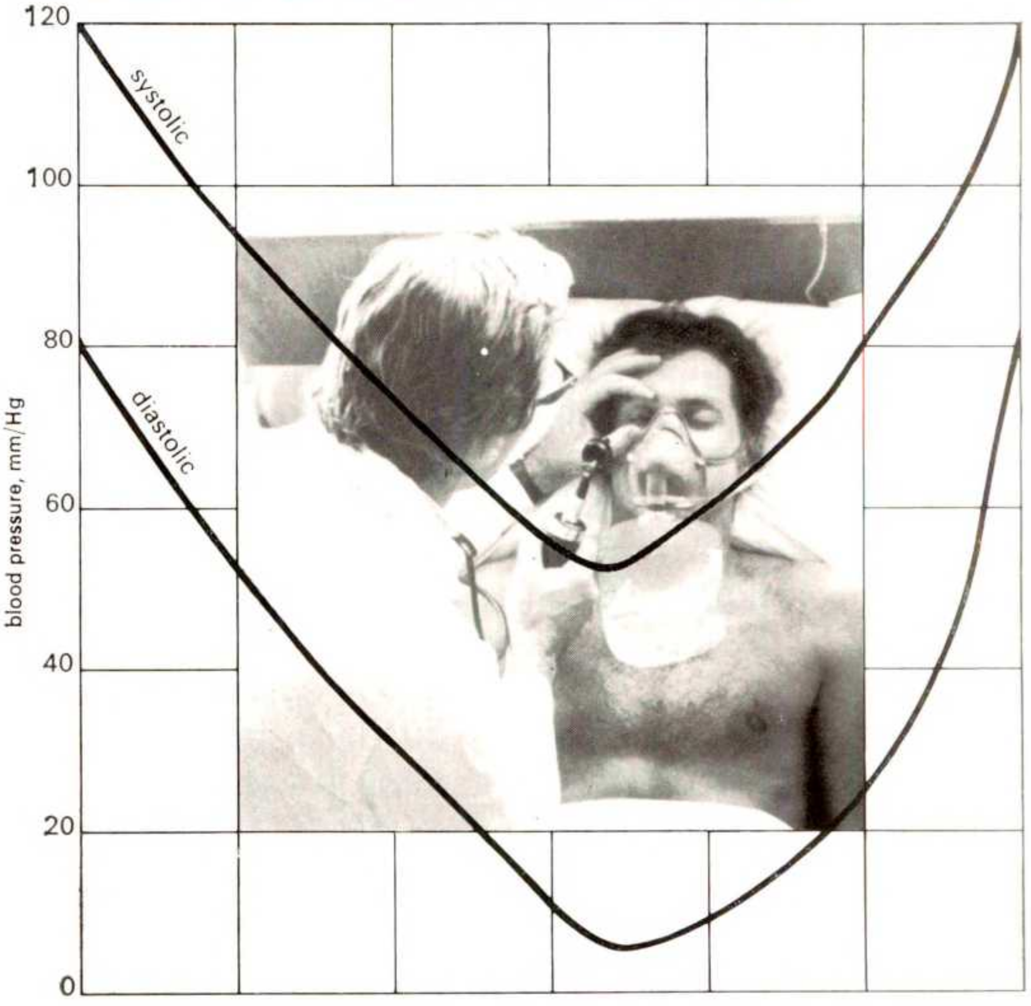

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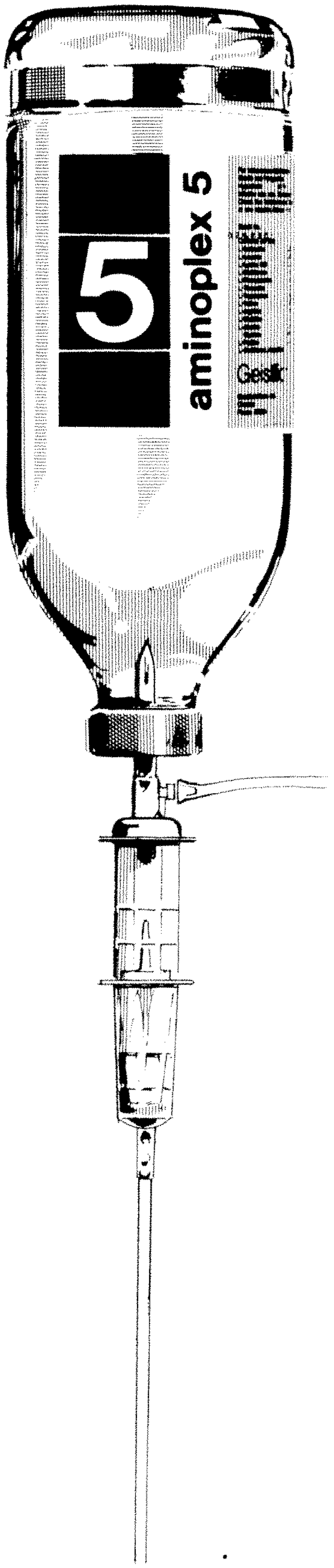

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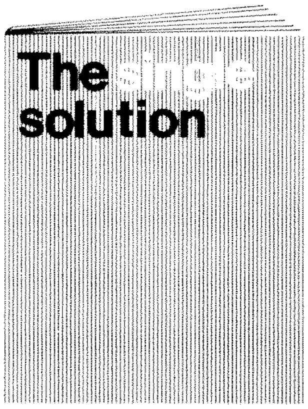

COMPARISON OF SINGLE-LAYER INVERTING, TWO-LAYER INVERTING, AND EVERTING ANASTOMOSES IN THE RABBIT COLON

By T. T. IRVIN and J. P. EDWARDS

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SUMMARY

Inverting methods of suture should be used in colonic anastomosis. A two-layer inverting anastomosis is usually recommended but it has been suggested that a single-layer technique is preferable and safer.

Single-layer inverting, two-layer inverting, and everting anastomoses were compared in the unprepared rabbit colon. Everting anastomoses gave inferior results by comparison with both inverting methods with respect to tensile strength, anastomotic leakage, and histological evidence of healing, but no difference was found between the single-layer and two-layer methods using these criteria and measurement of colonic collagen.

It was concluded that single-layer inverting methods of anastomosis had no particular advantages over the standard two-layer inverting method.

THERE can be little doubt that inverting methods of suture should be used in anastomosis of the colon (Goligher, Morris, McAdam, de Dombal, and Johnston, 1970) and the method of suture usually recommended is the two-layer inverting technique (Goligher, 1967; Muir, 1969; Turnbull and Kyle, 1969). Single-layer inverting techniques have been used less frequently in the colon, although Halsted (1887) suggested that this was the method of choice, and Gambee, Garnjobst, and Hardwick (1956) were favourably impressed with this method in clinical practice. Experimental evidence implies that the single-layer method is safer than the two-layer method in small-bowel anastomosis (Letwin and Williams, 1967), but there is little objective information regarding the relative merits of the two methods in anastomosis of the colon.

In the present study single-layer inverting, standard two-layer inverting, and everting anastomoses have been compared in the rabbit colon.

MATERIALS AND METHODS

Ninety-three male and female rabbits were anaesthetized with Nembutal by intravenous injection in a dose of 30 mg. per kg. of body-weight. Intestinal preparation was not used except for restriction of the diet to liquids only for 48 hours prior to surgery. The abdomen was opened through a midline incision and a 2-cm. segment of the right colon was resected. The resected specimen was retained for estimation of collagen content and the method of anastomosis—single-layer inverting, two-layer inverting, or everting—was allocated randomly in each case. The techniques used for the different types of anastomosis are shown in *Fig.* 1. The standard two-layer anastomosis comprised a continuous 0000 polyglycolic acid suture (Davis & Geck) incorporating all the coats of the bowel wall for the inner layer and an outer layer of interrupted 0000 silk Lembert sutures. The single-layer inverting anastomosis was made with interrupted 0000 silk vertical sutures through all the layers except the mucosa and the same suture was used through all the coats of the bowel wall for the single-layer everting anastomosis. Diet was restricted to fluids only for 72 hours after surgery and the animals were sacrificed in a random fashion at 0, 7, 14, 21, and 28 days after operation.

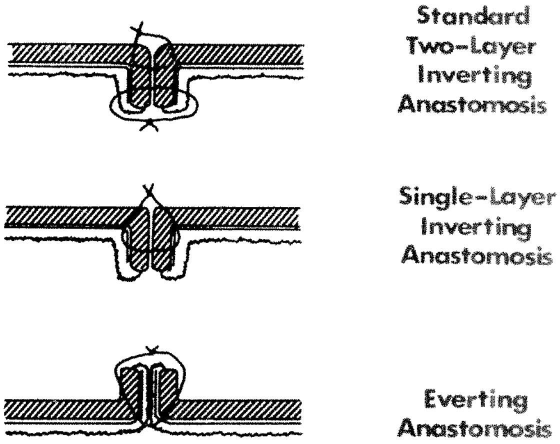

Standard Two-Layer Inverting Anastomosis
Single-Layer Inverting Anastomosis
Everting Anastomosis

FIG. 1.—Single-layer inverting, two-layer inverting, and everting methods of anastomosis.

At autopsy the presence of obstruction, peri-anastomotic sepsis, and anastomotic leakage was noted and a 12-cm. length of intestine including the anastomosis was resected. A barium-enema study was performed on most of the specimens and the degree of anastomotic stenosis was assessed on radiological examination by the method of McAdams, Meikle, and Taylor (1970). This method of assessment is shown in *Fig.* 2. The diameters of the anastomosis (a) and the bowel at two points 2 cm. proximal and distal to the anastomosis (b and c) were measured and the percentage reduction in the lumen or 'index of stenosis' was obtained from the calculation $100[1 - \{2a/(b + c)\}]$. The bursting pressure of each specimen was measured on a mercury manometer after distension of the specimen with air at a constant rate. Paraffin sections of the anastomosis were stained with haematoxylin and eosin and van Geison's stain for histological examination.

Half of each anastomosis was dried to constant weight using acetone and desiccation and the dried tissue was hydrolysed in a hot-air oven at 120° C. for 16 hours with 6 *N* hydrochloric acid. Collagen was estimated by a modification of the method of Neuman and Logan (1950) after neutralization of the hydrolysate with 6 *N* sodium hydroxide. Prior separation of hydroxyproline from the tissue hydrolysate was unnecessary since preliminary studies based on spectral characteristics of the chromogen obtained using the modified method revealed that the hydrolysate did not contain significant quantities of interfering substances. These observations are in accordance with previously published recommendations (LeRoy, 1967).

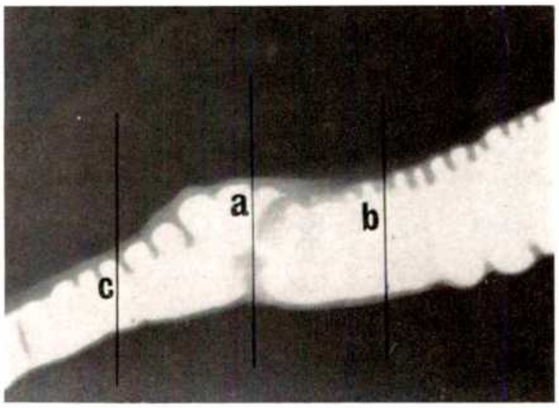


FIG. 2.—Barium-enema study of a colonic anastomosis in the rabbit. The percentage reduction in the lumen or the 'index of stenosis' is derived from the diameters of the anastomosis (a) and the bowel at two points 2 cm. proximal and distal to the anastomosis (b and c), using the calculation 100[1 – {2a/(b + c)}].

Table I.—THE INCIDENCE OF COMPLICATIONS ASSOCIATED WITH THE THREE METHODS OF ANASTOMOSIS

COMPLICATION	SINGLE-LAYER INVERTING ANASTOMOSIS		TWO-LAYER INVERTING ANASTOMOSIS		EVERTING ANASTOMOSIS	
	No.	Per cent	No.	Per cent	No.	Per cent
Intestinal obstruction	3	12	7	27	0	0
Leaking anastomosis	1	4	1	4	14	54
Intraperitoneal abscess	1	4	1	4	4	15

RESULTS

Mortality and Incidence of Anastomotic Complications.—Each method of anastomosis was tested in 31 animals, but 5 animals in each group were sacrificed immediately and anastomotic healing was studied in the remaining 26 rabbits in each group. Three deaths in the single-layer inverting group and 7 deaths in the two-layer inverting group resulted from intestinal obstruction and 2 deaths occurred in the everting group as a result of anastomotic dehiscence. Because of these deaths the numbers of animals available for sacrifice on the seventh, fourteenth, twenty-first, and twenty-eighth postoperative days differed slightly in the three groups. Thus, in the single-layer inverting group, 11 animals were sacrificed on the seventh day, 7 on the fourteenth day, 3 on the twenty-first day, and 2 on the twenty-eighth day. The corresponding numbers for the two-layer inverting group on these days were 11, 6, 2, and 0, and for the everting group, 10, 9, 3, and 2.

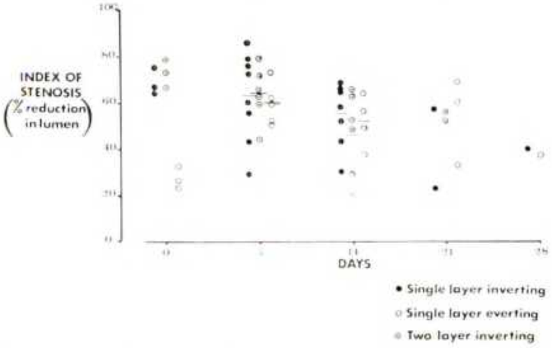


FIG. 3.—The 'index of stenosis' or percentage reduction in the bowel lumen measured in 21 single-layer inverting, 17 two-layer inverting, and 16 everting anastomoses.

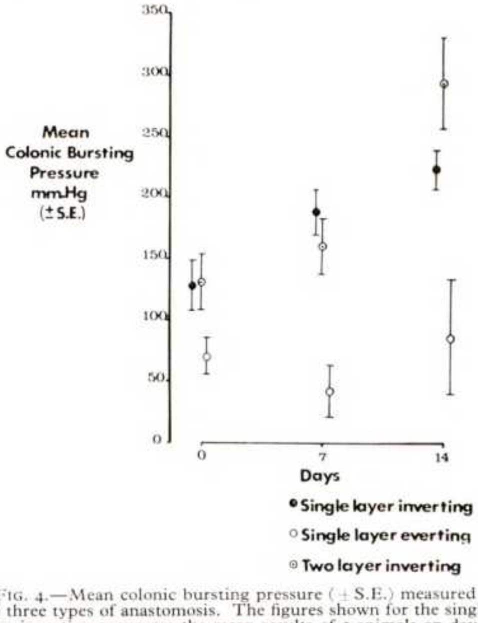


FIG. 4.—Mean colonic bursting pressure (± S.E.) measured in the three types of anastomosis. The figures shown for the single-layer inverting group are the mean results of 5 animals on day 0, 11 animals on day 7, and 7 animals on day 14, and the corresponding numbers of animals in the two-layer inverting group on these days are 5, 11, and 6, and for the everting group, 5, 10, and 9.

The incidence of complications associated with the three methods of anastomosis is shown in *Table I*. The complications comprised obstruction resulting in the death of the animal, anastomotic dehiscence, and perianastomotic abscesses unassociated with anastomotic leakage at the time of autopsy. The total incidence of complications associated with single-layer inverting, two-layer inverting, and everting anastomoses was 15, 35, and 69 per cent respectively. The complication rate in single-layer and two-layer inverting anastomoses was not significantly different but there was a significant difference between single-layer inverting and everting anastomoses ($\chi^2 = 7{\cdot}348$,

$P < 0\cdot01$). The difference between two-layer inverting and everting anastomoses was not quite statistically significant, but intestinal obstruction accounted for most of the complications arising with the two-layer method and it is doubtful if any significance should be attached to this complication since inverting anastomoses in the rabbit undoubtedly produce a degree of narrowing of the bowel lumen which has little resemblance to the situation in the human colon. There is no doubt, however, that the incidence of anastomotic dehiscence and intraperitoneal abscess was significantly higher after everting suture compared with either of the two methods of inverting suture ($\chi^2 = 12\cdot800$, $P < 0\cdot001$).

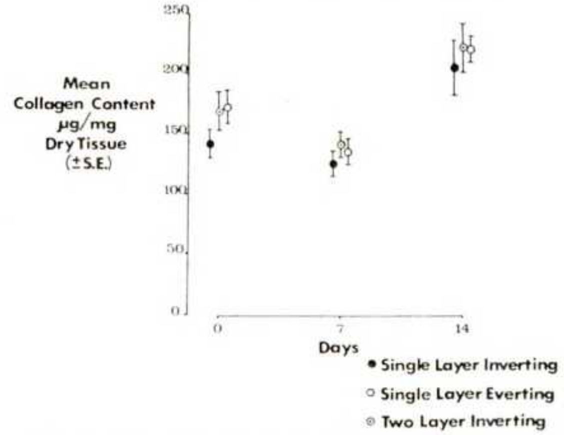
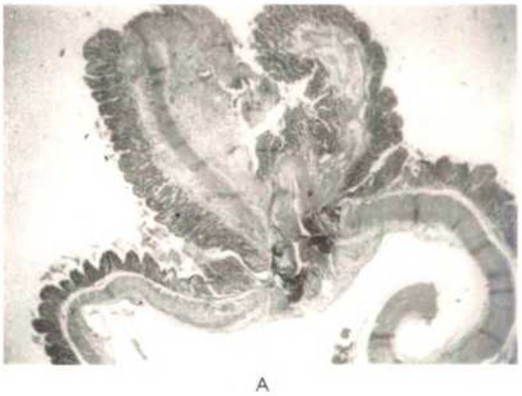


FIG. 5.—Mean collagen content (± S.E.) of the three types of anastomosis. The figures for the single-layer inverting group are the mean results of 10 animals on day 7 and 7 animals on day 14 and the corresponding numbers of animals in the two-layer group on these days are 11 and 6, and in the everting group, 10 and 9. The results in each group obtained on day 0 are measurements of normal colon resected at operation in the animals which were sacrificed subsequently on the seventh day.

Anastomotic Stenosis.—*Fig.* 3 shows the degree of stenosis found on radiological assessment of 21 single-layer inverting anastomoses, 17 two-layer inverting anastomoses, and 16 everting anastomoses. Measurements made on completion of the anastomosis showed that the everting suture produced less narrowing of the bowel than the two methods of inversion but, surprisingly, this difference was not apparent on subsequent assessment and the results at 7, 14, 21, and 28 days showed no difference between the three types of anastomosis.

Bursting Pressure.—*Fig.* 4 shows the mean colonic bursting pressure for the animals in the three groups sacrificed at 0, 7, and 14 days. The everting anastomosis was significantly weaker than both types of inverting anastomosis on the day of surgery ($P < 0\cdot05$) and the tensile strength of the everting anastomosis had actually diminished by 7 days after operation, whereas the bursting pressure had increased by this time in both types of inverting anastomosis and the latter were significantly stronger than everting anastomoses at 7 days ($P < 0\cdot001$) and 14 days ($P < 0\cdot01$). Rupture of the intestine on testing occurred invariably through normal bowel adjacent to the anastomosis at 14 days after both types of inverting suture, but there was no difference between single-layer and two-layer inverting anastomoses with respect to tensile strength.



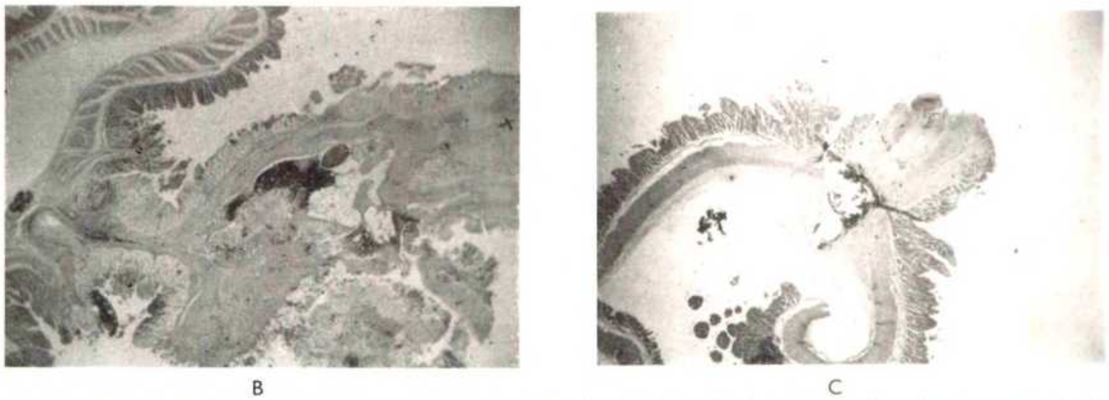


FIG. 6.—The variable degree of necrosis observed in the inverted cuff of tissue at 7 days after the two types of inverting anastomosis. In (A) most of the inturned tissue has survived in a single-layer inverting anastomosis but significant necrosis is shown in the single-layer anastomosis in (B), and (C) shows a two-layer anastomosis in which most of the tissue has sloughed. H. and E. (× 2·7.)

Collagen.—*Fig.* 5 shows the collagen content of the anastomoses in the three groups of animals sacrificed at 7 and 14 days after operation and the results are compared with the collagen content of the normal colon obtained at operation in the animals which were killed subsequently at 7 days. The mean collagen content of the three types of anastomosis at

7 days after operation was slightly lower than the control value in normal colon, but by 14 days the collagen content had increased beyond the values obtained in normal colon. However, there was no difference between the three types of anastomosis with respect to collagen content at 7 or 14 days.

Table II.—HISTOLOGICAL FEATURES OF THE THREE TYPES OF ANASTOMOSIS ASSESSED AT 7, 14, 21, AND 28 DAYS AFTER OPERATION WITH RESPECT TO COLLAGEN AND MUCOSAL UNION AND, IN THE CASE OF THE INVERTING ANASTOMOSES, THE PRESENCE OR ABSENCE OF SIGNIFICANT NECROSIS IN THE INVERTED CUFF OF TISSUE

HISTOLOGICAL FEATURE	DAY OF SACRIFICE AND TYPE OF ANASTOMOSIS											
	7 Days			*14 Days*			*21 Days*			*28 Days*		
	1	2	EV	1	2	EV	1	2	EV	1	2	EV
Necrosis of more than 50 per cent of inturned cuff of tissue	7	8	—	4	4	—	2	2	—	1	—	—
Collagen union present	9	8	4	7	6	7	3	2	3	2	—	2
Mucosal union present	0	0	0	2	2	0	1	1	0	2	—	2
Number of animals	11	11	10	7	6	9	3	2	3	2	0	2

1, Single-layer inverting anastomosis. 2, Two-layer inverting anastomosis. EV, Everting anastomosis.

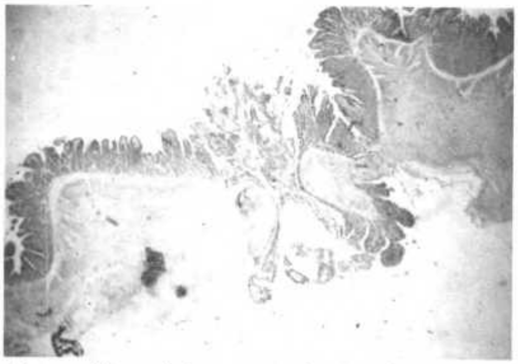


FIG. 7.—The typical appearance of an everting anastomosis at 7 days showing non-union of mucosa and connective tissue. H. and E. (× 2·7.)

Histological Features.—*Table II* shows the histological features of the three types of anastomosis assessed at 7, 14, 21, and 28 days after operation with respect to connective-tissue and mucosal union and, in the case of the inverting anastomoses, the presence or absence of significant necrosis in the inverted cuff of tissue. Some evidence of collagen union across the anastomosis was observed in the majority of single-layer and two-layer inverting anastomoses at 7 days and collagen union was present in all the inverting anastomoses by 14 days after operation. However, mucosal union in inverting anastomoses was less rapid and was not invariably present at 21 days after surgery. Examination of the inturned cuff of tissue in inverting anastomoses showed no difference between the single-layer and two-layer methods and *Fig.* 6 shows that a variable amount of tissue necrosis occurred with both methods of suture.

Connective-tissue and mucosal union in everting anastomoses was much delayed by comparison with the inverting methods of suture. *Fig.* 7 shows the typical appearance of an everting anastomosis at 7 days and there is no definite evidence of connective-tissue or mucosal union.

DISCUSSION

A controlled clinical trial comparing everting and inverting methods of suture in the colon (Goligher and others, 1970) demonstrated that everting anastomoses are prone to disruption and this has been amply confirmed in the present study. The tensile strength and healing of everting anastomoses in the rabbit colon were distinctly inferior to those found in inverting anastomoses and similar observations have been reported in previous experimental studies (Loeb, 1967; Hargreaves and Keddie, 1968; Mellish, Ty, and Keller, 1968; Gill, Fraser, Carter, and Hill, 1969; Trueblood, Nelson, Kohatsu, and Oberhelman, 1969; Abramowitz and Butcher, 1971). It is surprising, perhaps, that the collagen content of everting anastomoses, many of which were leaking or in close proximity to peritoneal sepsis, was no different from that found in inverting anastomoses, but Hawley (1972) found that the total collagen or hydroxyproline content of an anastomosis was not significantly altered in the presence of anastomotic dehiscence since increased lysis of mature collagen was matched by an increased rate of collagen synthesis in such cases.

An inverting method using two layers of sutures is usually recommended for intestinal anastomosis (Goligher, 1967; Muir, 1969; Turnbull and Kyle, 1969), but there is no clinical evidence which would indicate that this technique is any better than an inverting method using one layer of sutures. Indeed, Halsted (1887) suggested that a single layer of inverting sutures was the most acceptable method of intestinal anastomosis, and Gambee and others (1956) advocated this method, based on their clinical experience of 153 single-layer anastomoses. Moreover, Letwin and Williams (1967) showed that the single-layer inverting method gave better results than the two-layer method in the small bowel of the dog and they claimed that the amount of vascular damage and tissue necrosis was less in single-layer anastomoses. Similarly, the studies of Hamilton (1967), Gill and others (1969), and Orr (1969) moved these authors to recommend the single-layer inverting anastomosis as the safest method and the one least likely to interfere with the vascularity of the suture line. However, there have been few studies of single-layer and two-layer inverting anastomoses in the colon of experimental animals and it is significant, perhaps, that

McAdams and others (1970) found no difference between these methods in the dog colon.

In the present study of the rabbit colon we have found no difference between the two types of inverting anastomosis with respect to their tensile strength, collagen content, and the incidence of tissue necrosis and anastomotic complications. However, it would be wrong to dismiss the single-layer method on the basis of these results since there are important differences between man and the experimental animal with regard to intestinal anastomosis. Thus, the size of the suture material used in the experimental anastomosis is relatively greater than that which obtains in man, and the degree of luminal obstruction produced by inversion in the intestine of animals is similarly greater than that which is apparent in the human colon. Accordingly, the final decision regarding the merits of the single-layer inverting anastomosis must await the results of properly controlled clinical trials.

The results of a randomized, prospective, clinical trial comparing single-layer and two-layer inverting anastomoses are described on p. 457 of this JOURNAL.

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A RANDOMIZED PROSPECTIVE CLINICAL TRIAL OF SINGLE-LAYER AND TWO-LAYER INVERTING INTESTINAL ANASTOMOSES

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SUMMARY

Most surgeons recommend an inverting technique for anastomosis of the intestine using two layers of sutures, but it has been suggested that greater safety would be achieved by using an inverting method which involves only a single layer of sutures.

Single-layer inverting and standard two-layer inverting intestinal anastomoses were compared in a randomized prospective clinical study of 60 patients. A similar incidence of anastomotic dehiscence and obstructive complications occurred after both types of anastomosis and it was concluded that single-layer methods of anastomosis do not possess qualities which surpass the standard two-layer method.

MOST surgeons recommend that end-to-end anastomosis of the intestine should be accomplished by inversion of the cut edges of the bowel using two layers of sutures (Grey Turner, 1955; Dunphy and Pikula, 1959; Goligher, 1967; Muir, 1969; Turnbull and Kyle, 1969). There can be little doubt that inversion is necessary in intestinal anastomosis (Goligher, Morris, McAdam, de Dombal, and Johnston, 1970), but Halsted (1887) suggested that this can be achieved with the greatest safety by using a technique which involves only a single layer of sutures and some surgeons have been favourably impressed by the results of single-layer methods of anastomosis (Gambee, Garnjobst, and Hardwick, 1956). However, experimental studies of single-layer and two-layer inverting anastomoses have produced conflicting results and there have been no randomized clinical trials comparing these two methods.

Anastomotic dehiscence and serious, sometimes fatal, septic complications associated with the standard two-layer method of anastomosis remain a source of concern and it seemed logical to assess the merits of single-layer inverting anastomoses in a randomized prospective clinical trial, comparing this method with the standard two-layer method.

METHODS

Sixty patients undergoing resection with end-to-end anastomosis of the small or large intestine during the course of emergency or elective operations were studied and the method of anastomosis used in each case was allocated randomly. Thirty-one patients (17 males and 14 females) had a two-layer anastomosis and 29 patients (12 males and 17 females) were given a single-layer anastomosis. The average ages of the patients in the two-layer and single-layer groups were 57 years (S.D. ± 19) and 64 years (S.D. ± 13) respectively.

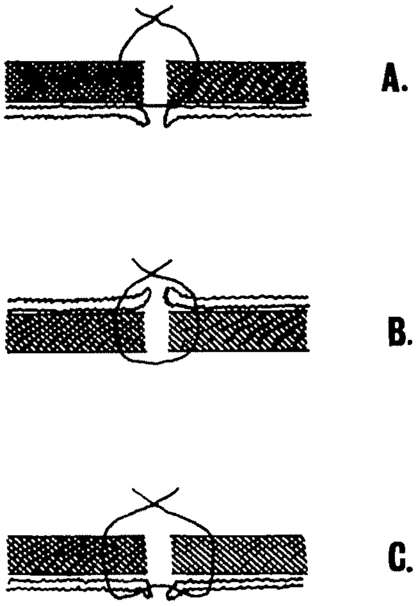

FIG. 1.—The methods used in single-layer inverting intestinal anastomoses. A, Submucosal suture. B, Suture inserted from the mucosal aspect through all the coats of the bowel. C, Gambee suture.

All the patients underwent intestinal preparation for 5 days prior to elective surgery. Mechanical preparation consisted of the daily administration of enemata and magnesium sulphate, and a single dose of castor oil was given on the day preceding operation. Diet was restricted to liquids only for 24 hours prior to surgery and intestinal antiseptics were used routinely in conjunction with mechanical bowel preparation. Phthalylsulphathiazole was administered daily for 5 days and kanamycin was given during the 48 hours prior to surgery.

The standard two-layer inverting anastomosis needs little description and, in our hands, consisted of an inner layer of continuous chromic catgut, including all coats of the bowel wall, and an outer layer of interrupted Lembert sutures, using silk as the suture material. The techniques used for single-layer inverting anastomoses are depicted in *Fig.* 1. Vertical, interrupted, atraumatic silk sutures were used in all cases. In 12 cases a submucosal suture (A) was used throughout. In 6 cases the posterior aspect of the anastomosis was made with sutures inserted from the mucosal aspect of the bowel through all the coats and knotted on the mucosa (B), and a submucosal suture (A) was used for the anterior aspect of the anastomosis. In the remaining 11 cases method B was used for the posterior layer but a Gambee suture (Gambee and others, 1956) was used for the anterior aspect of the anastomosis (C). The technique used in each case was left to the discretion of the surgeon.

The radiological appearance of the anastomosis was assessed by a barium-enema examination on the fourteenth postoperative day in all the surviving patients, with the exception of 1 patient who had undergone small-bowel resection, and anastomoses involving the rectum were also examined by sigmoidoscopy on the tenth postoperative day.

RESULTS

Similarity of the Groups.—The nature of the pathology, types of operation, and various other clinical features which may be of relevance to the success or failure of anastomotic healing were assessed in patients treated by single-layer anastomosis and in those given a standard two-layer anastomosis to determine whether or not these two groups of patients could be regarded as well matched.

Table I.—PATHOLOGY IN THE TWO GROUPS OF PATIENTS UNDER STUDY

PATHOLOGY	SINGLE-LAYER INVERTING ANASTOMOSIS		TWO-LAYER INVERTING ANASTOMOSIS	
	No.	Per cent	No.	Per cent
Carcinoma	17	59	13	43
Crohn's disease	5	18	6	20
Benign tumour	0	0	2	6
Diverticular disease	2	7	2	6
Loop colostomy	2	7	5	16
Mechanical obstruction	1	3	2	6
Intestinal infarction	1	3	1	3
Tuberculosis	1	3	0	0

Table II.—VARIOUS TYPES OF OPERATION IN THE TWO GROUPS OF PATIENTS UNDER STUDY

OPERATION	SINGLE-LAYER INVERTING ANASTOMOSIS		TWO-LAYER INVERTING ANASTOMOSIS	
	No	Per cent	No.	Per cent
Small-bowel resection	0	0	1	3
Right hemicolectomy	17	59	13	42
Transverse colectomy	0	0	1	3
Left hemicolectomy	2	7	3	10
High anterior resection	7	24	7	23
Subtotal colectomy and ileorectal anastomosis	1	3	1	3
Colostomy closure	2	7	5	16

Table III.—INCIDENCE OF VARIOUS CLINICAL FEATURES WHICH MAY BE OF RELEVANCE IN ANASTOMOTIC HEALING IN THE TWO GROUPS OF PATIENTS UNDER STUDY

CLINICAL FEATURE	SINGLE-LAYER INVERTING ANASTOMOSIS		TWO-LAYER INVERTING ANASTOMOSIS	
	No.	Per cent	No.	Per cent
Obesity	13	45	9	29
Anaemia (haemoglobin <12 g per 100 ml)	5	17	4	13
Steroid therapy	1	3	2	6
Palliative operation for carcinoma	5	17	3	10
Emergency operation	5	17	5	16
Defunctioning colostomy	2	7	2	6
Faecal loading of bowel or intestinal obstruction	12	41	11	35
Faecal soiling at operation	4	14	3	10
Peritoneal sepsis at operation	2	7	4	13
Postoperative antibiotic therapy	9	31	8	26

Table I shows the various types of pathology encountered in the two groups. Carcinoma of the colon and Crohn's disease were the most common indications for surgery and it is apparent that the two groups were similar with regard to pathology.

In *Table II* the incidence of the various types of surgical operation is compared in the two groups. The operation most frequently performed in each group was right hemicolectomy and it can be seen that the two groups were well matched with respect to the various surgical operations although there was a slightly higher incidence of colostomy closures in the group treated by two-layer anastomosis.

Table IV.—MORTALITY AND INCIDENCE OF ANASTOMOTIC DEHISCENCE IN THE TWO GROUPS OF PATIENTS UNDER STUDY

	SINGLE-LAYER INVERTING ANASTOMOSIS		TWO-LAYER INVERTING ANASTOMOSIS	
	No.	Per cent	No	Per cent
No of cases	29	—	31	—
No. of deaths	3	10	3	10
Clinical evidence of anastomotic dehiscence	2*	7	3*	10
Subclinical anastomotic dehiscence	3	10	2	6
Total incidence of anastomotic dehiscence	5	17	5	16

* Died as a result of anastomotic dehiscence.

Table V.—NATURE OF THE PATHOLOGY AND THE TYPES OF OPERATION IN 10 PATIENTS WHO DEVELOPED CLINICAL OR SUBCLINICAL EVIDENCE OF ANASTOMOTIC DEHISCENCE

ANASTOMOSIS	AGE AND SEX		PATHOLOGY	OPERATION	RESULT
Single-layer	64	F	Crohn's disease	Right hemicolectomy	Peritonitis—death
Single-layer	72	F.	Carcinoma	Subtotal colectomy	Peritonitis—death
Single-layer	66	F.	Diverticular disease	Left hemicolectomy	Subclinical dehiscence
Single-layer	54	M.	Carcinoma	Left hemicolectomy	Subclinical dehiscence
Single-layer	71	F.	Carcinoma	High anterior resection	Subclinical dehiscence
Two-layer	75	M.	Carcinoma	Right hemicolectomy	Peritonitis—death
Two-layer	71	M.	Intestinal infarction	Right hemicolectomy	Peritonitis—death
Two-layer	68	F.	Carcinoma	Colostomy closure	Peritonitis—death
Two-layer	67	M.	Carcinoma	High anterior resection	Subclinical dehiscence
Two-layer	69	M.	Carcinoma	High anterior resection	Subclinical dehiscence

In *Table III* the incidence of various clinical features which may be of relevance in anastomotic healing is compared in the two groups. Again, it appears that the groups were well matched. There was little difference between the two groups with regard to the incidence of obesity, anaemia, steroid therapy, palliative and emergency operations, defunctioning colostomy, faecal loading of the bowel and intestinal obstruction, faecal soiling and peritoneal sepsis at operation, and postoperative antibiotic therapy.

Mortality and Incidence of Anastomotic Dehiscence.—*Table IV* shows the mortality and incidence of anastomotic dehiscence in the two groups of patients given a single-layer or standard two-layer anastomosis. The mortality in each group was 10 per cent. One patient in the single-layer group died of respiratory complications on the twelfth postoperative day but there was no clinical evidence of anastomotic dehiscence in this case. Two deaths in the single-layer group and 3 deaths in the two-layer group resulted from anastomotic dehiscence and a further 3 cases in the single-layer group and 2 cases in the two-layer group were shown to have subclinical anastomotic dehiscence on postoperative barium-enema examination. Thus, the total incidence of anastomotic dehiscence was 17 per cent in the single-layer group and 16 per cent in the two-layer group.

Table V shows the nature of the pathology and the types of operation in the 10 patients who developed clinical or subclinical evidence of anastomotic dehiscence. Carcinoma was the pathology involved in 7 of the 10 cases, but anastomotic disruption was not confined to any one particular operation and occurred after anastomosis of the right colon, left colon, and rectum, and in 1 case after colostomy closure.

Postoperative Ileus or Mechanical Obstruction.—Six patients in each group developed ileus or some degree of mechanical intestinal obstruction during the postoperative period. In each group 3 of the patients who developed ileus also had either clinical or subclinical evidence of anastomotic disruption. No patient in either group required a further laparotomy for persisting mechanical obstruction.

DISCUSSION

An inverting technique using two layers of sutures is usually recommended for anastomosis of the intestine (Grey Turner, 1955; Dunphy and Pikula, 1959; Goligher, 1967; Muir, 1969; Turnbull and Kyle, 1969), but Halsted (1887) suggested that an inverting method employing only one layer of sutures provided the greatest margin of safety and some surgeons have been impressed by the results of single-layer inverting anastomoses. Gambee and others (1956) found that anastomotic complications accounted for a mortality of only 3 per cent in a study of 153 single-layer anastomoses, and Beling (1957) observed no complications in his series of 60 cases treated by single-layer anastomosis. Buchin and Van Geertruyden (1960) concluded that the single-layer inverting anastomosis was associated with a lower incidence of anastomotic disruption and postoperative intestinal dysfunction by comparison with the standard two-layer method, on the basis of a retrospective analysis of 437 anastomoses, of which 133 were single-layer anastomoses. However, there has been no comparison of the two methods in controlled clinical trials and rather conflicting results have accrued from experimental studies. Letwin and Williams (1967) showed that single-layer inverting anastomoses in the small bowel of the dog resulted in less tissue destruction and anastomotic disruption by comparison with two-layer anastomoses. Similarly, Orr (1969) compared single-layer and two-layer small-bowel anastomoses in the dog and he observed less tissue destruction and more rapid healing after single-layer anastomosis. On the other hand, McAdams, Meikle, and Taylor (1970) were unable to detect any significant difference between single-layer and two-layer inverting anastomoses in the colon of the dog and the incidence of anastomotic disruption was slightly higher after single-layer anastomoses. Similarly, we have found no difference between single-layer and two-layer inverting anastomoses in the rabbit colon with regard to tensile strength, collagen content, histological features, and the incidence of septic complications (*see* p. 453 of this JOURNAL).

In the present study the incidence of anastomotic complications associated with the single-layer method was not significantly different from that encountered with the standard two-layer method in a controlled clinical trial. Clinical or subclinical evidence of anastomotic dehiscence occurred in 17 per cent of single-layer anastomoses and in 16 per cent of two-layer anastomoses, and similarly there was no difference between the two methods of anastomosis with regard to postoperative obstructive complications. The patients treated by these two methods were well matched with respect to age, pathology, and the types of operation performed, and other clinical features such as peritoneal sepsis, faecal loading of the bowel, and faecal soiling which may be of particular relevance in the breakdown of intestinal anastomoses (Goligher, Graham, and de Dombal, 1970; Hawley, 1970; Dunphy, 1971), were evenly distributed between the two methods. It appears, therefore, that there was no bias which favoured either method of anastomosis.

The results of the present study imply that single-layer inverting methods of anastomosis do not possess qualities which surpass the standard two-layer method and it seems unlikely that the continuing problem of anastomotic disruption would be affected significantly by the more liberal use of the single-layer method in clinical practice.

Acknowledgements.—We are grateful to Miss Jane Horrocks and Mr. F. T. de Dombal for invaluable assistance in the computer-assisted analysis of the results.

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AETIOLOGY OF DISRUPTION OF INTESTINAL ANASTOMOSES

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SUMMARY

Various factors have been cited in the aetiology of disruption of intestinal anastomoses but their relative clinical importance is uncertain.

A retrospective study was made of 204 patients treated by resection and standard end-to-end anastomosis of the intestine.

Clinical evidence of anastomotic dehiscence occurred in 14 per cent of cases and the incidence of dehiscence was significantly increased in cases where faecal loading of the bowel obtained and after operations involving low anterior resection of the rectum or surgery for fixed tumours. The presence of a defunctioning colostomy did not remove the threat of anastomotic complications. A significant reduction in preoperative plasma proteins was found in patients who developed anastomotic dehiscence and the incidence of disruption was highest in patients over the age of 60 years.

RECENT experimental and clinical studies have suggested that numerous factors may compromise healing of colonic anastomoses. Thus, anastomotic technique, shock, peritoneal sepsis, inadequate bowel preparation, inexpert surgery, the nutritional status of the patient, and the nature of the operation must all be considered (Goligher, Graham, and de Dombal, 1970; Goligher, Morris, McAdam, de Dombal, and Johnston, 1970; Hawley, 1970; Whitaker, Dixon, and Greatorex, 1970; Dunphy, 1971; Daly, Vars, and Dudrick, 1972), but the relative clinical importance of these different aspects is uncertain.

In an attempt to elucidate the factors which may be of most importance in clinical practice to the success or failure of anastomotic healing we have reviewed the case records of patients undergoing intestinal resection with anastomosis in the Professorial Surgical Unit, Leeds General Infirmary, during the period 1968–72.

METHODS

The case records of 204 patients undergoing intestinal resection with anastomosis in the Professorial Surgical Unit at the Leeds General Infirmary during the period 1967–72 were studied. A standard method of end-to-end anastomosis of the intestine was used in all the cases, namely, double-layer inversion using continuous chromic catgut for the inner layer which incorporated all the coats of the bowel wall and interrupted silk for the outer layer of Lembert sutures. A further 62 cases underwent intestinal anastomosis during this period but were not included in the study as everting or single-layer methods of suture were used.

The patients underwent intestinal preparation for 5 days prior to elective surgery. Mechanical bowel preparation consisted of the daily administration of enemata and either magnesium sulphate or liquid paraffin by mouth. Castor oil was administered on the day preceding surgery in most cases and diet was restricted to liquids only for 24–48 hours prior to operation.

Intestinal antiseptics were used routinely in conjunction with mechanical bowel preparation. Phthalylsulphathiazole was administered daily for 5 days prior to surgery and, in most cases, broad-spectrum antibiotics in the form of kanamycin or neomycin were given during the 48 hours preceding operation.

The findings on postoperative barium-enema and sigmoidoscopic examinations in patients who had undergone resections of the left colon or rectum were available only in a proportion of cases and it was clearly impossible to document fully the incidence of subclinical anastomotic breakdown. Accordingly, we have studied only the clinical incidence of anastomotic dehiscence and every case of dehiscence described in the present study had unequivocal evidence of anastomotic breakdown *shown either by a faecal fistula or at further laparotomy for peritonitis.*

RESULTS

Mortality and Anastomotic Dehiscence.—The operative mortality in the 204 cases was 6·5 per cent. There was clinical evidence of anastomotic dehiscence in 28 cases (14 per cent) and this complication accounted for the fatal outcome in 10 of these patients.

Table I.—OPERATIONS PERFORMED IN 203 CASES AND THE RELATED INCIDENCE OF ANASTOMOTIC DEHISCENCE

OPERATION	NO ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE	PERCENTAGE DEHISCENCE
Small-bowel resection	14	2	13
Right hemicolectomy	52	7	13
Left hemicolectomy	10	0	0
High anterior resection	64	9	12
Low anterior resection	27	9*	25
Subtotal colectomy and ileo-rectal anastomosis	8	1	11

* Significantly higher incidence of dehiscence compared with the cumulative incidence of dehiscence after the other operations ($\chi^2 = 3·985$, $P < 0·05$)

The 204 cases comprised 98 males and 106 females, but the incidence of anastomotic disruption was virtually identical for each sex.

One patient died of a ruptured aortic aneurysm within 72 hours of operation and this case has been excluded from further study.

Type of Operation.—*Table I* shows the operations performed on the 203 cases and the respective incidence of anastomotic dehiscence. The term 'high anterior resection' implies that a colorectal anastomosis was performed above the reflection of the pelvic peritoneum, whereas 'low anterior resection' refers to cases in which the anastomosis was made below the pelvic peritoneum using rectum devoid of a serosal coat. A significantly higher incidence of anastomotic dehiscence was encountered after the latter operation compared with the cumulative incidence of dehiscence after all the other operations ($\chi^2 = 3{\cdot}985$, $P<0{\cdot}05$).

Fourteen per cent of the 203 patients underwent emergency operations involving resection of small bowel or the right colon, but there was no difference between emergency and elective operations with respect to anastomotic dehiscence. Likewise, 34 per cent of the operations were performed by junior staff, usually of senior registrar status, but the incidence of anastomotic dehiscence was not increased in such cases.

Table II.—INDICATIONS FOR SURGERY IN 203 CASES AND THE RELATED INCIDENCE OF ANASTOMOTIC DEHISCENCE

INDICATION FOR SURGERY	NO ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE
Carcinoma of colon	90	17
Benign tumour	8	0
Polyposis coli	3	0
Diverticular disease	24	5
Crohn's disease	34	3
Intestinal strangulation or infarction	15	2
Ileocaecal tuberculosis	1	1

Table III. RELATIONSHIP BETWEEN AGE AND ANASTOMOTIC DEHISCENCE

AGE (yr)	NO . ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE	PERCENTAGE DEHISCENCE
<60	91	7	7
>60	84	21*	20

* Significantly higher incidence of dehiscence in patients over the age of 60 ($\chi^2 = 6{\cdot}075$, $P<0{\cdot}02$).

Indications for Operation.—*Table II* compares the indications for surgery in the 203 cases with the respective incidence of anastomotic dehiscence. The most common conditions requiring operation were carcinoma of the colon or rectum, Crohn's disease, and diverticular disease, but there was no significant difference between the different types of pathology with respect to the incidence of anastomotic dehiscence.

Age.—*Table III* shows the relationship between age and anastomotic dehiscence. More than 50 per cent of the patients were over 60 years of age and the incidence of anastomotic breakdown in such cases was significantly higher than that encountered in patients below the age of 60 years ($\chi^2 = 6{\cdot}075$, $P<0{\cdot}02$).

Plasma Proteins.—*Table IV* shows the relationship between preoperative plasma-protein estimations and anastomotic dehiscence. Plasma-protein results were available in 106 cases and 17 of these developed anastomotic disruption. Patients who developed disruption had significantly lower total protein ($t = 2{\cdot}987$, $P<0{\cdot}01$) and plasma-albumin values ($t = 3{\cdot}499$, $P<0{\cdot}001$).

Malignant Disease.—The extent of the disease in 107 cases of carcinoma of the colon or rectum is compared with the incidence of anastomotic dehiscence in *Table V*. In all the cases information was available regarding the presence of metastases at operation, the opinion of the surgeon regarding the radical or palliative nature of the operation, and the extent of spread on pathological examination of the specimen using the criteria of Dukes (1940). Hepatic or peritoneal metastases were present in 24 per cent of cases and the operation was thought to be definitely palliative in 22 per cent of cases. Fifty-seven per cent of cases were classified as Dukes Stage C on pathological examination. It can be seen that the incidence of dehiscence was highest in those patients who had metastases, palliative operations, or Stage C lesions but none of these trends is statistically significant. In 16 cases the surgeon was uncertain regarding the radical nature of the operation because of the local extent of the tumour, and if these dubiously radical or 'uncertain' operations and the definitely palliative excisions are each compared with the radical operations it is apparent that there is a significantly higher incidence of anastomotic dehiscence in the former group ($\chi^2 = 5{\cdot}422$, $P<0{\cdot}02$).

Table IV.—CORRELATION BETWEEN PREOPERATIVE PLASMA PROTEINS (MEAN ± S.D.) AND ANASTOMOTIC DEHISCENCE

PLASMA PROTEIN	NO ANASTOMOTIC DEHISCENCE ($n = 89$)	ANASTOMOTIC DEHISCENCE ($n = 17$)	P
Total protein (g per 100 ml)	7 2±0·76	6·6±0·53	<0 01
Albumin (g per 100 ml)	3·9±0 52	3 4±0·71	<0 001

Table V.—ANASTOMOTIC DISRUPTION IN RELATION TO PALLIATIVE OR RADICAL OPERATIONS, THE PRESENCE OR ABSENCE OF METASTASES, AND THE EXTENT OF SPREAD ON PATHOLOGICAL EXAMINATION OF THE BOWEL IN 107 CASES OF LARGE-BOWEL CANCER

	NO ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE	PERCENTAGE DEHISCENCE
Metastases			
None	71	10	12
Hepatic and/or peritoneal metastases	19	7	27
Palliative surgery			
Radical	61	6	9
Palliative	18	6	25
Uncertain	11	5	31
Pathology (Dukes staging)			
'A' cases	10	0	0
'B' cases	32	4	13
'C' cases	48	13	21

Fixation of Bowel.—*Table VI* shows the relationship between fixity of the bowel at operation either by tumour or inflammation and the incidence of anastomotic dehiscence. The incidence of dehiscence was significantly higher after operations for carcinoma where the bowel was adherent to the parietes or other viscera compared with cases in which fixation of the bowel did not obtain ($\chi^2 = 11{\cdot}468$, $P<0{\cdot}001$).

Bowel Preparation, Faecal Soiling, and Peritoneal Sepsis.—In *Table VII* anastomotic dehiscence is correlated with the mechanical state of the bowel and the presence of faecal soiling and peritoneal sepsis at operation. Poor mechanical bowel preparation was associated with a significantly higher incidence of anastomotic dehiscence ($\chi^2 = 10{\cdot}252$, $P<0{\cdot}01$), but there is no evidence that faecal soiling or peritoneal sepsis contributed towards anastomotic complications.

Table VI.—RELATIONSHIP BETWEEN ANASTOMOTIC DEHISCENCE AND FIXITY OF THE BOWEL BY TUMOUR OR INFLAMMATION

FIXATION OF BOWEL	NO ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE	PERCENTAGE DEHISCENCE
No fixation	119	11	8
Fixation by tumour	23	11*	32
Fixation by inflammation	33	6	15

* Significantly higher incidence of dehiscence compared with no fixation ($\chi^2 = 11{\cdot}468$, $P<0{\cdot}001$)

Table VII.—ANASTOMOTIC DEHISCENCE CORRELATED WITH THE EFFICIENCY OF MECHANICAL BOWEL PREPARATION AND THE PRESENCE OF FAECAL SOILING OR PERITONEAL SEPSIS AT OPERATION

	NO ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE	PERCENTAGE DEHISCENCE
Mechanical bowel preparation			
Well prepared	116	9	7
Badly prepared or obstructed	59	19*	24
Faecal soiling at operation			
No soiling	154	22	13
Soiling	21	6	22
Peritoneal sepsis			
No sepsis	151	24	14
Sepsis	24	4	14

* Significantly higher incidence of anastomotic dehiscence compared with well-prepared cases ($\chi^2 = 10\,252$, $P<0\,01$)

Table VIII.—INCIDENCE OF ANASTOMOTIC DEHISCENCE IN 119 PATIENTS TREATED WITH OR WITHOUT A DEFUNCTIONING COLOSTOMY

	NO ANASTOMOTIC DEHISCENCE	ANASTOMOTIC DEHISCENCE	PERCENTAGE DEHISCENCE
Colostomy	42	10	19
No colostomy	59	8	12

Drains.—Intraperitoneal drains were placed routinely in the vicinity of the anastomosis with the exception of 12 cases. Two patients in the latter category developed clinical evidence of anastomotic disruption but the numbers are insufficient to warrant critical analysis.

Defunctioning Colostomy.—*Table VIII* shows the incidence of anastomotic dehiscence in 119 patients treated by resection of the left colon or rectum with or without a temporary defunctioning transverse colostomy. A colostomy was performed in 52 cases, but the incidence of disruption in this group was similar to that encountered in the group treated without a colostomy. However, it cannot be concluded that a defunctioning colostomy afforded no protection since it was reserved frequently for cases which might be expected to do badly. Thus, the incidence of low anterior resection was significantly higher amongst colostomy patients ($\chi^2 = 41{\cdot}921$, $P<0{\cdot}001$) and the cumulative incidence of poor mechanical bowel preparation, fixed tumours, peritoneal sepsis, and faecal soiling was also significantly higher in colostomy cases ($\chi^2 = 6{\cdot}975$, $P<0{\cdot}01$).

DISCUSSION

The results of recent studies on anastomotic healing imply that a wide variety of factors may be involved in the aetiology of anastomotic disruption. Thus, the methods of preoperative bowel preparation (Rosenberg, Graham, de Dombal and Goligher, 1971), faecal loading of the bowel (Goligher, Graham, and de Dombal, 1970), the use of intraperitoneal drains (Manz, La Tendresse, and Sako, 1970), the role of faecal contamination and peritoneal sepsis (Hawley, 1970; Rosenberg and others, 1971), and the relationship between blood-loss (Whitaker and others, 1970) and anastomotic healing have all come under scrutiny as well as consideration of the nutritional status of the patient (Daly and others, 1972) and attention to surgical technique (Dunphy, 1971). The present study of 204 patients treated by a standard method of end-to-end anastomosis of the intestine has identified the relative clinical importance of several of these aspects.

We previously suggested (Goligher, Graham, and de Dombal, 1970; Rosenberg and others, 1971) that poor mechanical preparation of the bowel was associated with an increased incidence of anastomotic disruption and this impression has been confirmed in the present study which has shown a highly significant correlation between faecal loading and anastomotic dehiscence. The clinical importance of preoperative antiseptics in colonic surgery has been demonstrated previously (Rosenberg and others, 1971) and need not be considered here since all the patients undergoing elective surgery in the present study were given antiseptics in conjunction with preoperative mechanical bowel preparation.

Hawley (1970) showed that faecal soiling and peritoneal sepsis significantly impaired the healing of colonic anastomoses in experimental animals and our earlier studies on smaller numbers of patients tended to support this thesis (Goligher, Graham, and de Dombal, 1970: Rosenberg and others, 1971). The present study has not confirmed that these factors are of significance in the aetiology of anastomotic disruption, but it should be noted that prophylactic broad-spectrum antibiotics were administered routinely in cases complicated by sepsis or faecal soiling at operation, and in the latter part of the study peritoneal lavage with antibiotic solutions was employed in a proportion of such cases. Thus, it is conceivable that such measures may have prevented anastomotic complications.

Low anterior resections of the rectum were associated with a significantly higher incidence of dehiscence compared with the other operations under study and it seems that the extraperitoneal rectum is less suited for anastomosis than the intraperitoneal rectum or colon. Examination of our results shows that the high incidence of dehiscence is not explained by an unduly large number of poor mechanical bowel preparations or fixed tumours in cases treated by low anterior resection.

Palliative operations and operations for the more advanced colonic tumours were associated with an increased incidence of anastomotic breakdown, but this trend was of statistical significance only in the cases where the tumour was actually adherent to the parietes or other viscera. It is interesting to relate this association between anastomotic disruption and the surgery of fixed tumours to some recent experimental and clinical studies. Conolly, Hunt, Sonne, and Dunphy (1969) found that the incidence of wound infection in experimental animals was increased after major surgical trauma, and Hawley (1970) showed a similar relationship between surgical trauma and lysis of mature collagen in the colon of experimental animals. In man Whitaker and others (1970) found that the incidence of anastomotic disruption was increased after operations which involved major blood-loss and they postulated that intra-operative shock and intestinal ischaemia interfered with anastomotic healing. Clearly, the relationship between surgical trauma and anastomotic healing is worthy of further investigation.

The significance of age as an aetiological factor in anastomotic disruption is uncertain. A significantly higher incidence of disruption was found in patients over the age of 60 years, but this may reflect merely the higher incidence of fixed tumours and low anterior resections in this age-group.

There seems little doubt that the nutritional status of the patient is relevant in the healing of intestinal anastomoses. A significant correlation was shown in the present study between hypoproteinaemia and anastomotic disruption, and Daly and others (1972) found that protein depletion in experimental animals significantly impaired the healing of colonic anastomoses.

The results of the present study amply confirm the common impression that a number of factors are involved in the aetiology of anastomotic dehiscence and the practical implications are considerable. Inadequate mechanical bowel preparation is involved in a significant proportion of cases and it seems likely that improved methods of mechanical preparation of the colon would result in a reduced incidence of anastomotic disruption. Our results have clearly shown that the presence of a defunctioning colostomy does not completely remove the threat of anastomotic dehiscence, but the precise value of a proximal colostomy needs to be evaluated in a randomized prospective trial. Improvement in the nutritional status of patients undergoing intestinal anastomoses may also prove worth while, but this too must be evaluated and further investigations are necessary to determine the factors which compromise anastomotic healing after extensive surgical procedures.

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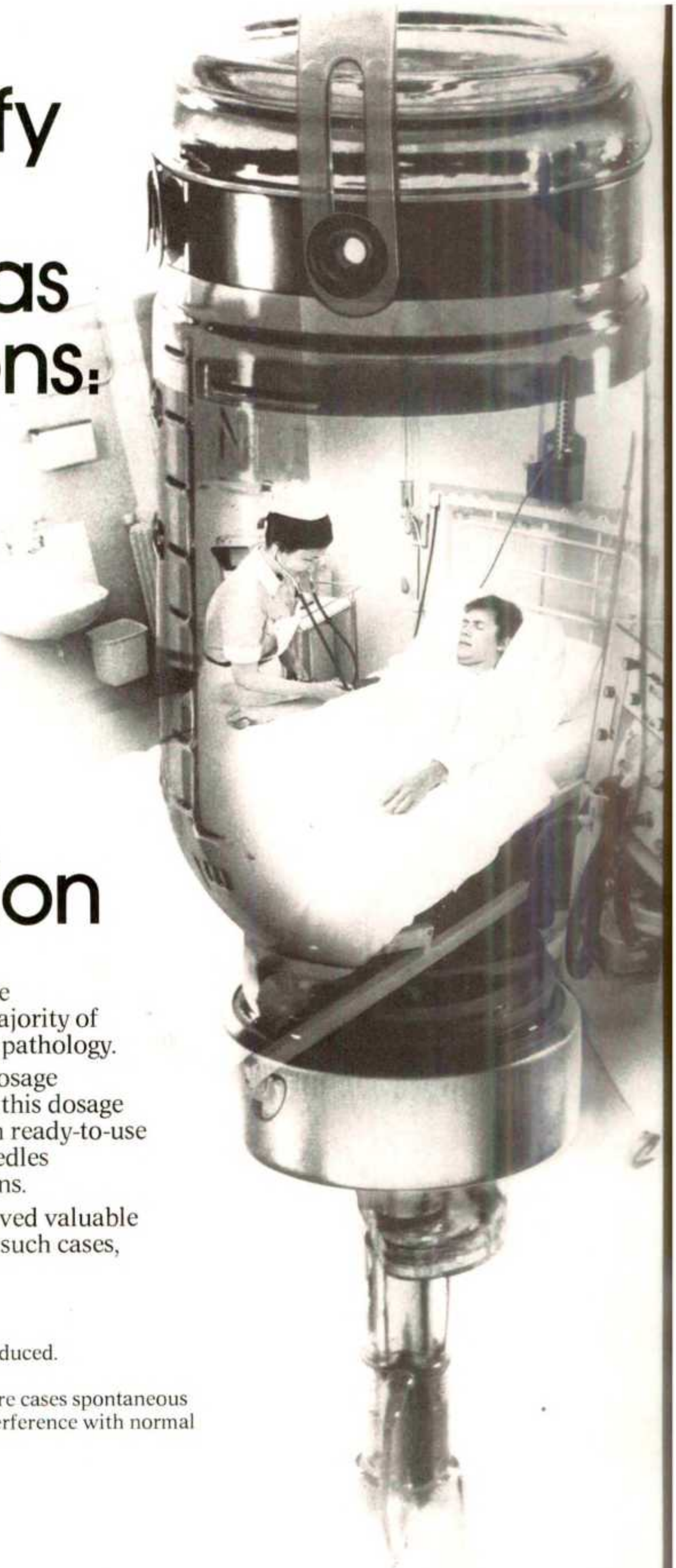

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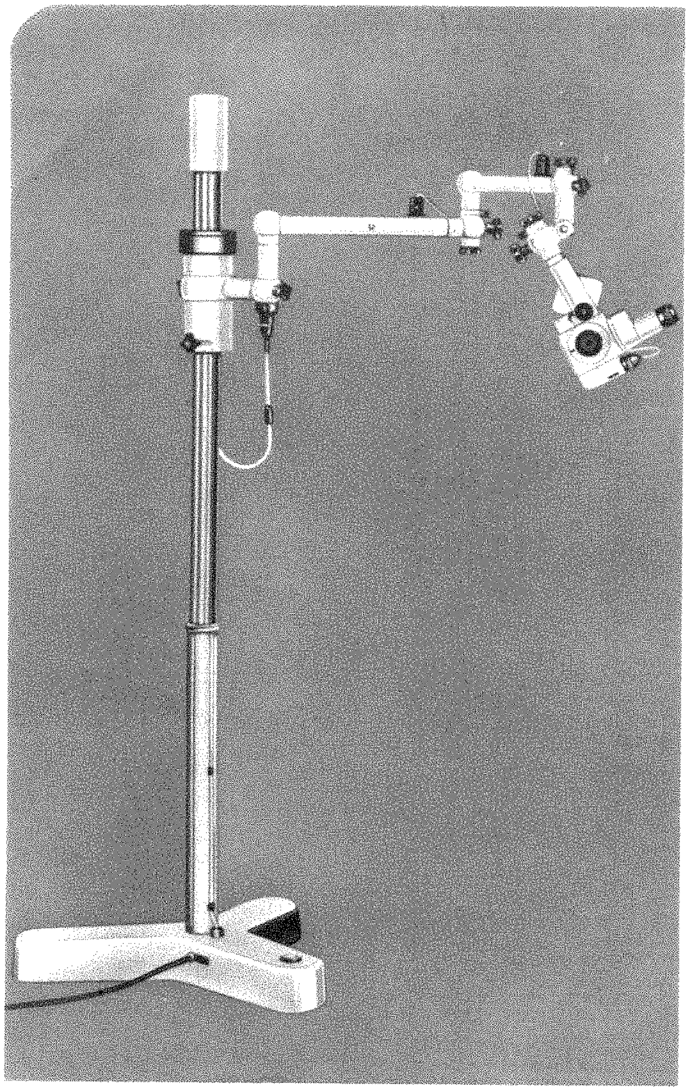

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NON-MALIGNANT BREAST MASSES IN AN AFRICAN POPULATION

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SUMMARY

The clinical manifestation of non-malignant breast masses in an African population is presented. The pattern of disease is affected by many factors, among which are social habits, poverty, and ignorance. The problems of diagnosis and treatment are discussed. Ulcerating benign masses simulate advanced malignancies and no hasty conclusion should be made on the latter without histological proof or evidence of distant metastases. There may be an indication for mammary amputation in some diseased pendulous breasts.

It is generally accepted that the incidence of cancer of the breast is lower in Africa and Asia than in Europe and North America (Doll, 1969; De Waard, 1969). While the causes of breast cancer continue to elude us, a number of aetiological factors are being closely examined with conflicting conclusions. Such factors include hormonal status (Bulbrook, Hayward, Spicer, and Thomas, 1962; Bulbrook and Hayward, 1967), genetic make-up (Macklin, 1959), marital status, parity, lactational habits, social class, and nutrition (Graham, Levin, and Lilienfeld, 1960; MacMahon and Feinleib, 1960; Lilienfeld, 1963; De Waard, 1969). Whatever part these factors play in mammary carcinogenesis, relatively little attention has been paid to other pathological effects that they may have on the breast. While the lower incidence of breast cancer in Africa and the clinical pattern may be due to complex social factors unrelated to the causation of the disease it is worth while to look more closely at the pattern of non-malignant breast masses in this environment with a view to seeing if similar differences exist.

MATERIALS FOR STUDY

One hundred and fifty-two non-malignant breast biopsies examined at the University College Hospital, Ibadan, in a 3-year period between 1969 and 1971 were studied. Fifty unselected case histories were also available for detailed clinical evaluation. The nomenclatures and histological criteria were based on those recommended by the World Health Organization International Reference Centre for the Histological Definition and Classification of Breast Tumours (1968).

FINDINGS

Frequency.—In the years under review 15,706 biopsy samples were examined in the Department of Pathology of the University College Hospital. The non-malignant breast mass biopsies therefore constitute about 0·8 per cent of the total number of biopsies. This compares with 166 cases of carcinoma of the breast recorded at the Cancer Registry of the hospital over the same period.

Age and Sex.—There were 139 females to 13 males in this series. The age range of the patients was 13–72 years. The average age of the patients with benign mammary dysplasia (B.M.D. group) was 32 years, while patients with benign or apparently benign tumours (fibro-adenoma group) had an average age of 22 years. Eighty per cent of the fibro-adenoma group presented by the third decade of life as compared with 50 per cent of the B.M.D. group.

Other Clinical Features.—The majority of the patients were educated women and can be considered more sophisticated than the average Nigerian female of the same age-group. About 50 per cent of the women were married and parity ranged between 0 and 9. Sixty per cent of the women were nulliparous. The length of history varied between 1 week and 10 years and the duration of symptoms in 48 per cent of the patients was less than 6 months. Twenty-two per cent of the patients were lactating at the time of the clinical examination. The masses were equally distributed in both breasts and were bilateral in 10 per cent of cases. There were two or more lumps in one breast in 8 per cent of the cases and 12 per cent had ulceration of the overlying skin.

Pathology.—*Table I* shows the histological diagnoses in the patients studied. The size of tumour excised varied between 1 and 28 cm. in diameter and the weight range was 1–4400 g.

Table I.—HISTOLOGICAL DIAGNOSIS OF BENIGN BREAST MASSES IN 152 NIGERIANS

DIAGNOSIS	NO. OF CASES	PERCENTAGE (APPROX.)
Group A		
Benign mammary dysplasia	61	40
Group B		
Benign or apparently benign tumours	65	43
Chronic abscesses	14	9
Others (epidermal inclusion cyst, parasitic cyst, galactocele, tuberculosis, etc.)	12	8
Total	152	100

Of the 65 cases with benign or apparently benign tumours, 60 were fibro-adenomas most of which had mixed intra- and pericanalicular patterns. The weight range of the fibro-adenomas was 1–2320 g. with an average of 129 g. Ten of the 13 males had unilateral 'idiopathic' gynaecomastia.

DISCUSSION

The pathology of non-malignant breast affections in an African population has attracted little attention. The literature on them has been scanty and textbooks have, at best, been vague and often silent. By general clinical experience the foregoing analysis is a considerable underestimate of the frequency of inflammatory breast disease. This is accounted for by the fact that the majority of breast infections resolve spontaneously or respond to warm applications or self-medication of antibiotics. This, however, does not invalidate the results of the present review since our motivation was to document breast masses which are non-cancerous in a tropical environment.

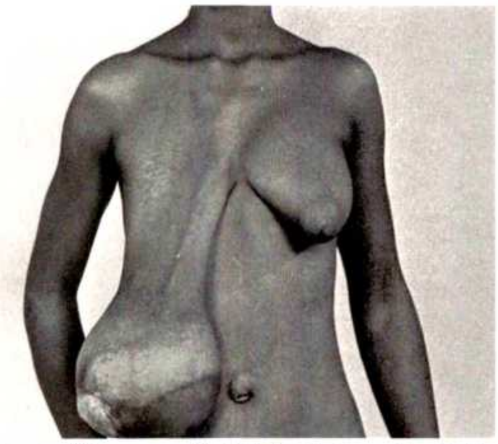

FIG. 1.—This 25-year-old girl had noticed a swelling in the right breast for 2 years. It got rapidly bigger during pregnancy and ulcerated shortly before her confinement following topical applications. She presented with a 'fungating' breast mass and ipsilateral axillary lymphadenopathy. The photograph was taken after a course of antibiotics. Lymph-node biopsy showed 'non-specific' reactive hyperplasia. Histology of the excised breast mass showed fibro-adenoma

Fibro-adenoma.—The commonest benign mammary mass was a fibro-adenoma which constituted 39·5 per cent of the total number of excised specimens. Templeton (1971) reported 56 fibro-adenomas out of 168 non-malignant histological specimens examined in Mulago Hospital, Kampala, Uganda: this was an incidence of 33·3 per cent. We agree with him that this may represent an underestimate since African women seldom attend hospitals with early, painless disease owing mainly to socio-economic reasons. It is therefore not surprising that nurses and students constituted about half the total cases reviewed from a teaching hospital in a university city. It is, however, worthy of note that Ellis (1937) examined the breasts of 140 patients in Bida, Northern Nigeria, and reported that 72 of them had 'nodularity' and 20 had cysts. No mention was made of fibro-adenomas. There are two possible reasons for this: either there were no fibro-adenomas in the cases examined or some of the 'cysts' were fibro-adenomas. It is clear that the overall incidence in this population needs further study.

The age-range of the patients with fibro-adenoma was 13–41 years, giving an average of 22·4 years. This contrasts with an average age of 30 years in 108 cases surveyed by Kinder in the United Kingdom in 1954. This is interesting as it has also been observed that carcinoma of the breast occurs about a decade earlier in Nigeria than in Europe and America (Pearson, 1963).

While 48 per cent of the cases presented within 6 months of discovering a lump in the breast, no less than 22 per cent waited for 18 months or more before seeking medical advice. It therefore is not surprising that over 70 per cent of the cases of carcinoma of the breast in Nigeria present in Stages III and IV (Manchester Classification).

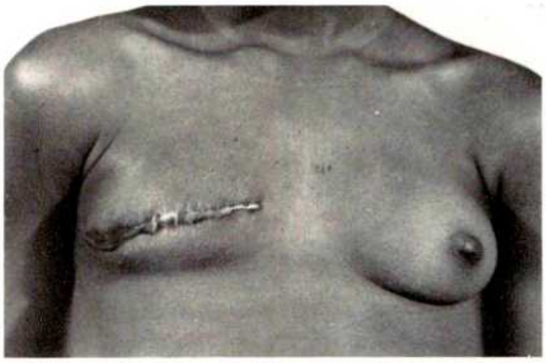

FIG. 2.—This 15-year-old girl presented with a 3-year history of progressive swelling of the right breast which had been 'treated' with topical applications. Extensive skin destruction with sloughing of the nipple made mastectomy inevitable. The tumour was thought to have totally replaced the breast at operation. Note the extent of the hypertrophy of the remnant breast 3 months later.

That fibro-adenomas in Africans are large at the time of clinical presentation has been noted before (Davey, 1968; Edington and Gilles, 1969). The diameters of the fibro-adenomas varied between 1 and 28 cm. and the weight range was between 1 and 2320 g., giving an average of 129 g. This contrasts with fibro-adenomas in the United Kingdom where tumours of more than 2·54 cm. in diameter are seldom seen (Handley, 1964). In 3 of the fibro-adenomas there were areas which examined in isolation could have been described as Brodie's tumour (cystosarcoma phyllodes). We therefore agree with Treves and Sunderland (1951) that microscopic detail and clinical behaviour are the essential criteria in the diagnosis of cystosarcoma phyllodes. Of its many synonyms, 'giant fibro-adenoma' is the most misleading.

Benign Mammary Dysplasia.—Benign mammary dysplasia accounted for 40 per cent of the present series. These were histologically confirmed, thus eliminating the guesswork of clinical examination whereby 'nodularity' is equated with mammary dysplasia. The true incidence in an African population is still unknown. Templeton (1971), by a rough calculation of the population at risk in Uganda, suggested that mammary dysplasia is about five hundred times more common in Europeans and seventy times more common in Asian women than in Africans. The studies of Ellis (1937) in Northern Nigeria in which 51 per cent of his patients had 'nodularity' have been referred to above. He concluded that in Bida 'nodularity' is about twice as common as in England. It would seem that the facts might lie between the two views, considering that of 500 British women examined by D'Abreu in 1935, 28·8 per cent had nodularity of the breast. Our proposed epidemiological survey of breast masses in a fixed village population in Western Nigeria might provide an answer.

The age-range of the patients in this group was 13–63 years, the average age being 31·7 years. This suggests that the patients with benign mammary dysplasia are about 10 years older than patients in the fibro-adenoma group. Where clinical details were

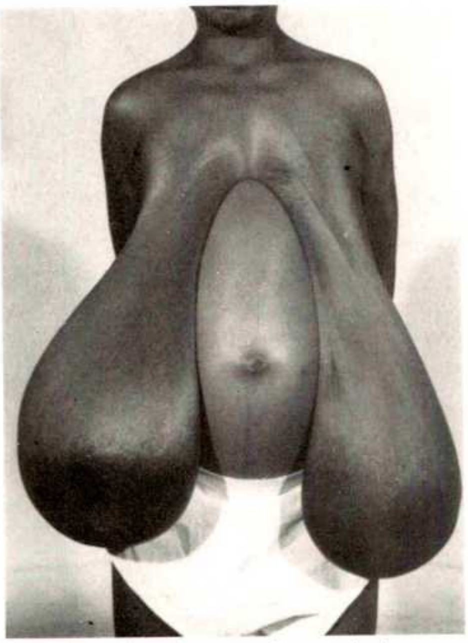

FIG. 3.—Gross bilateral mammary hypertrophy in a 22-year-old girl who was about 30 weeks pregnant. Histology confirmed bilateral benign mammary dysplasia.

available, about 30 per cent of the patients were lactating at the time of clinical presentation. No great significance can be attached to this as the cases under review are few. Although 60 per cent of all the patients in this study were nulliparous and, therefore, had presumably not lactated, about 70 per cent of the patients with benign mammary dysplasia had an average parity of 2. It would therefore seem that benign mammary dysplasia is much more common in patients who have suckled their infants since all African women breast-feed their infants. If that were true one would expect mammary dysplasia to be more common in an African population of high parity in which prolonged lactation is the rule. Since a parity of 2 cannot be considered high, perhaps prolonged lactation may be a contributory factor in the pathogenesis of some mammary dysplasias.

Other Breast Affections.—The other breast affections presenting as masses do not deserve extensive discussion except to note the rarity of tuberculosis of the breast in this series. This is surprising in an environment where tuberculosis is a common disease. In our view tuberculosis of the breast is commoner than it would seem from this series though a 'tuberculoma' of the breast is rare. Breast lesions in miliary tuberculosis are well known (Handley, 1964). While we do not wish to enter into the controversy as to whether primary or secondary tuberculosis of the breast is more frequent, we note that the commonest cause of upper limb lymphoedema in Western Nigeria is tuberculosis (Ngu, 1962). It is likely that not a few of these had lesions originating in the ipsilateral breast which eventually become oedematous following lymphatic obstruction, thus making clinical detection difficult.

DIAGNOSIS AND TREATMENT

The diagnosis of non-malignant breast masses in Nigerians can sometimes be difficult. Such difficulty often arises from late presentation at a hospital, superimposed infection commonly due to tattooing by the 'native doctor', and skin excoriations from powerful topical applications. It is therefore not unusual to see a patient with a benign ulcerating breast mass, *peau d'orange*, and palpably enlarged axillary lymph-glands on the ipsilateral side (*Fig.* 1). A clearly definable edge of the mass should raise a suspicion of a benign mass but this is sometimes not possible where sepsis is considerable. A high index of suspicion, a 'negative' axillary lymph-node biopsy, and response to a short course of antibiotics often provide an answer in a week. Subsequent histological examination of the excised lump would be confirmatory.

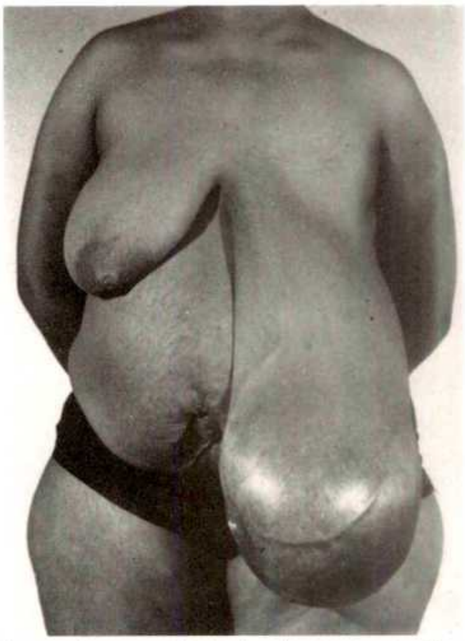

FIG. 4.—A 27-year-old schoolteacher (parity, 3) with a 12-month history of progressive enlargement of the left breast following confinement. The diagnosis was a galactocele.

The problems of treatment are accounted for by skin destruction for the reasons mentioned above. Supplementary to this is the necessity to preserve the breast not only for cosmetic reasons but also for function. The latter reason is especially important as most of the patients are young and suckling is the most satisfactory method of feeding the infant in a predominantly underprivileged society. The balance of judgement should always scale towards conservatism notwithstanding the extent of skin destruction. While 'cosmetic salvage' can often be achieved, 'functional salvage' is usually less successful, especially when the nipple has sloughed.

Large fibro-adenomas should always be shelled out. The initial clinical impression is that of total replacement of the breast by the large tumour. Careful palpation not invariably reveals a compressed rim of normal breast tissue which may quantitatively equal the normal opposite breast. *Fig.* 2 shows a young girl who had a 'mastectomy' for extensive ulceration and destruction of the right breast owing to a fibroadenoma. Note the extent of hypertrophy of the remnant breast after 3 months. Occasional difficulties may arise where the large mass turns out to be a malignant Brodie's tumour. One such case was in a 12-year-old girl in whom the tumour recurred 6 months after enucleation. This was enucleated again and it recurred 10 months later. The patient then had a sector mastectomy and has had no problems for 2 years.

Mammary hypertrophy is not uncommon in parous African women. Some are associated with obesity and others with benign mammary dysplasia (*Fig.* 3), but most are normal. There is no relation to parity, lactational histories, and degree of sophistication. Problems, however, do arise where a pendulous breast is the seat of neglected mammary dysplasia (*Fig.* 4). McIndoe and Dee Rees (1958) held the view that there is no place for amputation in benign breast lesions. Cases of this sort must be the exceptions since it is difficult to accept such breasts as satisfactory organs of lactation or as cosmetically desirable even after the excision of the breast lesions. Any form of mammaplasty in this circumstance is tantamount to amputation.

Acknowledgements.—We are grateful for the co-operation of all our colleagues in the preparation of this paper. Professor A. O. Williams of the Department of Pathology has been most kind. The staff of the University of Ibadan Medical Illustration Unit have been helpful. We thank Mr. T. Odeyale for his secretarial assistance.

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STREPTOKINASE THERAPY IN DEEP-VEIN THROMBOSIS

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R. G. MAHAFFY, and M. ALLARDYCE
ABERDEEN ROYAL INFIRMARY

SUMMARY

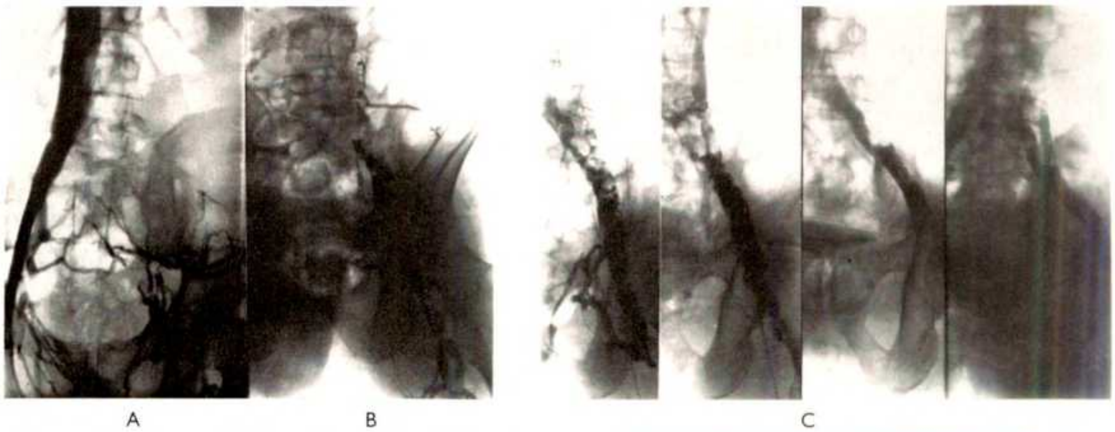
Experience with the use of streptokinase in the treatment of iliofemoral venous thrombosis is described. Streptokinase in a dose sufficient to induce systemic controlled defibrination was administered via an indwelling cannula which was used for repeated phlebography during the course of lysis and for several days afterwards. Of 40 patients treated, 10 had complete clearance and 24 partial clearance of the thrombus with the establishment of an iliofemoral channel. In 5 patients lysis did not occur and in 1 it was followed by early rethrombosis.

Thrombectomy under phlebographic control remains the treatment of choice for non-occlusive iliofemoral venous thrombosis (Mavor, 1971). However, experience suggests that where occlusion is present and of some duration complete operative clearance is more difficult and the incidence of post-thrombectomy rethrombosis rises (Mavor and Galloway, 1969). In this respect in many cases of occlusive iliofemoral venous thrombosis non-occlusive clot has been present for a considerable time before the appearance of symptoms of venous occlusion, so that thrombectomy is inevitably a late procedure in these cases. The use of streptokinase in doses sufficient to induce systemic fibrinolytic activity in the management of rethrombosis following iliofemoral venous thrombectomy has been encouraging (Mavor, Bennett, Galloway, and Karmody, 1969). This has led us to use the drug in the primary treatment of iliofemoral venous thrombosis in selected patients.

This report covers the results of the use of streptokinase both in rethrombosis after venous thrombectomy and for the primary treatment of iliofemoral venous thrombosis.

PATIENTS AND METHODS

A total of 40 patients were given streptokinase: 39 for iliofemoral venous thrombosis (1 bilateral) and 1 for axillary vein thrombosis. Of the 40 patients (16 males and 24 females), 19 had post-thrombectomy rethrombosis. In all these patients an indwelling saphenofemoral catheter had been inserted at the conclusion of thrombectomy; regular follow-up phlebograms through this cannula had shown rethrombosis. The remaining 21 patients (1 with bilateral iliofemoral venous thrombosis) were treated with streptokinase as the initial treatment. Only 1 of the 40 patients had an associated pulmonary embolus. This patient had a massive pulmonary embolus associated with non-occlusive iliofemoral venous thrombosis; this was the only non-occlusive thrombus in the series which was treated with streptokinase as the initial treatment.



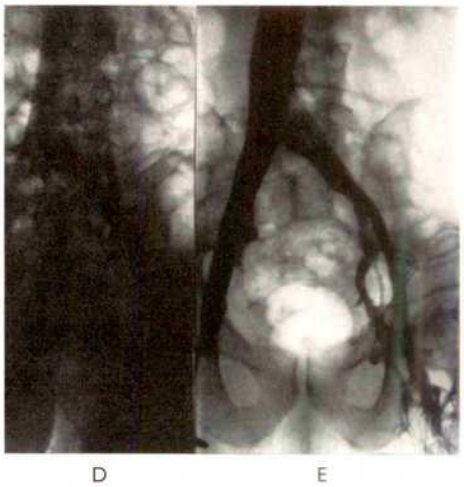


FIG. 1.—Phlebograms showing left occlusive iliofemoral venous thrombosis (A) which was treated by thrombectomy following which rethrombosis occurred (B). Streptokinase was administered and lysis was phlebographically obvious at 8 hours (C) and progressed to restore complete patency by 48 hours (D). This was maintained at the final phlebogram obtained 4 months later (E).

In patients with iliofemoral venous thrombosis streptokinase was administered through an indwelling saphenofemoral catheter by means of a constant-infusion Palmer pump (Mavor and Galloway, 1969). During the infusion of streptokinase phlebography was performed serially to determine the response of thrombus to thrombolytic therapy. After the cessation of streptokinase therapy the cannula was left in situ and heparinized saline (15,000 units in 500 ml. of normal saline in 24 hours) was instilled to maintain patency. Serial phlebograms were obtained for up to 10 days. For the administration of streptokinase and for monitoring the response to thrombolytic therapy in the patient with axillary vein thrombosis a tributary of the basilic vein was used instead of the long saphenous vein.

The titrated dose of streptokinase calculated on the basis of the streptase test was infused over a period of 40 minutes. This was followed by a fixed dose of 750,000 units over the first 4 hours and in each subsequent 8-hour period of treatment until phlebographic evidence of lysis occurred. In 15 cases this régime was modified to a 12-hour infusion with a total dose of 1·5 million units plus the initial dose. Before infusion, streptokinase (Hoechst Pharmaceuticals Ltd., Hounslow, Middlesex) was made up as a solution in 0·9 per cent NaCl at room temperature. The activity of the streptokinase was not measured and the units refer to those given by the manufacturers. It was assumed that the material was stable over the period of infusion. All the patients were given 10 mg. of prednisolone, starting on the day preceding infusion and lasting till the day after infusion was discontinued. Phlebograms were obtained in all the patients before infusion, and then 4, 8, 12, 24, 36, and 48 hours after infusion. Thereafter phlebograms were obtained daily until the cannula was removed 7–10 days after infusion. All the patients were also assessed clinically and phlebographically 4–6 months after streptokinase therapy.

The degree of lysis shown on the phlebogram at 7–10 days was used as a criterion for dividing the patients into three groups. In group 1 complete lysis had occurred (*Fig.* 1). In group 2 lysis had occurred but residual thrombus remained or recurred before the final phlebogram was taken, although a venous channel persisted (*Fig.* 2). In group 3 patients had either no lysis or initial lysis was followed by complete rethrombosis so that no channel remained in the iliofemoral segment. Patients in groups 1 and 2 had a normal leg.

Regular coagulation and fibrinolytic assays were made during and after the infusion of streptokinase to ensure that systemic excess fibrinolytic activity had been produced and that no severe coagulation defect had been induced. Plasma fibrinogen, plasminogen, euglobulin lysis time, Quick one-stage prothrombin time, and thrombin clotting times were measured serially during and for 24–48 hours after the cessation of streptokinase therapy, as described elsewhere (Mavor and others, 1969). Some patients were also given anticoagulant drugs, without apparent effect on the incidence of rethrombosis (Mavor, Dhall, Walker, Dawson, Duthie, and Allardyce, 1973).

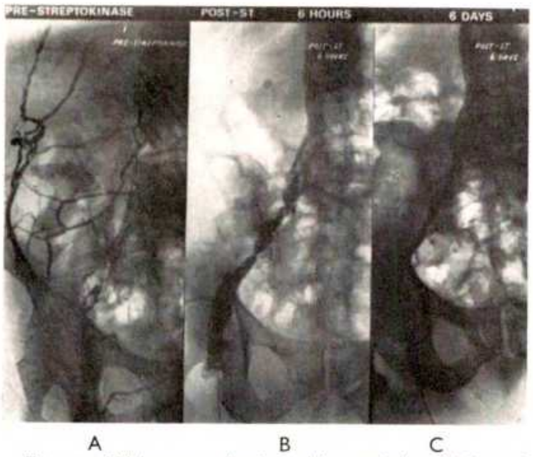


FIG. 2.—Phlebograms showing right occlusive iliofemoral venous thrombosis (A) which was treated with streptokinase following which a channel was established by 6 hours (B) which persisted. C, 6-day phlebogram.

RESULTS

The results of streptokinase therapy are shown in *Tables I–III*, corresponding to the three groups into which the patients were divided according to the final 7–10-day phlebographic assessment.

Table I shows the clinical details of the 10 patients in group 1 who initially had complete clearance of thrombus. Eight of the 10 patients had occlusive and 2 had non-occlusive thrombus at presentation. Five patients had been subjected to thrombectomy for occlusive thrombus; streptokinase was an additional measure to lyse post-thrombectomy thrombus. The details of loading dose (mean 400,000 units; range 100,000–1,000,000 units), total dose (mean 2·5 million units; range 1·6–4·2 million units), and infusion times (mean 23·5 hours; range 12–48 hours) are shown in *Table I*. Although all these patients had complete clearance of thrombus initially, 2 cases were found to have an occluded iliofemoral venous segment at the follow-up phlebogram 4 months later.

Table II shows the clinical details of the 24 patients in group 2. Of the 24 patients, 11 had had thrombectomy and in the remaining streptokinase was the initial treatment. These patients were, therefore, comparable to those in group 1 with respect to choice of initial treatment. Twenty-two cases had occlusive iliofemoral venous thrombosis and the remaining 2 had non-occlusive thrombus for which both patients had had thrombectomy initially. Details of loading dose (mean 190,000 units; range 100,000–500,000 units), total dose (3·65 million units; range 1·2–7·0 million units), and infusion times (mean 33·9 hours; range 8–83 hours) are shown in *Table II*. These patients had larger streptokinase doses over more extended periods of time than those in group 1. It is clear that streptokinase therapy was successful in establishing a patent venous channel in all the patients who presented with occlusive iliofemoral venous thrombosis. In the remaining 2 patients who had had a previous thrombectomy and had started to rethrombose this process was halted by streptokinase so that progression to occlusive thrombus was checked. Phlebographic assessment 4–6 months later showed that of the 24 patients in group 2, 12 remained with a venous channel through the iliofemoral venous segment and the remaining 12 developed occlusive thrombosis. It should be emphasized that of the 12 cases remaining with a channel 4 months later, 10 originally had had complete occlusion.

Table I.—CLINICAL DETAILS OF 10 PATIENTS WHO HAD COMPLETE CLEARANCE OF THROMBOSIS ON THE 7–10-DAY PHLEBOGRAM (GROUP 1)

CASE NO.	AGE AND SEX		STREPTOKINASE		INFUSION TIME (hr.)	COMPLICATIONS
			Loading Dose (units)	Total Dose (units × 10^6)		
1	50	F.	100,000	4·7	47	Profuse bleeding from wound
2	56	M.*	750,000	1·25	12	Nil
3	36	F.	100,000	1·6	12	Nil†
4	50	M.	250,000	2·7	22	Nil
5	63	M.*	100,000	1·6	12	Asthmatic attack requiring cessation of streptokinase
6	42	M.	1,000,000	2·5	12	Wound haematoma
7	29	F.	1,000,000	2·5	12	Nil†
8	48	M.	500,000	4·0	48	Rigors and fever
9	79	F.	100,000	2·35	32	Nil
10	68	M.	100,000	2·05	26	Nil

Cases 6–10 had post-thrombectomy rethrombosis.
* Non-occlusive iliofemoral thrombosis.
† Complete occlusion of the iliofemoral venous segment on the follow-up phlebogram at 4–6 months after streptokinase therapy.

Table III shows the clinical details of the 6 patients classed in group 3. Of these 6 cases, 4 had occlusive and 2 had non-occlusive thrombus. Three patients (2 for occlusive and 1 for non-occlusive thrombus) had had thrombectomy as the initial treatment and thrombolytic therapy was instituted to counteract post-thrombectomy rethrombosis. Five cases showed no lysis whatsoever and in 1 (non-occlusive) the lesion progressed to occlusive clot while the patient was receiving streptokinase. The details of loading dose (mean 275,000 units; range 100,000–1,000,000 units), total dose (mean 2·3 million units; range 1·4–4·6 million units), and infusion times (mean 21·1 hours; range 7–54 hours) shown in *Table III* match closely with those for group 1 patients.

Table II.—CLINICAL DETAILS OF 24 PATIENTS WHO HAD PARTIAL CLEARANCE OF THROMBOSIS ON THE 7–10-DAY PHLEBOGRAM (GROUP 2)

CASE NO.	AGE AND SEX	STREPTOKINASE		INFUSION TIME (hr.)	COMPLICATIONS
		Loading Dose (units)	Total Dose (units × 10^6)		
1	56 F.	100,000	1·6	12	Nil†
2	60 F.	500,000	2·0	12	Nil
3	46 F.	100,000	1·2	8	Septicaemia; streptokinase discontinued†
4	67 F.	100,000	5·3	54	Nil†
5	55 M.	100,000	3·1	29	Nil†
6	38 F.	100,000	4·6	52	Nil
7	36 M.	100,000	3·1	26	Wound haematoma and infection
8	36 M.	250,000	7·0	50	Nil
9	40 M.	100,000	4·6	72	Nil
10	38 F.	100,000	5·63	45	Nausea, rigor, pyrexia, haematoma†
11	58 F.	100,000	2·1	16	Bleeding from cannula site requiring cessation of streptokinase
12	47 F.	100,000	7·5	83	Nil
13	44 F.	250,000	1·75	12	Nil†
14	73 F.	100,000	2·35	28	Nil
15	24 F.*	100,000	7·6	76	Wound haematoma
16	62 F.	100,000	1·6	12	Nil
17	37 F.	250,000	1·7	12	Nil
18	38 M.	100,000	2·35	21	Bleeding from cannula site†
19	55 F.	500,000	3·5	26	Bleeding requiring cessation of streptokinase†
20	54 M.	500,000	5·4	48	Wound haematoma†
21	75 F.	100,000	2·85	27	Nil
22	67 F.	100,000	3·1	28	Wound haematoma
23	57 M.	250,000	3·25	29	Severe wound infection and septicaemia
24	52 M.	500,000	4·5	36	Severe wound bleeding

Cases 14–24 had post-thrombectomy rethrombosis.
* Non-occlusive iliofemoral thrombosis.
† Complete occlusion of the iliofemoral venous segment on the follow-up phlebogram at 4–6 months after streptokinase therapy.

Table III.—CLINICAL DETAILS OF 6 PATIENTS WHO HAD NO CLEARANCE OF THROMBOSIS ON THE 7–10-DAY PHLEBOGRAM (GROUP 3)

CASE NO.	AGE AND SEX	STREPTOKINASE		INFUSION TIME (hr.)	COMPLICATIONS
		Loading Dose (units)	Total Dose (units × 10^6)		
1	25 F.*	100,000	4·6	54	Nil†
2	61 F.	100,000	2·35	20	Nil†
3	37 F.	100,000	1·6	8	Nil†
4	32 F.*	100,000	1·6	12	Nil†
5	52 M.	1,000,000	2·5	12	Rigors†
6	66 M.	250,000	1·4	7	Profound decrease in fibrinogen†

Cases 4–6 had post-thrombectomy rethrombosis.
* Non-occlusive iliofemoral thrombosis.
† Complete occlusion of the iliofemoral venous segment on the follow-up phlebogram at 4–6 months after streptokinase therapy.

GENERAL CONSIDERATIONS

1. Thrombolysis and Age of Thrombus.—In patients who had undergone thrombectomy and had developed rethrombosis, the age of the thrombus was accurately known from the repeated phlebographic assessment during the postoperative period. Nineteen post-thrombectomy patients developed rethrombosis of varying degree and were treated with streptokinase. On phlebographic evidence the thrombus was less than 24 hours old in 7 patients, and in the remaining cases it had a varying age from 24 hours to 10 days. Of the 7 thrombi less than 24 hours old, 5 showed satisfactory thrombolysis, and of the remaining 12 patients with thrombi older than 24 hours, 9 showed successful lysis, 3 being failures. From these results it was apparent that within certain limits the age of thrombus was not a significant factor influencing the onset and extent of lysis.

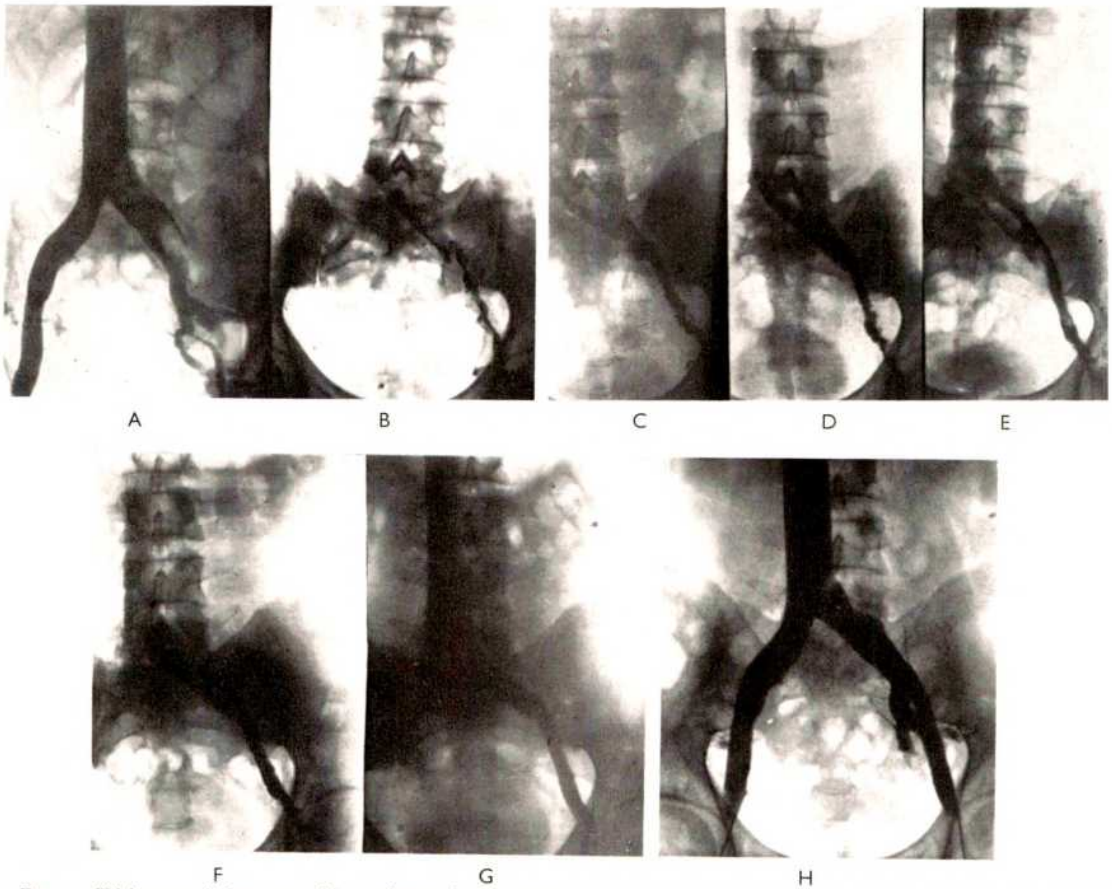


FIG. 3.—Phlebograms before streptokinase therapy by intra-osseous injection (A), and via cannula (B) showing left non-occlusive iliofemoral thrombosis. Streptokinase was administered with resultant progressive lysis at 20, 28, and 45 hours (C, D, and E). Further lysis had occurred by 3 days (F) and complete patency was achieved 11 days after streptokinase therapy (G). A check phlebogram at 4 months showed maintained patency (H).

2. Dosage and Duration of Infusion.—The duration of infusion (*Tables I–III*) was not found to bear a close relationship to the degree of lysis observed phlebographically. Of 15 patients given infusions of 12 hours or less, 5 showed complete lysis (group 1), 6 partial lysis (group 2), and 4 no lysis (group 3). In 1 of the 4 cases with no lysis the infusion was discontinued after 7 hours because the plasma fibrinogen showed a rapid decline from 784 to 183 mg. per 100 ml. In the 11 patients who showed lysis radiological changes were obvious 4 hours after the initiation of treatment. In 1 patient partial rethrombosis occurred after this time and persisted for 9 days, after which complete lysis occurred (*Fig.* 3).

In the remaining 25 patients who were given infusions with a lower initial dosage but a larger total streptokinase dosage (2·1–7·6 million units) over prolonged periods of time (16–17 hours) the maximal lysis also occurred approximately 36–48 hours after the initiation of streptokinase therapy. Thereafter the vein remained patent or rethrombosis commenced and progressed. Administration of these larger amounts of streptokinase did not guarantee eventual lysis. Furthermore, in 1 patient in group 3 complete thrombosis occurred even while the drug was being administered.

3. Complications.—The chief complication of streptokinase therapy was bleeding, usually from the cannula site; this occurred in 10 patients, necessitating the cessation of therapy in 2 cases. Apart from a haematoma in 1 patient who was given a short infusion, bleeding was related to prolonged streptokinase therapy over 12 hours and associated anticoagulant drugs. Rigors, pyrexia, and nausea complicated streptokinase administration in 3 patients, but was not severe enough to require cessation of therapy. In 1 patient an asthmatic attack was precipitated and the infusion was discontinued. Wound infection and septicaemia complicated therapy in 2 patients, requiring discontinuation of treatment in 1. This was undoubtedly due to technical difficulties with the infusion pump and cannula.

In some patients a pronounced but unexplained decrease in the haemoglobin was observed. None of the patients developed evidence of haemolysis or of blood-loss into the gastro-intestinal or genito-urinary tracts.

4. Laboratory Results.—Laboratory measurements of fibrinogen were made serially during streptokinase therapy in order to detect dangerous hypofibrinogenaemia. There was little relationship between haemorrhage and the level of fibrinogen in these 40 patients, but in 1 patient streptokinase therapy was discontinued because of a rapid decrease in fibrinogen. Although there was a rapid massive fall in plasminogen and shortening of the euglobulin lysis time (even when mixed with control plasma), these measurements did not correlate with clinical severe haemorrhage in the patients. Likewise, measurements of plasminogen and euglobulin lysis time did not show a dangerous bleeding state in any patient. The results of the haematological investigations in these patients have been critically evaluated for factors underlying thrombolysis and rethrombosis after streptokinase therapy and these will be described separately (Mavor and others, 1973).

DISCUSSION

Iliofemoral venous thrombosis is a potentially dangerous disease (Mavor and Galloway, 1969; Mavor, 1971) which poses a serious therapeutic challenge. Thrombectomy gives excellent results in the treatment of early non-occlusive venous thrombosis. However, thrombectomy is difficult in many left-sided cases and is contra-indicated in late disease, in cases where recurrent pulmonary embolism has produced severe cardiorespiratory failure, and also in post-thrombectomy rethrombosis. The need to restore venous patency to relieve venous obstruction and to avert pulmonary embolic episodes remains urgent in these patients. The use of thrombolytic therapy with streptokinase in such clinical situations is reported in this paper.

Although the aim in this study was the induction of systemic fibrinolytic activity, the administration of streptokinase via a saphenofemoral cannula takes cognizance of the clinical and experimental evidence which suggests that for its optimal action streptokinase should be delivered into the vicinity of the thrombus (Karmody and Galloway, 1969; Mavor and others, 1969). Furthermore, the in situ cannula allows a readily accessible means of phlebographic observations of the course of lysis. Such visual assessment of the iliofemoral venous segment provides an objective yardstick of success or failure of streptokinase therapy, and if a true measure of benefit of therapy is to be recorded this must be continued for a period of several days beyond the cessation of therapy.

Using such an objective control it has been found that neither preceding surgery nor the age of the thrombus is a critical factor in thrombolysis with streptokinase; in 19 patients with post-thrombectomy rethrombosis the thrombolytic response was almost identical to that in 21 patients with spontaneous venous thrombosis. In the 19 post-thrombectomy patients the age of the thrombus was accurately known from regular follow-up phlebograms. Whether the thrombus was fresh (less than 24 hours) or old (24 hours–10 days) the results of thrombolysis with streptokinase were similar. This finding is in keeping with our clinical experience in patients with iliofemoral venous thrombosis treated initially with streptokinase. In such situations one might expect that a recent thrombus, as judged by a short history, would lyse consistently and readily. However, clinically this is not always so. Conversely, occasionally patients with thrombi several days or even weeks old show rapid and satisfactory lysis; in 1 patient in this series satisfactory lysis occurred in thrombus of over 14 days' duration.

When the patients are divided according to phlebographic criteria into three groups, 34 of the 40 patients following therapy had direct venous drainage into the inferior vena cava either via a normal iliofemoral segment or one with some residual mural thrombus in it. Clinically these 34 patients had a good result. The remaining 6 failed to derive any benefit from the treatment. At present there seems to be no way of predicting the initial response or final result after streptokinase therapy. This stems from an almost complete lack of knowledge of the pharmacology of streptokinase in relationship to thrombolysis. Clearly a factor of major importance is the activity of plasmin on the surface of thrombus and within it. Yet quantitative information regarding penetration of thrombi by streptokinase, plasminogen, and plasmin is lacking. Whether the structural morphology of thrombi plays a role in their susceptibility to lysis by streptokinase is unknown, but presumably diffusion is dependent upon it. Further, the administration of streptokinase by infusion assumes that the material is stable in various vehicle solutions *in vitro* for several hours. Some preliminary studies (Walker, 1972), however, tend to cast doubt on the validity of this assumption. For the present the assessment of the dissolution of thrombi by radiological means constitutes the only clinical measurement of the degree of clot lysis in individual patients.

In comparing the three groups (*Tables I–III*) a large variation will be noted in the loading dose and the total streptokinase dose given. The loading dose was based on the streptase test. This test purports to measure the spontaneous anti-streptokinase antibody in the patient's plasma and the loading dose is adjusted to allow for the neutralization of streptokinase activity. It might have been expected that patients requiring a high loading dose would be resistant to thrombolytic therapy. However, no correlation is apparent between the susceptibility to thrombolysis and the initial titration dose. Furthermore, the final outcome in terms of restoration of complete or partial patency of the iliofemoral venous segment does not correlate with the total dose or with the duration of infusion of streptokinase. In earlier cases a large total dose of streptokinase was administered over an extended period of time in the hope that eventual lysis would occur, but experience has shown that if the thrombus is susceptible to lysis, thrombolysis begins immediately and the results are apparent phlebographically at 4–8 hours. Furthermore, lysis characteristically continues for some time after the cessation of therapy, being generally maximal at approximately 36–48 hours. In some instances complete thrombolysis may be eventually achieved several days after the cessation of therapy. After maximal lysis the vein remains patent, or in some instances where lysis is incomplete, rethrombosis of varying degree occurs, often despite continuing streptokinase infusion. As a result of these observations a smaller total streptokinase infusion dose, lasting 12 hours 40 minutes (loading dose over 40 minutes, then 1·5 million units over 12 hours), was used without compromising the incidence of good results and, when lysis occurred, the final degree of lysis. This may be related to the known adsorption by formed fibrin of plasminogen (Sherry, Fletcher, and Alkjaersig, 1959), which once activated to plasmin seems to retain its activity despite the discontinuation of its activator. On the basis of these observations it has become our practice to standardize the infusion time to 12 hours 40 minutes. This has recently been further modified to an 8-hour 40-minute infusion (40 minutes for the titration dose followed by a fixed dose of 1·5 million units over 8 hours). A short infusion time and small dosage carry important advantages in minimizing the cost. In our experience it is not possible to achieve stable anticoagulant control with drugs such as Warfarin and heparin over this short period and consequently these drugs are omitted from our current practice. Disadvantages do not result from this omission in terms of the incidence of successful lysis or rethrombosis (Mavor and others, 1973). Present evidence suggests, therefore, that streptokinase dosage schedules of 24–48 hours or more are not only unnecessary but also may be harmful in terms of complications, especially when combined with anticoagulant therapy.

That benefits accrue for the patient who has an immediate good response to streptokinase and then maintains complete or partial patency is clear. However, it is surprising that on an objective phlebographic follow-up study 2 of the 10 patients in group 1 and 12 of the 24 patients in group 2 showed complete occlusion of their iliofemoral venous segments 4–6 months after thrombolytic therapy. Certainly, from these results it would seem that the chances of insidious venous occlusion occurring subsequently is related inversely to successful thrombolysis with streptokinase. However, it is possible that the patients may have further thrombotic episodes which are unrelated to their treatment with streptokinase. Nevertheless, the incidence of late rethrombosis at 4 months after successful thrombolysis in these patients is certainly higher than in patients who have undergone thrombectomy for non-occlusive iliofemoral venous thrombosis. These findings indicate the need for further investigation into the problem of rethrombosis.

CONCLUSIONS

1. Streptokinase has been shown to be useful in the treatment of occlusive iliofemoral venous thrombosis.
2. The saphenofemoral catheter technique allows the administration of the drug in the vicinity of the thrombus and also facilitates phlebographic assessment of lysis as required.
3. Lysis of the thrombus starts immediately and is usually maximal 36–48 hours after the initiation of infusion.
4. A short infusion period of 12 hours 40 minutes during which 1·5 million units plus the loading dose are given has been shown to be as effective as an extended infusion period with larger doses. In all cases the streptase test was used to calculate the loading dose.
5. Bleeding was the chief complication and occurred in patients in whom the duration of infusion exceeded 12 hours and in whom anticoagulant drugs had also been administered.

Acknowledgements.—We acknowledge the valuable co-operation of the physicians and surgeons of Aberdeen General and Special Hospitals in referring these patients to us for study and treatment. We are also indebted to Hoechst Pharmaceuticals Ltd. for financial assistance and research grants to one of us (M. G. W.) and for the supply of streptokinase. We would also like to acknowledge the financial assistance of Aberdeen General Hospitals, and the co-operation of the Department of Pathology, Aberdeen University.

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VOLVULUS OF THE CAECUM: CAECOPEXY BY POLYVINYL ALCOHOL SPONGE

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SUMMARY

Six cases of caecal volvulus were encountered. In one, with a gangrenous caecum, a right hemicolectomy was carried out. In the other five, with a viable caecum, caecopexy using a strip of polyvinyl alcohol sponge was carried out. No complications or recurrences have followed this form of treatment.

CAECAL volvulus is a rare but serious type of intestinal obstruction. It comprises less than 1 per cent of all cases of intestinal obstruction. The early diagnosis of volvulus of the caecum is essential to the success of surgical treatment, because delay has the danger of allowing gangrene to occur and thus mortality rises with delay (Villet, 1959; Wolf and Wilson, 1966).

Six cases of caecal volvulus have been encountered. In the first case the caecum was gangrenous and a right hemicolectomy was done. In the subsequent 5 cases caecopexy was performed using a strip of polyvinyl alcohol sponge. No complications or recurrences have followed this form of treatment.

In this paper a method of caecopexy using polyvinyl alcohol sponge is described and the importance of early diagnosis and treatment in volvulus of the caecum is stressed.

CASE REPORTS

Case 1.—A woman aged 48 years presented with severe generalized abdominal pain of 24 hours' duration. She had also vomited and was constipated. She had had a hysterectomy for a fibroid uterus 8 years before. On examination the patient had a distended abdomen with generalized tenderness. On auscultation there were increased intestinal sounds. A plain radiograph of the abdomen showed dilated loops of small intestine. A preoperative diagnosis of intestinal obstruction of unknown nature was made.

Operation was carried out through a right paramedian incision and revealed a volvulus of the caecum. The torsion was in a clockwise direction. Detorsion of the volvulus was carried out. The caecum was gangrenous and therefore a right hemicolectomy with ileotransverse anastomosis was performed. There were no postoperative complications.

Case 2.—A woman aged 30 years in the 28th week of pregnancy presented with abdominal cramping pains, vomiting, and constipation of 2 days' duration. On examination there was generalized mild tenderness which was more marked in the right lumbar region.

A diagnosis of acute appendicitis was made and a laparotomy was performed. A volvulus of the caecum was found. The torsion was in a clockwise direction. Treatment consisted of detorsion and caecopexy with polyvinyl alcohol sponge.

The postoperative course was uneventful and the pregnancy was continued to full term.

Case 3.—A man aged 35 years presented with continuous abdominal pain in the right iliac fossa of 8 hours' duration. Initially the pain had been intermittent and colicky but later it had become continuous. The patient also had nausea and vomiting but he had passed a motion the morning before the onset of the pain. He had had an appendicectomy 3 years earlier.

On examination, the right iliac fossa was distended and somewhat tender. Auscultation of the abdomen revealed increased intestinal sounds. A plain radiograph of the abdomen showed multiple small intestinal fluid levels. A diagnosis of small intestinal obstruction was made with a possibility that it might be caused by a caecal volvulus.

At laparotomy through a right paramedian incision a volvulus of the caecum in a clockwise direction was found. Detorsion of the volvulus revealed a viable distended caecum. Caecopexy with polyvinyl alcohol sponge was carried out. The patient made an uneventful recovery. He was well and symptom-free 8 years after operation.

Case 4.—A man aged 44 years complained of pain in the right iliac fossa of 36 hours' duration with nausea and vomiting. He gave a history of chronic constipation with frequent purgation. On examination he had marked tenderness in the right iliac fossa. A tentative diagnosis of acute appendicitis was made and the abdomen was entered through a McBurney's incision; a volvulus of the caecum was found. The McBurney's incision was closed and a right paramedian incision was made. The torsion was in a clockwise direction. Detorsion and caecopexy with polyvinyl alcohol sponge were carried out. The patient was followed up for 2 years and no recurrence of symptoms occurred.

Case 5.—A woman aged 34 years presented with severe colicky pains in the umbilical region of 24 hours' duration. At first the pains were intermittent, but later they became continuous. She had vomited several times and had had no bowel motion since the onset of the symptoms. She had a history of appendicectomy 10 years before.

On examination the patient had a distended abdomen with generalized tenderness. Auscultation revealed increased intestinal sounds. The patient had had similar symptoms, but of a lesser degree, several times in the past 2 years; the symptoms had usually been relieved by an enema. On the present occasion an enema increased her symptoms markedly and therefore it was decided to perform a laparotomy.

Exploration of the abdomen revealed a volvulus of the caecum in a clockwise direction. The caecum was viable. Detorsion and caecopexy with polyvinyl alcohol sponge were carried out. The patient was followed up for 6 months with no recurrence of symptoms.

Case 6.—A man aged 30 years underwent a difficult appendicectomy, the appendix being pre-ileal and severely inflamed; the appendicectomy operation was lengthy although the caecum was freely mobile. His postoperative course was uneventful and the patient was discharged from hospital on the sixth postoperative day. On the same day the patient complained of severe abdominal colic and vomiting and on examination it was found that he had a distended abdomen with severe tenderness in the right iliac fossa. He was kept under observation for a few hours, but aggravation of his symptoms indicated small intestinal obstruction and abdominal exploration was performed. Volvulus of the caecum was found and the torsion was in a clockwise direction. The caecum being viable, caecopexy with polyvinyl alcohol sponge was carried out. The patient was followed up for more than 1 year after the operation with no recurrence of symptoms.

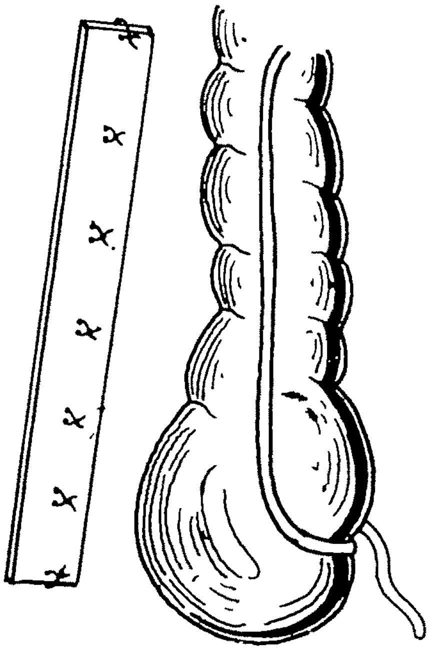

FIG. 1.—Strip of polyvinyl alcohol sponge sutured to the lateral abdominal wall.

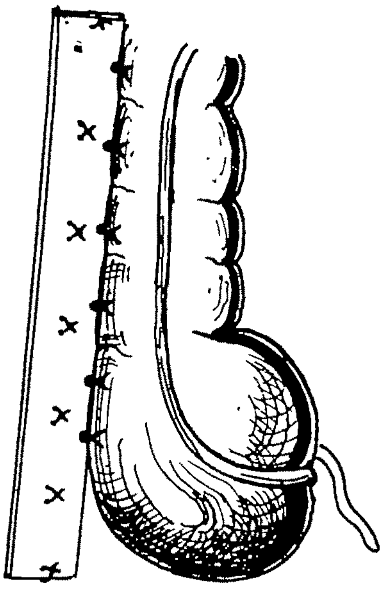

FIG. 3.—Medial layer of sutures completed.

SUMMARY OF CASES

Of the 6 cases in this series 3 were males and 3 were females. Their ages ranged from 30 to 48 years. The duration of symptoms before presentation was from 8 hours to 2 days.

One patient had a history of hysterectomy 8 years earlier and 2 patients had had an appendicectomy several years previously. In 1 case the caecal volvulus followed a few days after appendicectomy. Only 1 patient gave a history of chronic constipation and frequent purgation. One patient was in the 28t week of pregnancy. Recurrent symptoms of caecal volvulus had occurred in 1 case.

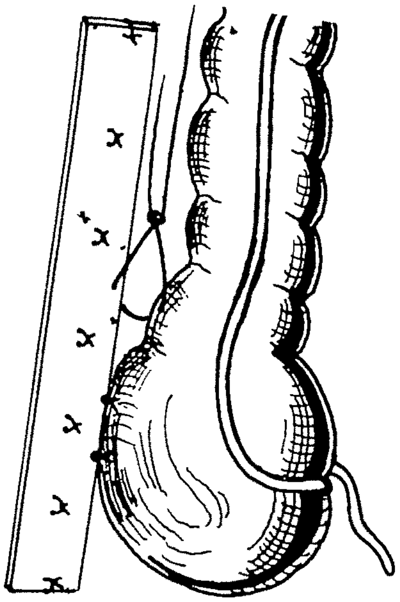

FIG. 2.—Medial layer of sutures being taken

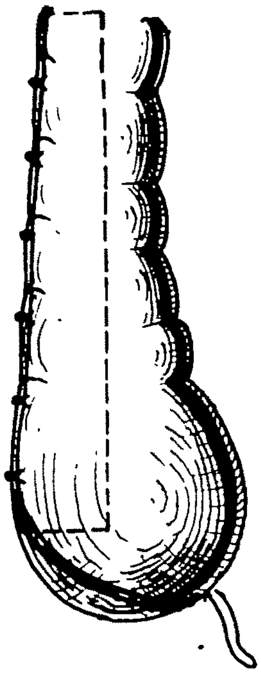

FIG 4.—Lateral layer of sutures completed. The strip of polyvinyl alcohol sponge is completely buried.

Preoperative diagnosis was small intestinal obstruction in 4 cases, with a possibility of caecal volvulus in 1 of them. In the other 2 cases the preoperative diagnosis was that of acute appendicitis.

The torsion in all 6 cases was in a clockwise direction. No distal obstruction was found in any of the cases.

One case was treated by hemicolectomy because of gangrene of the caecum and the other 5 cases were treated by caecopexy with polyvinyl alcohol sponge. None of the 5 cases treated by caecopexy had any recurrence of symptoms, 1 of them being followed for 8 years.

CAECOPEXY WITH POLYVINYL ALCOHOL SPONGE

At laparotomy when the condition of caecal volvulus is diagnosed the distended loop of bowel is decompressed by needle suction and, if the bowel wall is viable and there are no perforations, caecopexy with polyvinyl alcohol sponge is performed.

A strip of polyvinyl alcohol sponge, 4 × 15 cm., is cut, soaked in saline, and fixed along its centre with silk sutures to the lateral abdominal wall, so that it lies parallel to the line of the caecum and ascending colon (*Fig.* 1). Then, using fine silk (00), the medial edge of the polyvinyl alcohol sponge is sutured to the caecum and the proximal part of the ascending colon, including the peritoneum of the lateral abdominal wall in the stitches (*Figs.* 2, 3), with five to six sutures. The lateral edge of the strip is then sutured in the same way to the colon and caecum (*Fig.* 4). On completing this, the strip of polyvinyl alcohol sponge is completely buried lateral to the caecum and ascending colon, attaching them to the lateral abdominal wall. Closure of the abdomen without drainage terminates the operation.

DISCUSSION

Aetiology.—An abnormally mobile caecum is a necessary prerequisite for the development of caecal volvulus. This may occur as a complete malrotation (Holman, 1940; Godfrey, 1945; Butler, 1958; Armitage, 1961) or more commonly as a mobile caecum with an ileocaecal mesentery (Krippaehne, Vetto, and Jenkins, 1967) producing a volvulus by rotation about a fixed point.

Abnormal fixation of the ascending colon by a transverse band (Melchior, 1949; Krippaehne and others, 1967) or by adhesions produced by previous operations may also be predisposing factors. This was not present in any of the cases of this series.

Other precipitating factors associated with caecal volvulus are distension of the caecum by distal obstructing lesions, chronic constipation and frequent purgation (*Case* 4), pregnancy (*Case* 2), and pelvic tumours that displace the caecum upwards. Jordan and Beahrs (1953) suggested that withdrawal of abdominal packs or undue manipulation of the ileocaecal region at operation might precipitate volvulus. In *Case* 6 the volvulus occurred a few days after appendicectomy.

Pathological Process.—Most cases of caecal volvulus twist in a clockwise direction, the caecum passing laterally, then upwards, and finally to the left. In fact, all the cases in this series had twisted in a clockwise direction. Closed-loop obstruction rarely occurs before 180° of torsion, which may be considered physiological provided that there are none of the aetiological factors present. When torsion exceeds 180° two types of rotation may be noted in the included loop of bowel (Gerwig, 1969): twisting of the two segments of bowel one on the other as well as twisting of each part on its longitudinal axis. These two factors combine to effect a closed-loop obstruction. It is not the number of rotations but the tightness of the twist that produces vascular occlusion. As the torsion tightens the first circulatory impairment to the walls of the intestine is venous. The thin walls of the veins in contrast to the thick walls of the arteries are more easily compressed. Occlusion of the venous return is followed by arterial ischaemia with eventual progression to gangrene and perforation.

Clinical Picture.—Caecal volvulus occurs predominantly in the 40–60-year age-group (Meyers, Heifetz, and Baue, 1972). In the present series the ages of the patients were between 30 and 48 years with a mean of 37 years.

A review of the literature has shown that the sex ratio is variously reported as 2 : 1 in favour of females (Villet, 1959) and 3 : 1 in favour of males (Gardiner, 1947). In this series there were 3 males and 3 females.

The signs and symptoms of volvulus of the caecum are essentially the same as those of small-bowel obstruction. The onset is rapid and is generally characterized by severe intermittent colicky pains which are initially closely spaced and then become continuous. Nausea and vomiting occur early. After the existing gas and faeces in the large bowel have been eliminated, absolute constipation ensues. Rectal bleeding is uncommon but has been recorded (May, 1966; Krippaehne and others, 1967).

Frequently a history of milder attacks of similar acute abdominal pain is elicited and suggests a recurrent form of the disease (Villet, 1959). Seventy-three of the 100 patients reviewed by Donhauser and Atwell (1949) had a history of previous subacute or chronic symptoms. These episodes may have been aborted by a change in position or an enema, resulting in forceful elimination of gas or faeces per rectum with dramatic relief of symptoms. One case in the present series (*Case* 5) had this recurrent form of the disease.

The majority of patients on examination have a distended abdomen with tenderness which is most marked in the right lower abdomen. In some cases a large gas-filled loop may be palpated. The location of the segment depends upon the original location of the caecum, the length of the mesentery, and the amount of dilatation in the isolated loop (Gerwig, 1969). Often the loop migrates in the upper abdomen and may simulate gastric retention that can be excluded by passing a nasogastric tube.

A fulminating form of caecal volvulus with a short history of severe pain and tenderness has been described (Hinshaw, Carter, and Joergenson, 1959; Wolf and Wilson, 1966), and at laparotomy gangrene of the caecum is found.

Radiology.—Plain radiography of the abdomen and barium-enema examination would in some cases confirm the diagnosis of caecal volvulus. However, since all the cases present as emergencies operation should not be delayed by waiting for a barium-enema examination to be done.

McGraw, Kremen, and Rigler (1948) have documented the radiological findings, which can be summarized as follows:—

1. The caecum is greatly distended and often presents in an ectopic position. It may be possible to distinguish a caecal from a sigmoid loop by the direction of the gas shadow which faces the left lower quadrant in caecal volvulus and the right lower quadrant in sigmoid volvulus.

Frequently the distended caecum is located in the left upper quadrant of the abdomen where it may be mistaken for gastric retention, especially as both conditions have a single fluid level. Evidence that the shadow is a dilated caecum rather than the stomach may be found in the relative lack of gastric contents on aspiration and by the upright radiograph of the abdomen which usually reveals a separate air-bubble in the stomach.

2. Distended loops of small intestine which are located to the right of the caecal shadow.

3. Demonstration of the ileocaecal valve when the caecum is outlined by gas.

4. A spiral distorsion of the mucosal folds at the site of obstruction.

5. A single fluid level is seen in caecal volvulus in contrast with sigmoid volvulus which usually has two fluid levels.

6. Gas is absent from the transverse colon and beyond.

These radiological signs are not present in every case. Wolf and Wilson (1966) had radiological signs of caecal volvulus from plain radiographs in 13 out of 22 cases, and Dowling and Gunning (1969) in 2 out of 7 cases. In the present series plain radiography was done in 2 cases but in neither case was any of the radiological signs of caecal volvulus apparent.

Barium-enema examination reveals a 'bird's beak' deformity at the site of torsion in the right lower quadrant.

Management.—Emergency surgery is almost always required for all forms of caecal volvulus. The best way to treat caecal volvulus is greatly disputed in the literature. It is advisable to decompress the distended caecum by needle suction so that it can be twisted and its viability assessed.

There is general agreement that when gangrene and perforation of the bowel are present right hemicolectomy is required if the patient's general condition is satisfactory. This was carried out in the present *Case* 1. Exteriorization has been recommended for late cases and where the general condition of the patient is poor (Young, Morrison, and Wilson, 1947).

When the bowel is viable detorsion alone, caecostomy, appendicostomy, caecopexy, and right hemicolectomy have all been recommended.

Detorsion alone, caecostomy, and appendicostomy have not prevented recurrence (Melchior, 1949; Nelson and Bowers, 1956), and indeed caecostomy may provide an axis around which the caecum could rotate. In addition Krippaehne and others (1967) have reported gangrene of the abdominal wall following caecostomy, which is sometimes associated with persistent fistulas that should be formally closed.

Right hemicolectomy is an unnecessarily drastic procedure for a case with a viable bowel. However, it was advised by Melchior (1949) and Meyers and others (1972) because of the high recurrence rate after caecal fixation by sutures. Indeed, Saint (1958) found a completely mobile caecum 1 year after caecopexy by sutures to the lateral gutter. Dixon and Meyer (1948) have suggested a fixation technique whereby an incision is made in the peritoneum of the posterior iliac fossa, creating a retroperitoneal pocket into which the caecum and ascending colon are placed, and the peritoneum is sutured to the anterior taenia coli. Successful treatment by this method has been reported (Nelson and Bowers, 1956; Bell and Powers, 1962) with alleviation of symptoms and no recurrences.

The technique of caecopexy by a strip of polyvinyl alcohol sponge described in this paper is an easy procedure and allows fibrosis to develop between the caecum and ascending colon on the one side and the lateral abdominal wall on the other. No complications or recurrences have ensued in the 5 cases treated by caecopexy in this series.

CONCLUSION

Six cases of caecal volvulus have been operated upon. One had a gangrenous caecum and therefore a right hemicolectomy was carried out. The other 5 cases have been treated by caecopexy using a strip of polyvinyl alcohol sponge to initiate fibrosis between the colon and lateral abdominal wall. No complications or recurrences followed this technique. The importance of early diagnosis and treatment to prevent the development of gangrene of the bowel is stressed.

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TWO CASES OF IDIOPATHIC VOLVULUS OF THE SMALL BOWEL

BY J. C. POSTLETHWAITE AND P. A. DUPONT
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SUMMARY

Volvulus of the entire small bowel about its mesentery without predisposing anatomical defects is rare in the Western world but more common in less developed countries. Two cases are described, the aetiology is discussed, and a valuable diagnostic sign is highlighted. It is suggested that the high mortality is avoidable by prompt diagnosis and early surgery.

VOLVULUS of the small intestine about its mesentery is a well-known complication of congenital defects of gut rotation in both children and adults (Devlin, 1971).

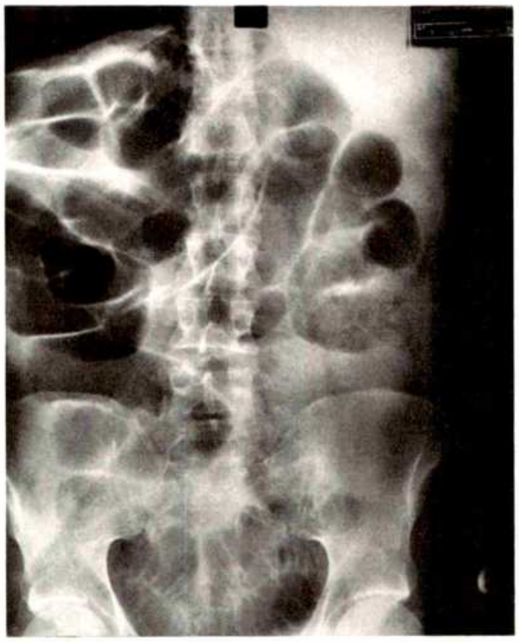

FIG. 1.—*Case* 1. Supine radiograph of the abdomen, demonstrating jejunal bowel pattern in the pelvis.

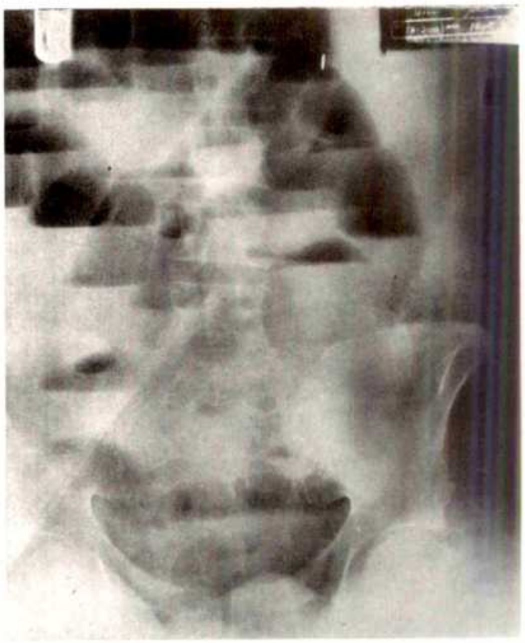

FIG. 2.—*Case* 1. Erect radiograph of the abdomen, demonstrating multiple small-bowel fluid levels.

Primary volvulus occurring without any obvious predisposing cause is rare and is probably decreasing in incidence in Europe and America (Vick, 1932; Walker, 1960), although it is common in India (Agarwal and Singh, 1966), Africa (Kerr and Kirkaldy-Willis, 1946), and Iran (Vaez-Zadeh, Dutz, and Nowrooz-Zadeh, 1969). The cases of primary small-bowel volvulus described here occurred in previously fit Englishmen.

CASE REPORTS

Case 1.—A 31-year-old white Englishman presented as an emergency with a 12-hour history of severe colicky and generalized abdominal pain of sudden onset, accompanied by bilious vomiting. Shortly before the onset of the pain he had consumed 6 pints of beer, as was his habit most evenings. He had a past history of a single hospital admission as a child for undiagnosed abdominal pain.

On examination the patient was distressed, shocked, apyrexial, and in obvious pain. His abdomen, which bore no scars, was distended and uniformly tender, and bowel-sounds were obstructive in type. There were no herniae present, and rectal examination revealed a few soft faeces.

A full blood-count, erythrocyte-sedimentation rate, plasma urea, and electrolytes were all within normal limits. A chest radiograph was normal. Abdominal radiographs (*Figs.* 1, 2) showed distended loops of small bowel and numerous fluid levels. Loops with a jejunal mucosal pattern were seen to lie in the lower half of the abdomen, and the featureless small-bowel pattern occupied the upper half. A clinical diagnosis of acute small-bowel obstruction with probable strangulation was made, and after a short period of intravenous fluid therapy and gastric aspiration the patient underwent laparotomy. He was found to have an 180° anti-clockwise volvulus of the small bowel about its mesentery. The jejunal segment was heavily loaded with fluid and hung down into the pelvis, its mesentery being drawn tautly downwards across the origin of the rest of the small-bowel mesentery. The distal small bowel was displaced upwards into the upper abdomen. There was free blood-stained fluid, and the small bowel was distended and plum-coloured, but viable. The small bowel was deflated and the volvulus was reduced. The anatomy of the small-bowel mesentery was normal. The abdomen was closed without any attempt at enteropexy.

The patient's recovery was marred only by a pneumococcal chest infection, which responded quickly to treatment with antibiotics. He was discharged 10 days postoperatively and has had no further symptoms. A barium-meal and follow-through examination has demonstrated no congenital defects of the alimentary tract.

Case 2.—A 30-year-old white Englishman presented in the Casualty Department, St. Mary's Hospital, London, with a 2-hour history of very severe generalized abdominal pain with colicky exacerbations, the maximal pain being umbilical and to the right of the umbilicus. After admission he had vomited copiously, the vomit being mainly bilious. The patient stated that for the week prior to these severe symptoms he had had vague abdominal pains but no other symptoms. He had no previous medical history or hospital admission.

On examination the patient appeared to be in considerable pain and was obviously in agony during the colicky exacerbations, when he curled up in the left lateral position or in the knee–elbow position. The abdomen was a little distended; there were no scars or herniae. On palpation there was generalized tenderness with an impression of a vague mass to the right of the umbilicus. Bowel-sounds were reduced and obstructive in type. Rectal examination was non-contributory. Haematological investigation revealed haemoconcentration, with a haemoglobin of 22·6 g., packed-cell volume of 71·5 per cent, and blood-urea of 56 mg. per 100 ml. Radiographs of the chest were normal, whilst those of the abdomen revealed dilated obstructed small-bowel loops, mainly to the right of the umbilicus. After rapid rehydration and nasogastric aspiration the patient was submitted to laparotomy 6 hours after the onset of his acute symptoms. A 180° volvulus of the small bowel about its mesentery was found which after reduction revealed that 90 per cent of the small bowel, from a few centimetres from the duodenojejunal flexure to a few centimetres from the ileocaecal region, was distended, black, and gangrenous. No arterial pulsation was found and no other bowel or mesenteric abnormality was noted. Improvement was attempted by conservative methods only and after an hour only minimal improvement was obtained. The abdomen was closed routinely. The patient gradually deteriorated over the next 4 days and died on the fourth day after surgery.

A post-mortem examination was carried out, the pathologist noting irregular ulceration and membranous exudates of the small bowel which he postulated might have predisposed to the volvulus.

DISCUSSION

The aetiology of primary volvulus of the entire small intestine was discussed by Wilms (1906), who considered that mesenteric rotation occurred frequently following food intake. Spasokukozki (1909) considered that bulky poorly digested food accompanied by hypermotility were causative factors. Vaez-Zadeh and others (1969) postulated that the heavily laden jejunum sinks into the pelvis, displacing empty distal bowel upwards, thus initiating rotation of the mesentery. The frequency of the condition in countries in which unprocessed vegetables form a large part of the diet adds strength to this theory (Kerr and Kirkaldy-Willis, 1946).

Spasmodic reports of the condition in England and the United States (McKechnie and Priestly, 1936; Weber, 1945; Walker, 1960; Renton, 1965), however, do not confirm dietary factors as a cause. In the present *Case* 1 it is possible that a high intake of alcohol led to the heavily laden jejunum prolapsing into the pelvis. Marginal abnormality of mesenteric dimension has been described (Vaez-Zadeh and others, 1969) but does not bear critical examination.

Tagart (1950) described the knee–elbow position adopted by sufferers as the 'position of relief', and considered this an important diagnostic sign; this was a prominent finding in the present *Case* 2. *Case* 1 illustrated a useful diagnostic invesgtiation, i.e., the presence of jejunal bowel pattern in the lower abdomen on a plain abdominal radiograph, while the featureless distal small bowel is seen to ride high in the upper half of the abdomen.

Most writers are agreed that the right course of action is to resect any gangrenous bowel, if it is not too extensive, and to return the decompressed intestine without enteropexy (Rowlands, 1929; Woods, 1945; Maingot, 1957). Kerr and Kirkaldy-Willis (1946) described a method of exteriorization and enterotomy to decompress and fix the bowel.

Several reports from Europe, Scandinavia, and the United States quote a high mortality due mainly to late diagnosis (Svane, 1965), which supports a 'look-and-see' policy when faced with signs of unexplained acute obstruction.

Acknowledgements.—We wish to thank Mrs. M. W. Ghilchik and Mr. G. Jantet for permission to publish details of patients under their care and for their interest and advice in the preparation of the text.

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ASSESSMENT OF ACUTE BLOOD-LOSS BY DETERMINATION OF CHANGE IN RED-CELL VOLUME

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SUMMARY

A method is described for the quantitative measurement of acute blood-loss from any source by determination of change in the red-cell volume. The accuracy and sensitivity of this method have been assessed in 23 patients admitted to hospital with acute gastro-intestinal bleeding. The method was sufficiently sensitive to detect a change in red-cell volume of 3 per cent. Reproducible results were obtained, duplicate measurements of red-cell volume deviating from the mean by less than 4 per cent. Completely separate daily measurements, in subjects not undergoing further haemorrhage, deviated from the mean by less than 5 per cent.

THERE is a need for a universally applicable method for the accurate quantitative measurement of blood-loss in order to study the physiological and metabolic changes occurring in patients undergoing acute haemorrhage. We have therefore developed a technique for measuring changes in red-cell volume (R.C.V.). The conventional method of carrying out a single R.C.V. determination using ^{51}Cr-labelled red cells (Sterling and Gray, 1950) has been modified in several respects in order to enable three completely separate R.C.V. measurements to be carried out at daily intervals. We have assessed the accuracy and sensitivity of this method under clinical conditions by studying 23 patients admitted to hospital with acute upper gastro-intestinal bleeding.

MATERIALS AND METHODS

Preparation of Labelled Red-cell Stock.—In order to avoid the need to repeat the time-consuming labelling process, a stock of each patient's labelled red cells was prepared and aliquots were used for daily R.C.V. estimations. Special attention was paid to the dilutions made and extra care was taken with sterile procedures, but otherwise the labelling technique was essentially the same as that described by Mollison and Veall (1955).

Approximately 35 ml. of the patient's blood were placed in a sterile 50-ml. bottle containing 10 ml. of acid–citrate–dextrose solution, and this bottle was used as the stock container. All transfers to and from it were made through a Subaseal stopper using syringes. The red cells were labelled with 120 μc. ^{51}Cr (approximately 1 μg. of Cr as sodium chromate), then washed three times with saline, and finally made up to 40 ml. in saline prior to storage at 4° C. until required for use. The efficiency of the labelling procedure was always greater than 90 per cent.

Subsequent dilutions and volumes taken for injection were adjusted so that the amounts of ^{51}Cr in the second and third injections were respectively about two and four times larger than that in the first injection; the total amount administered in three such injections did not exceed 100 μc. ^{51}Cr. This improved the sensitivity of measuring the radioactivity in circulating red cells following the second and third injections, in the presence of radioactivity from the prior injection, while ensuring that the total body radiation dose was small (<30 mrad).

First R.C.V. Determination.—Five ml. of the stock of labelled red cells (15 μc. ^{51}Cr) were injected using a glass syringe, care being taken to ensure efficient entry of red cells into the circulation. The actual volume injected was later accurately determined by weighing the volume of water required to fill the syringe to the same mark as that used for the red-cell suspension, the average volume being calculated from at least three such calibrations. In order to determine the amount of radioactivity injected, an aliquot (2 ml.) was withdrawn from the stock of labelled red cells for duplicate haematocrit and counting measurements. For the latter, aliquots (0·1 ml.) were diluted to 4 ml. with water, after which the remainder of the 2-ml. sample was centrifuged and aliquots (0·1 ml.) of the supernatant were similarly diluted. Venous blood samples (10 ml.) were withdrawn from the patient at 15, 25, and 30 minutes after the injection and collected in heparinized tubes. On account of the small amount of radioactivity injected the red cells of these samples were concentrated by centrifugation prior to counting. A 4-ml. aliquot of the packed red-cell fraction was taken for counting and samples were also removed for haematocrit determination.

All the radioactivity measurements were made using a well-type NaI scintillation counter (Ekco type N550A) set to accept the ^{51}Cr photopeak. A small amount of solid Saponin was added to all the counting samples which contained blood in order to lyse the red cells and so avoid variations in counting efficiency due to sedimentation. Counting times were adjusted to reduce the counting error to less than 2 per cent for all the samples except the supernatant of the injected red-cell suspension. The correction which allowed for supernatant radioactivity was found to be so small that this degree of accuracy was unwarranted.

Haematocrit determinations were made using the microhaematocrit technique. Plain capillary tubes containing blood were sealed with Critoseal vinyl plastic putty (Biological Research Inc.). These were centrifuged for 5 minutes in a Hawksley centrifuge, after which measurements were made using a Hawksley Microhaematocrit Reader.

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R.C.V. was calculated for each of the blood samples taken 15, 25, and 30 minutes after injection, using the following formula:—

$$\text{First R.C.V. (ml.)} = \frac{{}^{51}\text{Cr in injected red cells}}{{}^{51}\text{Cr per ml. red cells in withdrawn blood sample}},$$

$$= \frac{(C_1 V/0{\cdot}1) - [C_2 V(1-H_1)/0{\cdot}1]}{C_3/4 \cdot H_3}$$

$$= \frac{40 H_3 V}{C_3}[C_1 - C_2(1-H_1)],$$

where C_1 is the radioactivity (counts per second) in a 0·1-ml. aliquot of the injected red-cell suspension; C_2 is the radioactivity (counts per second) in a 0·1-ml. aliquot of the supernatant of the injected red-cell suspension; C_3 is the radioactivity (counts per second) in a 4-ml. aliquot of the packed red-cell fraction of a blood sample withdrawn from the patient; H_1 is the haematocrit of the injected red-cell suspension (expressed as a fraction); H_3 is the haematocrit of the packed red-cell fraction of a blood sample withdrawn from the patient (expressed as a fraction), and V is the volume (ml.) of the injected red-cell suspension. The second term in the numerator of the above expression is the correction for residual ^{51}Cr in the fluid fraction of the injected red-cell suspension. This correction factor was always less than 1 per cent and confirmed that the cells had been efficiently washed prior to injection.

Second and Third R.C.V. Determinations.—A second R.C.V. determination was carried out about 24 hours after the first. Immediately before the second injection a 10-ml. sample of blood was withdrawn from the patient for counting as previously described, in order that the concentration of radioactivity remaining in the circulating red cells as a result of the first injection could be measured and corrected for. After a single washing with sterile saline the stock of labelled red cells was resuspended in saline to a volume of 40 ml., and 10 ml. (25 μc. ^{51}Cr) were injected. The calibration of the syringe and the subsequent procedure were essentially the same as described for the first R.C.V. determination. The second R.C.V. was calculated from the following formula:—

$$\text{Second R.C.V. (ml.)} = \frac{40V[C_1 - C_2(1-H_1)]}{(C_3/H_3) - (C_4/H_4)},$$

where C_1, C_2, C_3, H_1, H_3, and V have their previous notation as referred to the second injection. C_4 is the radioactivity (counts per second) in a 4-ml. aliquot of the packed red-cell fraction of a blood sample withdrawn from the patient immediately before the second injection and H_4 is the haematocrit value of this fraction. The second term in the denominator of the above equation represents the correction for the amount of ^{51}Cr present in circulating red cells at the time of the second injection as a result of the first injection.

For the third R.C.V. determination, which was carried out after a further 24 hours, the stock of red cells was washed as before and resuspended in sterile saline to a volume of 25 ml. After a 10-ml. sample of blood had been taken from the patient in order to measure the amount of residual radioactivity from the first and second injections, 20 ml. (55 μc. ^{51}Cr) of the labelled red-cell suspension were injected. The subsequent procedure and calculations were the same as those used for the second R.C.V. determination.

RESULTS

Reproducibility of the 15-, 25-, and 30-minute Values in Individual R.C.V. Determinations.—Repeated R.C.V. determinations, as described above, were made on 23 patients with acute gastro-intestinal haemorrhage. Three successive R.C.V. measurement were made on 7 patients and two measurements only were made on the remainder, giving a total of 53 R.C.V. determinations. For all except 1 patient three values were obtained at each R.C.V. determination, based on the measurement of blood samples taken 15, 25, and 30 minutes after the injection of labelled red cells.

In *Fig.* 1 the R.C.V. values calculated from the 25-minute blood samples have been plotted separately against those based on the 15- and 30-minute samples. In each case there is a high degree of correlation with the 25-minute values ($r > 0{\cdot}99$) and the regression lines are both very close to the 45° line, representing perfect agreement. It is apparent, however, that the calculations based on the measurement of blood samples taken at 15 minutes gave lower estimates of R.C.V. than those based on the 25- and 30-minute samples in some of the patients with relatively large red-cell volumes. These results suggest that mixing of labelled red cells within the total circulating red-cell mass had not been completed within 15 minutes in such patients. For this reason all R.C.V. estimations were taken as the mean of the two values based on the measurements of the 25- and 30-minute blood samples.

Reproducibility of Separate, Successive R.C.V. Determinations.—In 10 of the patients investigated no loss of blood occurred after the first injection of labelled red cells, as shown by the absence of radioactivity in the faeces collected during the investigation and for 10 days afterwards. Three R.C.V.s were measured in 4 of these patients and only 2 in the other 6 patients. The results of these determinations are shown in *Fig.* 2, in which the first R.C.V. is plotted against the second and third R.C.V.s. Taking the second and third R.C.V.s together as a single group, the regression on the first R.C.V. is very close to the 45° line, representing perfect agreement, and the correlation coefficient is $+0{\cdot}98$. When the first and second R.C.V.s and the first and third R.C.V.s were considered as pairs of measurements, individual values differed from the mean of paired values by less than $+3$ per cent in 12 out of 14 cases, and by less than $+5$ per cent in all the cases.

Sensitivity of the Method.—In 13 patients whose faeces contained radioactivity there was a mean fall in R.C.V. of 42 per cent, whereas in 10 patients whose faeces contained no detectable radioactivity there was a mean rise of 2·3 per cent ($P < 0{\cdot}01$ by Wilcoxon's rank test). There was no overlap between the two groups with the exception of 1 patient who had a rise in R.C.V. of 94 ml. (4·1 per cent) despite the presence of radioactivity in his faeces (*Fig.* 3). This result is probably misleading, however, because the patient almost certainly had an episode of bleeding after the completion of the final R.C.V. determination, since he had a sudden episode of breathlessness, followed by a fall in the haemoglobin level from 14·6 to 7·3 g. per 100 ml. over the course of the next 2 days.

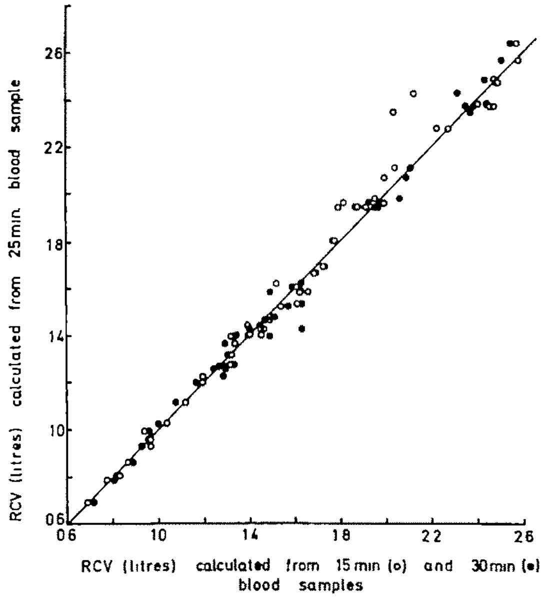

FIG. 1.—Relationship between the R.C.V. calculated from a blood sample taken 25 minutes after the injection of ^{51}Cr-labelled red cells and the R.C.V.s calculated from blood samples taken 15 and 30 minutes after the injection. The 45° line representing perfect agreement is shown.

Prior to completion of the final R.C.V. measurement he had shown no evidence of haemorrhage, and hourly measurements of pulse-rate, blood-pressure, and central venous pressure had remained steady.

If the latter result is ignored, radioactivity was detectable in the faeces of all the patients who had a fall in the R.C.V. of 3·1 per cent or more, but was not detectable in the faeces of those who had a fall in the R.C.V. of 1·3 per cent or less. Thus on the evidence of the present results a fall in the R.C.V. of about 3 per cent indicates the sensitivity of the method for detecting blood-loss. For a 70-kg. man this represents about 150 ml. of whole blood.

DISCUSSION

Methods currently available for the quantitative measurement of blood-loss all have disadvantages. Measurement of faecal radioactivity following the injection of ^{51}Cr-labelled red cells gives no indication of the timing of any episode of haemorrhage (Hughes and Burkinshaw, 1962), and is only applicable to gastro-intestinal bleeding. Although successive measurements of blood-volume based on plasma-volume determination using ^{125}I albumin can now be made quite easily by semi-automatic methods (Williams and Fine, 1961; Hobbs, 1965), plasma volume is affected not only by haemorrhage but also by the passage of fluid into and out of the extracellular space. Furthermore, calculation of blood-volume from plasma volume involves assumptions about the relationship between venous and total body haematocrit that are not necessarily valid under conditions of acute haemorrhage (Hope and Verel, 1955). Although red-cell survival is reduced in patients having recurrent haemorrhage (Tudhope, 1958), this does not give an accurate quantitative assessment of the size of the haemorrhage. Whole-body counting methods in which ^{59}Fe is used to label haemoglobin

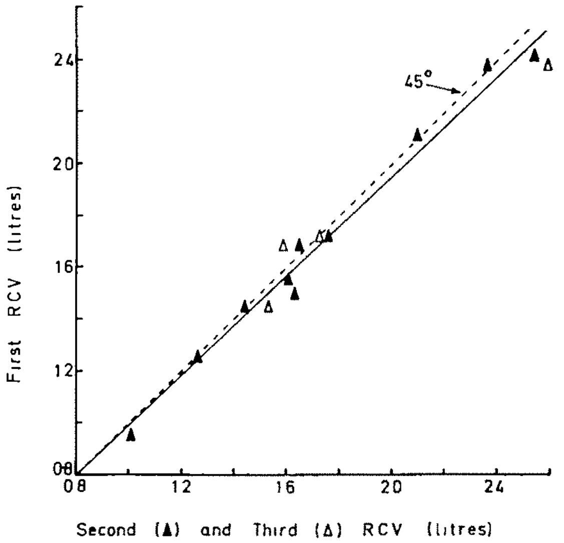

FIG. 2.—Relationship between the first R.C.V measurement and the second and third measurements (made at intervals of 1 and 2 days respectively) in patients who did not re-bleed. The regression of the second and third R C V.s on the first R.C.V. and the 45° line representing perfect agreement are shown.

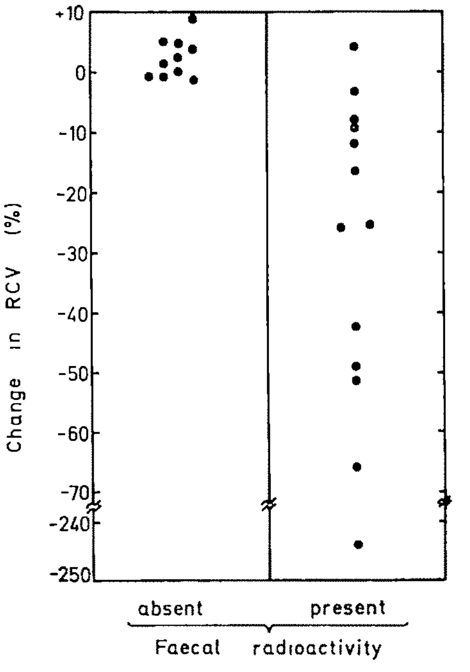

FIG. 3.—Percentage change in R.C.V. in 13 patients who re-bled and 10 patients who did not, as indicated by the presence or absence of ^{51}Cr in the faeces.

(Stack, Smith, Jones, and Fletcher, 1969) require an initial delay period of several days to allow incorporation of the tracer, and only measure blood-loss if the shed blood has been completely eliminated from the body by the time of the measurement.

Successive measurements of R.C.V. provide a more direct and specific assessment of blood-loss and are not affected by haemodilution or haemoconcentration. They also give an indication of the timing of any episode of haemorrhage. The method is reasonably sensitive, being able to detect a fall in R.C.V. of about 3 per cent of the total R.C.V. The accuracy of this technique for measuring changes in R.C.V. is best assessed from the reproducibility of individual R.C.V. measurements, under circumstances in which the R.C.V. can be expected to remain constant. Separate measurements based on the 25- and 30-minute blood samples deviated from the mean of the two measurements by less than ± 4 per cent in 98 per cent of cases, although slightly less consistent results were obtained using the 15-minute samples, probably because of incomplete mixing of the tracer during the first 15 minutes. Separate daily R.C.V. measurements in patients undergoing no further haemorrhage, as indicated by the absence of faecal radioactivity, showed a mean daily rise in R.C.V. of 38 ml. This can probably be attributed to the release of new red cells from the bone-marrow. The average rate of red-cell production in normal subjects is 14–20 ml. per day but this may be increased three to four times in severe haemorrhage (Tudhope, 1958). Despite this, daily measurements of the R.C.V. were reproducible, successive measurements on an individual patient deviating from the mean of two or three values measured in that patient by less than ± 5 per cent in all the patients with no recurrent haemorrhage.

This method of measuring the change in the R.C.V. has been found of value in correlating blood-loss with change in the central venous pressure (Northfield and Smith, 1970). It is probably applicable to the quantitative measurement of acute blood-loss from any source.

Acknowledgements.—We are grateful to Sir Francis Avery Jones and Dr. T. D. Kellock for allowing us to study patients admitted under their care.

These studies formed part of a M.D. thesis submitted to the University of Cambridge by one of the authors (T. C. N.).

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THE EFFECT OF INTESTINAL PREPARATION ON FLUID AND ELECTROLYTE BALANCE

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SUMMARY

It has been suggested that circulatory instability in elderly patients after the induction of anaesthesia is frequently accounted for by undiagnosed hypovolaemia, particularly in cases of intestinal cancer when preoperative mechanical bowel preparation has been used.

In the present study measurements were made in 25 patients undergoing mechanical bowel preparation for large-bowel cancer surgery.

Blood-volume measurements remained within normal limits after bowel preparation, and in 5 patients no change was found in total body exchangeable sodium, extracellular fluid volume, and plasma volume measured before and after bowel preparation.

Fluid and electrolyte balance studies in 11 cases showed that renal conservation of sodium occurred in the 24 hours preceding surgery and this is probably accounted for by diminished dietary intake. Circulatory instability after the induction of anaesthesia was commonly encountered but in most cases this was not the result of preoperative dehydration.

It has been suggested that dehydration and occult hypovolaemia are commonly present in elderly patients submitted to elective surgical operations (Beling, Bosch, and Carter, 1972; Waltemath and Harkness, 1963). These factors are held to be at least partly responsible for the high incidence of arterial hypotension encountered in this age-group after the induction of anaesthesia, particularly in malnourished patients and patients with intestinal carcinoma (Scott, 1961).

In our experience significant arterial hypotension is a common finding after the induction of anaesthesia in patients with large-bowel cancer and it seemed probable that a significant degree of dehydration might obtain in such patients since they are all subjected to a vigorous schedule of mechanical bowel preparation and intestinal antisepsis. Accordingly, we have studied the effects of intestinal preparation on the fluid and electrolyte balance in patients with carcinoma of the colon and rectum, and also the circulatory response to the induction of anaesthesia.

Table I.—PROTOCOL FOR THE 5-DAY COURSE OF INTESTINAL PREPARATION

DAY	APERIENT	ENEMAS OR SUPPOSITORIES	BOWEL ANTISEPTIC	DIET
1	Magnesium sulphate, 1 g. t d.s	Soap-and-water enema or 2 Dulcolax suppositories in evening	Sulfathaladine, 2 g 4-hourly during day	Ordinary
2	Magnesium sulphate, 1 g. t d.s	Soap-and-water enema or 2 Dulcolax suppositories in evening	Sulfathaladine, 2 g 4-hourly during day	Ordinary
3	Magnesium sulphate, 1 g t d.s	Soap-and-water enema or 2 Dulcolax suppositories in evening	Sulfathaladine, 2 g 4-hourly during day	Ordinary
4	Magnesium sulphate, 1 g. t.d s.	Soap-and-water enema or 2 Dulcolax suppositories in evening	Sulfathaladine, 2 g 4-hourly during day + kanamycin, 1 g 4-hourly	Ordinary
5	Castor oil, 2 oz. at 6.00 a m	Soap-and-water enema or 2 Dulcolax suppositories in evening	Sulfathaladine, 2 g. 4-hourly during day + kanamycin, 1 g. 4-hourly	Liquid
6 (day of operation)	None	None	Sulfathaladine, 2 g 4-hourly + kanamycin, 1 g up to 4–5 hours before operation	None

MATERIAL AND METHODS

Twenty-five patients undergoing preparation for elective large-bowel surgery were studied; informed consent was obtained in each case. Details of the 5-day course of intestinal preparation are shown in *Table I*. Mechanical bowel preparation was achieved with magnesium sulphate, enemata, suppositories, and castor oil, and intestinal antisepsis was obtained with sulphonamides and kanamycin. Diet was withheld during the 24-hour period prior to surgery and no oral intake, apart from the intestinal antiseptics, was permitted within 10 hours of operation.

Group 1.—In 14 patients (8 males and 6 females) plasma volume measured a few hours prior to surgery was the only investigation performed. The average age of these patients was 60 years (S.D. ± 9). Twelve of the patients were found at operation to have carcinoma of the colon or rectum, 1 patient was found to have Crohn's disease of the colon, and in the remaining case the pathology was diverticular disease of the sigmoid colon.

Group 2.—In 11 cases of large-bowel cancer (8 males and 3 females) fluid and electrolyte balance, changes in body-weight, and the haemodynamic response to surgery were measured. The average age of the patients in this group was 71 years (S.D. ± 7). In 5 cases plasma volume, total body exchangeable sodium, and extracellular fluid volume were also determined.

Patients were weighed to the nearest 100 g. on a metabolic scale each day. The haemoglobin and haematocrit, plasma and urinary sodium, potassium, urea, and osmolarity were also estimated daily. The haemoglobin and haematocrit were measured electronically on a Coulter counter and the urea and electrolytes were determined on an Autoanalyzer. Osmolarity was measured by freezing-point depression on an advanced osmometer.

Radio-isotopic studies were made prior to the 5-day course of intestinal preparation and again in the 24-hour period preceding surgery, in the latter case plasma-volume measurements being made within a few hours of operation. In group 1 patients plasma volume (P.V.) was measured using ^{125}I-labelled human serum albumin (H.S.A.). Plasma activity was assayed using a well-type scintillation counter in blood samples taken 20, 40, and 60 minutes after injection and the plasma volume was obtained by retrapolation of the dilution curve to zero time. The total blood-volume was estimated from the venous haematocrit after correction for the body : venous haematocrit ratio (Chaplin, Mollison, and Vetter, 1953).

In group 2 patients P.V., 24-hour total exchangeable sodium (Na^{e+}), and bromine 'space' (as a measure of extracellular fluid volume) were measured on two occasions. ^{125}I- or ^{131}I-labelled H.S.A., ^{24}Na sodium chloride, and ^{82}Br ammonium bromide (in doses of 5, 40, and 40 μc. respectively) were given as a single intravenous injection and blood samples were collected (*see above*) for P.V. measurement. All the urine was collected in the following 24 hours and a pooled aliquot was assayed for activity lost during equilibration. A plasma sample was obtained at 24 hours for assay of ^{24}Na and ^{82}Br activity and for the measurement of plasma sodium on the Autoanalyzer.

The plasma and urine activities due to the different radio-isotopes were separated by pulse-height analysis using a well-type sodium iodide scintillation counter and ^{24}Na and ^{82}Br standards. Radio-iodine, which was excluded in this procedure in order to obtain good physical separation of ^{24}Na and ^{82}Br, was assayed after a period of 7 days, thus taking advantage of the differential decay rates. For the first plasma volume ^{125}I was used, and for the second ^{131}I. A pulse-height setting which excluded ^{125}I was used for assay of the samples comprising the second P.V. measurement. The dilution 'spaces' for ^{24}Na and ^{82}Br were calculated in the usual way from the administered dose (less the activity lost in urine) and the 24-hour plasma activity. The Na^{e+} was calculated from the sodium space and the specific activity of ^{24}Na.

A minimum of 10,000 pulses was collected for each count, and duplicate counts were carried out on all the assay samples. Duplicate counts did not vary one from the other by more than 2 per cent.

In group 2 cases blood-pressure, pulse, and central venous pressure were recorded before the administration of the anaesthetic premedication and again after the induction of anaesthesia. Central venous pressure was measured with a saline manometer after the insertion of a catheter via an antecubital vein into the superior vena cava under radiographic control. The sternal angle was used as the zero reference point. Opiate and atropine were administered intramuscularly 45–60 minutes before the induction of anaesthesia. Thiopentone was used for the induction of anaesthesia and was given slowly by intravenous injection until the loss of the eyelash reflex occurred. A dose of 6–8 mg. of pancuronium was administered as a muscle relaxant, intermittent positive-pressure ventilation was commenced with a 50 per cent nitrous oxide/oxygen mixture, and the various circulatory parameters were then measured.

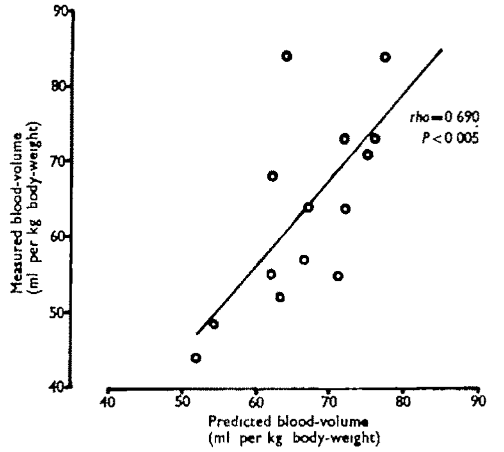

FIG. 1.—The highly significant correlation between the measured blood-volume and the predicted results based on body-weight and height in 14 patients in group 1.

Table II.—CORRELATION BETWEEN PREOPERATIVE WEIGHT-LOSS, CENTRAL VENOUS PRESSURE, AND BLOOD-PRESSURE CHANGE ON THE INDUCTION OF ANAESTHESIA IN 11 PATIENTS IN GROUP 2

AGE AND SEX	SYSTOLIC BLOOD-PRESSURE (mm. Hg)			CENTRAL VENOUS PRESSURE BEFORE PREMEDICATION (cm H_2O)	PLASMA VOLUME (ml. per kg body-weight)		WEIGHT-LOSS IN 24 HOURS BEFORE OPERATION (percentage of body-weight)
	Before Premedication	Before Induction	After Induction		Before Bowel Preparation	Before Premedication	
66 F	140	142	90	−4·0	38·7	39·5	1·3
75 F.	130	135	70	+2·5	—	—	0·8
59 F.	135	135	115	+3·5	44·7	46·1	1·3
65 M.	145	105	90	−4·0	—	—	1·6
67 M.	140	120	75	−4·0	54·4	62·8	0·6
75 M	140	130	90	−4·0	—	—	3·9
83 M	150	170	80	−4·5	49·5	48·2	0·6
68 M.	140	140	115	−1·0	—	—	2·6
66 M.	155	160	140	−4·0	—	—	2·5
71 M.	145	160	90	−9·5	—	—	4·9
81 M.	150	170	135	−5·5	52·3	59·4	3·0

It quickly became apparent that the important preoperative changes in body-weight occurred within the 24-hour period prior to surgery and two further groups of patients were studied during this period to determine the relative effects of intestinal preparation and fluid and dietary restriction on preoperative weight-loss.

Group 3.—Nine patients (7 males and 2 females) were weighed at the beginning and end of the 24-hour period prior to haemorrhoidectomy. The average age of these patients was 60 years (S.D. ± 6). Intestinal preparation was not used in this group but oral intake consisted of fluids only during the period of study. As in the group 2 cases, no oral intake was permitted during the 10 hours preceding operation.

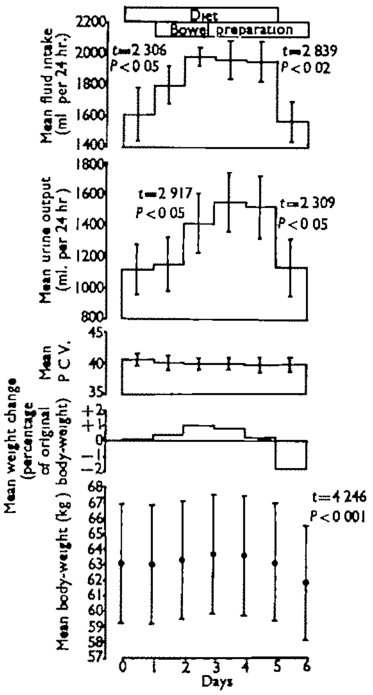

FIG. 2.—The mean fluid intake, urine output, haematocrit, and body-weight in 11 patients in group 2 undergoing a 5-day course of bowel preparation. There was a statistically significant increase in fluid intake and urine output during the course of bowel preparation until the 24-hour period preceding surgery when a significant reduction in fluid intake and urine output occurred. Haematocrit did not change significantly but there was a significant reduction in body-weight during the 24-hour period preceding surgery.

Group 4.—Nine patients (7 males and 2 females) were similarly studied prior to operation for groin hernia, peptic ulcer, or cholelithiasis. The average age of the patients in this group was 59 years (S.D. ±

13). Diet was not restricted in this group except during the 10-hour period prior to surgery when no oral intake was permitted.

RESULTS

Group 1.—*Fig.* 1 shows the statistically significant correlation between the blood-volume measured in 14 patients at the end of the 5-day course of intestinal preparation and the predicted value derived from height and body-weight using the method of Nadler, Hidalgo, and Bloch (1962). The average measured blood-volume was 63·7 ml. per kg. (S.D. ± 12·2), which was not significantly different from the expected value of 66·5 ml. per kg. (S.D. ± 7·5).

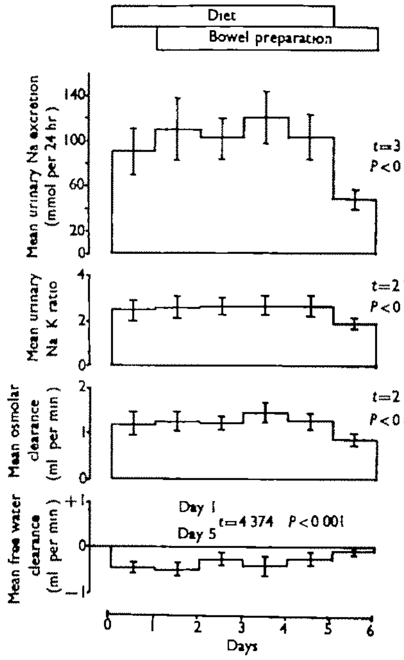

FIG. 3.—Mean urinary sodium excretion, sodium : potassium ratio, osmolar clearance, and free-water clearance in 11 patients in group 2 undergoing a 5-day course of bowel preparation. There was a statistically significant reduction in urinary sodium excretion, sodium : potassium ratio, and osmolar clearance during the 24-hour period preceding surgery. Free-water clearance remained negative but there was a statistically significant trend towards positive values during the course of bowel preparation.

Group 2.—*Fig.* 2 shows the fluid-balance measurements in 11 patients during the 5-day course of intestinal preparation. It can be seen that the average fluid intake increased significantly during the course of the study, as did the urine flow, until the 24-hour period prior to surgery when there was a statistically significant reduction in the fluid intake, urine flow, and body-weight. There was no significant change in the haematocrit during the period of study.

The data on urinary solute and water excretion in group 2 patients are shown in *Fig.* 3. Little change was observed until the 24-hour period preceding surgery when there was a statistically significant reduction in the urinary sodium excretion, the urinary sodium : potassium ratio, and osmolar clearance. Although free-water clearance remained negative, there was a significant trend towards positive values during the course of intestinal preparation.

Fig. 4 shows the plasma volume, total body exchangeable sodium (Na^e+), and extracellular fluid volume (E.C.F.) measurements obtained in 5 of the group 2 patients before and after the 5-day course of bowel preparation. No definite trend is apparent and there is no significant difference between the results before and after bowel preparation.

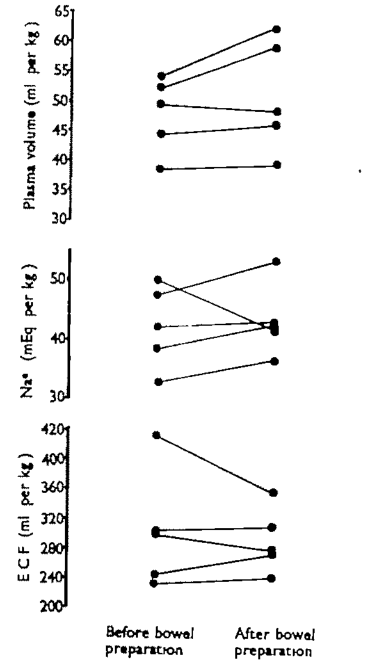

FIG. 4.—Plasma volume, total body exchangeable sodium (Na^e+), and extracellular fluid volume (E.C.F.) measurements in 5 patients in group 2 before and after bowel preparation.

Table III—COMPARISON OF AVERAGE WEIGHT-LOSS DURING THE 24-HOUR PERIOD BEFORE OPERATION IN GROUPS 2, 3, AND 4

GROUP	NO. OF PATIENTS	WEIGHT 24 HOURS BEFORE OPERATION (kg.)	WEIGHT BEFORE OPERATION (kg.)	WEIGHT-LOSS	
				kg.	Per cent
2. Bowel preparation and dietary restriction	11	63·1 ± 3·8	61·9 ± 3·6	1·3 ± 1·0	1·9
3. Dietary restriction. No. bowel preparation	9	72·0 ± 5·2	70·5 ± 5·1	1·5 ± 0·2	2·0
4. No dietary restricton. No bowel preparation	9	65·3 ± 4·0	64·3 ± 4·0	1·0 ± 0·2	1·5

Systolic blood-pressure changes resulting from premedication and the induction of anaesthesia in group 2 patients are correlated with the preoperative central venous pressure, plasma-volume, and body-weight measurements in *Table II*. The combined effects of premedication with opiates and the induction of anaesthesia with thiopentone produced a fall in the systolic blood-pressure of 50 mm. Hg or more in 7 of the 11 patients but, with the exception of 1 case, there was no obvious difference between the venous pressure, body-weight, or plasma-volume measurements in hypotensive and normotensive subjects. In 1 patient anaesthetic hypotension was associated with a preoperative central venous pressure of -9.5 cm. H_2O and a weight-loss amounting to almost 5 per cent of the body-weight.

Groups 3 and 4.—*Table III* shows the average change in body-weight of patients in groups 2, 3, and 4 during the 24-hour period preceding surgery. Group 2 cases were permitted fluids only by mouth whilst the 5-day course of intestinal preparation was completed. Patients in groups 3 and 4 had no bowel preparation but group 3 cases were permitted fluids only by mouth, whereas no dietary restriction was imposed on group 4 cases apart from the usual preoperative overnight fast. There was no statistically significant difference between the weight-loss of patients in groups 2, 3, and 4. The average weight-loss expressed as a percentage of body-weight was 1·9 per cent in group 2, 2·0 per cent in group 3, and 1·5 per cent in group 4.

DISCUSSION

It is alleged that dehydration and hypovolaemia are commonly present in elderly patients and, when unrecognized, may result in circulatory instability during anaesthesia (Beling and others, 1952; Scott, 1961; Waltemath and Harkness, 1963). It has been suggested that such problems are magnified in certain diseases including large-bowel cancer, and certainly one might expect dehydration to result in such cases from intensive preoperative mechanical bowel preparation. There is a lack of clinical data on the subject, however, and it appears that the diagnosis of dehydration or hypovolaemia is often based on subjective impressions alone rather than the results of objective measurement. Indeed, in the only previous study of the effects of intestinal preparation Trinkle, Fisher, Ketcham, and Berlin (1964) found no significant difference between the blood-volume measurements in 5 patients before and after a 5-day course of intestinal preparation.

In the present study we have found no conclusive evidence that a significant degree of hypovolaemia obtains in patients undergoing operation for large-bowel cancer (*Figs.* 1, 4), and there is no indication that intestinal preparation has a significant effect on the fluid and electrolyte status of such cases until the 24-hour period preceding surgery, when there is significant weight-loss and a reduction in urinary sodium excretion (*Figs.* 2, 3). Associated with the renal conservation of sodium, probably as a result of increased aldosterone secretion, there is a reduction in urine osmolarity and an increased clearance of free water. It appears, however, that intestinal preparation plays a small part in such changes since similar changes in body-weight were found in patients who had no bowel preparation but who were also subjected to dietary restriction (*Table III*). It seems probable, therefore, that the altered pattern of urinary salt and water excretion results largely from dietary restriction of salt.

Circulatory upset occurred in a proportion of patients during the induction of anaesthesia, but it could not be correlated with hypovolaemia or dehydration with the possible exception of 1 case. In this instance, anaesthetic hypotension was associated with a preoperative weight-loss amounting to almost 5 per cent of the body-weight and a central venous pressure of -9.5 cm. H_2O. Absolute measurements of the central venous pressure must be interpreted with extreme caution or perhaps not at all (Ryan and Howland, 1966), but it seems probable that significant dehydration obtained in this case although there was no evidence of azotaemia or change in the venous haematocrit. There are many other possible explanations for circulatory upset, of course, such as the depressant action of opiates and barbiturates, the vasodilator properties of anaesthetics or muscle relaxants, or pathological changes in the blood-gases (Jenkins and Beck, 1963), but nitrous oxide and pancuronium should have little effect on the blood-pressure (Eisele, Trenchard, Stubbs, and Guz, 1969; Kelman and Kennedy, 1971) and it seems likely that arterial hypotension in our patients resulted from the central effects of opiate premedication and thiopentone induction and the mechanical effects of positive-pressure ventilation.

It is concluded, therefore, that there is little evidence that intestinal preparation results in significant fluid and electrolyte imbalance in cases of large-bowel cancer or that such patients are hypovolaemic when anaesthetized. Nevertheless, circulatory upset on the induction of anaesthesia is frequently encountered. These patients respond well to fluid administration but it would be incorrect to assume that the majority are dehydrated.

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THE RESPONSE OF THE LOWER OESOPHAGEAL SPHINCTER TO A TEST-MEAL STIMULUS

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SUMMARY

The response of the lower oesophageal sphincter to test meals has been assessed using two manometric techniques. Tests in which the sphincteric pressures were continuously monitored proved to be the most satisfactory and test meals which were predominantly meat extract provided the greatest stimulus. Normal subjects increased the sphincteric pressure 86·7 per cent above the basal levels within 30 minutes of the introduction of the test meal, whereas patients with symptomatic hiatus hernia had diminished responses with pressure increases of only 30 per cent above basal levels. Patients with peptic ulceration or stricture of the oesophagus failed to respond to any form of test meal.

THERE is a great deal of evidence that the function of the lower oesophageal sphincter determines competence at the gastro-oesophageal junction (Cohen and Harris, 1971). Though the study of the lower oesophageal sphincter by intraluminal manometry has been undertaken for a number of years its value in the clinical situation has proved somewhat limited. In this report we have assessed the effect of test meals on sphincteric function using two techniques in an attempt to improve the clinical value of this type of investigation. The results suggest a possible role for test meals for the investigation of patients with symptoms of gastro-oesophageal reflux.

MATERIALS AND METHODS

Manometric investigation of the lower oesophageal sphincter area was performed using water-filled polyethylene tubes (external diameter, 1·4 mm.; internal diameter, 1·2 mm.) each with a side-hole (1·2 mm. diameter) at 5, 10, and 15 cm. from distal end respectively. These tubes were constantly perfused with water at 0·6 ml. per minute and were connected via strain-gauge transducers (Statham PEA D 300) to an amplified electromanometer (Cardiac Recorders Ltd.), the deflexions being recorded on moving photographic paper. Respiratory movements were monitored simultaneously from a pneumograph strapped around the chest.

In the first series of experiments intraluminal pressures in the oesophagus and stomach were determined by the technique described by earlier workers (Fyke, Code, and Schlegel, 1956; Atkinson, Edwards, Honour, and Rowlands, 1957). A triple-lumen tube was swallowed into the stomach and then withdrawn at 0·5-cm. intervals with pressure measurements being made from two tubes at each point for at least five full respiratory cycles. This technique results in a profile of the intraluminal pressures exerted by the lower oesophageal sphincter. The pressure tracings obtained in this way were measured using the end-inspiratory and end-expiratory excursions. The latter gave the more consistent reading and are, therefore, reported in this paper. After recording the sphincteric pressure profile under resting conditions, the test meal was introduced into the stomach through the most distal side-hole of the third tube. Sphincteric profiles were repeated after 15, 30, 60, 120, and 180 minutes.

In the second series of tests a quadruple-lumen tube was constructed using polyethylene tubing of similar dimensions to that described previously, with a cross-section diameter of 0·5 cm. One of these tubes was used to introduce the test meal into the stomach. The second tube had a side-hole (1·2 mm. diameter) 15 cm. from the distal end and was used to record pressures exerted in the upper part of the stomach. Five centimetres above this level the side-hole of the third tube measured pressure in the lower oesophageal sphincter. The fourth tube had a side-hole 5 cm. higher and recorded pressures in the lower oesophagus. The protocol for this technique called for the measurement of the sphincteric profile in the way outlined above, and then the tube system was fixed to the nose so that pressures could be continuously and simultaneously recorded from the stomach, lower oesophageal sphincter, and the lower oesophagus. Particular care was necessary in the fixation of the tube system in patients with hiatus hernia because of the frequent displacement of the cardia into the thoracic cavity. In all the subjects it proved important that the side-hole recording the sphincteric pressure was situated at the point of maximum sphincteric pressure. The pressure tracings were analysed by measuring the mean pressure recorded from any one side-hole over a period of at least 1 minute before the introduction of the test meal and for 2 hours afterwards.

Two types of test meal were used. The majority of the meals consisted of a commercial meat-extract preparation in which three cubes of desiccated meat extract (Oxo) were crumpled and dissolved in 200 ml. of water at 37° C. The other test meal consisted of 25·2 g. of skimmed-milk powder, 27·6 g. of glucose, and 14·8 g. of corn oil (Lundh, 1962). This mixture was easily homogenized in 200 ml. of water at 37° C. The test meals were introduced into the stomach via the tube system and with the subject's knowledge of their content.

Sphincteric profile test meals were carried out in 12 normal subjects (6 tests with the meat extract, 6 tests with the Lundh test meal). Continuous pressure-monitoring tests were performed in 8 normal subjects with the meat-extract test meal. Two groups of patients with gastro-oesophageal reflux were studied. Nine patients with hiatus hernia had symptoms of heartburn and regurgitation severe enough to warrant surgery. Another group of 5 patients had, in addition, severe dysphagia and were found to have an early stricture in the lower oesophagus or severe oesophagitis with peptic ulceration. The mean age of the normal subjects studied was 42 years and of the patients with hiatus hernia 54 years (range, 42–75 years). All the pressure values are presented as the mean plus 1 standard error of the mean.

RESULTS

1. Sphincteric Profiles following the Meat-extract Test Meal.—

a. Effect on Sphincteric Pressure.—From each sphincteric pressure profile the maximum pressure was noted. *Fig.* 1 shows the mean maximum sphincteric pressure under resting conditions and for 3 hours following the meat-extract test meal. The mean resting pressure of 20·3 ± 3·4 cm. H_2O reached a peak of 28·2 ± 3·3 cm. H_2O at 60 minutes after meat-extract stimulation and thereafter fell towards resting levels.

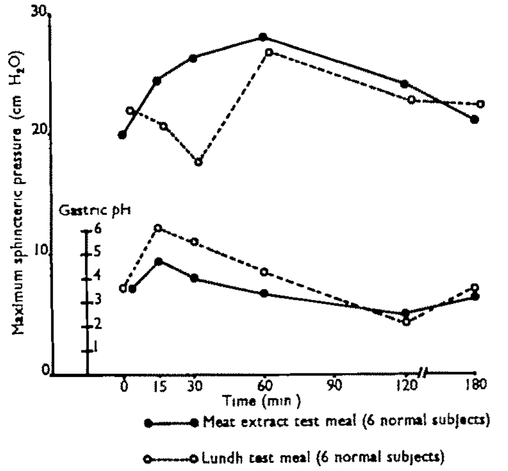

FIG. 1.—The mean lower oesophageal sphincteric pressures and mean gastric *p*H in normal subjects following stimulation with meat-extract (6 tests) or a Lundh (6 tests) test meal using the withdrawal technique.

Assuming a rise in sphincteric pressure of at least 5 cm. H_2O to be a positive response to meat extract, 4 of the subjects tested showed measurable changes in sphincteric tone. The 2 remaining subjects showed minor decreases in pressure.

A comparison of the sphincteric pressures measured by the two recording tubes in the same individual often showed a poor correlation, with maximum sphincteric pressures often varying up to 5 cm. H_2O at the same point of time after meat-extract stimulation.

The changes in sphincteric pressure were appreciated most easily by noting the percentage change in maximum sphincteric tone compared with the resting pressure. Thus the mean maximum percentage increase in sphincteric pressure within 30 minutes of meat-extract stimulation was 20·0 ± 9·0 per cent and within 60 minutes 32·4 ± 8·1 per cent (*Table I*).

b. Length of Sphincteric Area.—The mean sphincteric length of 4·2 ± 0·36 cm. was unaltered by meat-extract stimulation and was similar in the recordings of both tubes. There did not seem to be any change in the position of the sphincteric pressure area in relation to the point of respiratory reversal and thus it was assumed that the test meal did not cause alterations in anatomico-spatial relationships of the cardia.

c. Gastric Pressure and Pressure in the Lower Oesophagus.—The mean fundal pressure of 12·2 ± 0·68 cm. H_2O showed only minor changes in pressure following meat-extract stimulation. No significant changes were recorded in oesophageal pressures.

Table I.—MEAN MAXIMUM PERCENTAGE INCREASE IN SPHINCTERIC PRESSURE OVER RESTING LEVELS

	TIME AFTER MEAT EXTRACT GIVEN (min.)		
	30	45	60
Withdrawal technique			
Normal subjects	20·0 ± 9·0	—	32·4 ± 8·1
Continuous technique			
Normal subjects	86·7 ± 29·0	86·7 ± 29·0	88·3 ± 29·4
Hiatus hernia	29·8 ± 9·9	33·0 ± 11·7	36·8 ± 11·7
Hiatus hernia with stricture	0	0	0

d. pH Changes in the Gastric Aspirate.—Since routine radiological screening of the position of the tube system was not undertaken it is not certain from which gastric site the aspirate was sampled, though it was likely to be from the main body of the stomach. The *p*H of the samples under resting conditions varied from 1·8 to 6·4 with a mean of 3·6 ± 0·7. Following the introduction of meat extract (*p*H 5·8) the *p*H of the gastric aspirate became slightly more alkaline (*Fig.* 1) for 30 minutes but remained at about a mean of *p*H 3·0 for the remainder of the test.

2. Sphincteric Profiles following the Lundh Test Meal.—

a. Effect on Sphincteric Pressure.—*Fig.* 1 shows the mean sphincteric pressure under basal conditions and for the 3 hours following the Lundh test meal. Pressures observed during the first 30 minutes of the test showed a mean decrease in pressure to 17·6 cm. H_2O at 30 minutes. This decrease was seen in 4 of the 6 tests. Eventually 4 of the 6 subjects had distinct increases in maximum sphincteric pressures and the mean resting pressure rose from 22·0 ± 2·8 to 26·8 ± 3·0 cm. H_2O.

b. Length of Sphincteric Area.—The mean sphincteric length for the 6 subjects was 3·56 cm. The mean length at 120 and 180 minutes was 4 cm. but this was not taken to be indicative of any change in the length of the sphincteric area.

c. Gastric Pressure and Pressure in the Lower Oesophagus.—The mean fundal pressure for these tests was 13 ± 0·8 cm. H_2O under resting conditions and only minor changes were observed over the course of 3 hours. Similarly, the pressures exerted in the lower oesophagus were unaffected by the test meal.

d. pH Changes in the Gastric Aspirate.—The *p*H of the Lundh test meal was 6·2. Thus, the *p*H of the gastric aspirate immediately following the introduction of the meal rose to 6·0 and then gradually declined as the stomach became more acidic over the next 2 hours (*Fig.* 1).

3. Continuous Pressure Monitoring of the Sphincter following a Meat-extract Test Meal.—

a. Responses in 8 Normal Subjects.—The sphincteric pressure increased within 5–10 minutes after the introduction of the meat extract, reaching a peak at 20 minutes and then slowly declining towards the basal level over the next hour (*Fig.* 2). All the normal subjects showed a sphincteric pressure increase of 5 cm. H_2O or more and the mean sphincteric pressure rose from 29·4 ± 2·7 cm. H_2O to a mean maximum of 45·4 ± 4·1 cm. H_2O some 20 minutes after the meat-extract stimulation. All except 1 subject reached the peak of sphincteric pressure increase by 30 minutes and thereafter the mean sphincteric pressure declined. The pressure recorded by the gastric tube also showed minor increases following the meat extract which paralleled the changes seen in the sphincteric pressure (*Fig.* 2).

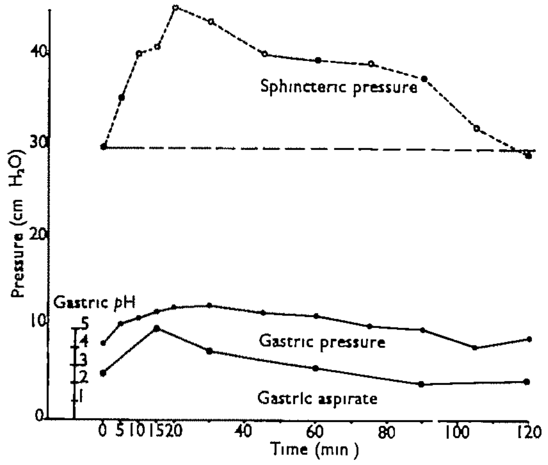

FIG. 2.—The mean sphincteric and gastric pressures and the mean *p*H of gastric aspirate in 8 normal subjects following stimulation with meat extract and using the continuous recording technique.

The mean gastric *p*H rose from 2·6 ± 0·3 to a mean maximum of 5·1 ± 0·2 (range 4·2–6·2) at 15 minutes after the meat extract (*Fig.* 2). Thereafter the gastric contents became more acidic and very little contamination of the gastric aspirate by meat extract was found after 45 minutes.

b. Responses in 9 Patients with Symptomatic Hiatus Hernia.—The mean pressure recordings of the 9 patients are shown in *Fig.* 3. The mean basal sphincteric pressure was 28·4 ± 2·4 cm. H_2O, which was similar to that in the group of normal subjects. Two of the patients had no pressure increase following the test meal and the remainder all showed increases in excess of 5 cm. H_2O. The mean sphincteric pressure for the group reached a maximum of 33·6 ± 2·4 cm. H_2O and then declined towards basal levels by 75 minutes. The timing of the peak pressure response was more variable and delayed than that in normal subjects. At 120 minutes after stimulation 6 patients still showed a sphincteric pressure elevated above resting levels (*Fig.* 3). The mean gastric pressure in these patients rose slightly from a mean of 12·5 ± 1·8 cm. H_2O to a mean maximum of 15·2 ± 2·1 cm. H_2O at 30 minutes after the test meal and then declined to basal levels (*Fig.* 3). No changes were noted in the oesophageal pressure with meat extract stimulation. The mean *p*H of the gastric aspirate rose from 3·0 ± 0·3 to 4·9 ± 0·2 at 15 minutes.

c. Sphincteric Responses in 5 Patients with a Symptomatic Hiatus Hernia and Evidence of a Peptic Stricture.—Some difficulty was experienced in defining the lower oesophageal sphincter in this group of patients. The mean sphincteric pressure was 8·6 ± 1·2 cm. H_2O. None of these patients showed any variation in this low resting sphincteric pressure with meat-extract stimulation.

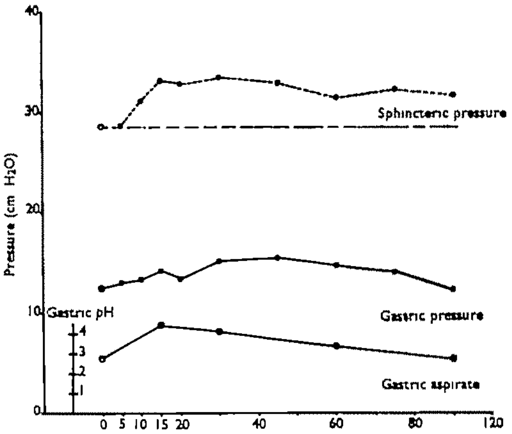

FIG. 3.—The mean sphincteric and gastric pressures and the mean *p*H of the gastric aspirate in 9 patients with a symptomatic hiatus hernia following stimulation with meat extract and using the continuous recording technique.

d. Percentage Change in Sphincteric Pressure.—In *Table I* the mean percentage increase in sphincteric pressure above the resting tone is shown for the three groups. It can be seen that normal subjects respond to the meat extract more quickly and to a greater degree than the patients with an uncomplicated but symptomatic hiatus hernia. In normal subjects the mean percentage increase within 30 minutes of stimulation was 86·7 ± 29·0 per cent, compared with 29·8 ± 9·9 per cent in patients with a symptomatic hiatus hernia. Since some patients reached the peak of sphincteric pressure later than 30 minutes the mean percentage increase within 60 minutes of the test meal rose to 88·3 ± 29·4 per cent in normal subjects and 36·8 ± 11·7 per cent in the patients with hernia. The differences between these two groups are significant at 30 minutes ($P < 0·05$). Patients with a complicated hiatus hernia had no response to the test meal.

DISCUSSION

The basic technique of oesophageal manometry demands a tube system of low volume with open end or side-holes and a constant flow of fluid along the tubes (Pope, 1970). The high pressure zone of the lower oesophageal sphincter is well shown by the withdrawal technique and demonstrates the position, shape, length, and the level of resting tone of the sphincter. The use of this technique has been criticized by Kaye and Showalter (1971) on the grounds of poor reproducibility in the same individual. This is a criticism with which we would concur and would add that it has proved to be a relatively insensitive method of detecting changes in the lower oesophageal sphincter pressure following a test meal. The static tube system with a side-hole continuously monitoring the lower oesophageal sphincter pressure is more convenient for both the patients and the investigators, and this method proved a highly sensitive method of detecting change in the lower oeosophageal sphincter pressure following a test meal. However, it is not always easy to site the tube so that the point of maximum sphincteric pressure is monitored, nor can it be certain that changes in position of the side-hole do not occur, particularly in patients with hiatal hernia in whom the sphincteric pressure is very low or where severe oesophagitis and fibrosis are present.

The meat-extract test meal has previously been used to assess antral function in patients with peptic ulceration (Welbourn and Burns, 1964; Giles and Clark, 1966). Since the lower oesophageal sphincter has been shown to respond to both endogenous and exogenous circulating gastrin (Giles, Mason, Humphries, and Clark, 1969; Castell and Harris, 1970), the meat-extract test meal may also be useful as a natural and physiological stimulus for assessing sphincteric function. The stimulus to the gastric antrum for gastrin release is probably a direct chemical one. However, it may be related, in part, to alkalinization of the gastric antrum, since the *p*H of the meat extract and the gastric aspirates for 1 hour following the meal remain relatively alkaline.

The effect of the meat-extract test meal in normal subjects was to produce an immediate and marked rise in the lower oesophageal sphincter pressure, with a mean rise of 86·7 per cent above the resting levels within 30 minutes of the stimulus. The initial pressure increase could no doubt be attributable to gastrin release from the antrum. However, since the *p*H of the gastric contents always declined below 3·0 within 60 minutes of the stimulus, it is unlikely that the gastric antrum continued to release gastrin. The persistent elevation of pressure in some subjects at 2 hours after meat extract had been given may be due to low levels of circulating gastrin or to some other mechanism. It is clearly advantageous that the sphincter maintains an elevated tone for an extended period of time following a meal, though it must be admitted that previous experience with the meat-extract test meal, under slightly different conditions, suggested that the stimulus to gastric acid secretion had completely waned by 60 minutes (Giles and Clark, 1966).

Routine use of the Lundh type of test meal was precluded by the fact that 4 of the 6 normal subjects tested showed significant falls in the lower oesophageal sphincter pressure during the early part of the test. Pressure increases were ultimately seen, though less than after meat extract. The decreases in the lower oesophageal sphincter pressure with this test meal may be related to the corn-oil content, which has previously been reported to produce inhibition of the lower oesophageal sphincter pressure (Castell and Nebel, 1971). The mechanism for this inhibition must be speculative, but it is probable that it is produced by release of secretin from the duodenum or is due to the action of enterogastrone.

Cohen and Harris (1971) have been able to correlate closely the occurrence of gastro-oesophageal reflux to the resting tone of the lower oesophageal sphincter and have questioned the relevance of the clinical diagnosis of hiatus hernia, the implication being that the function of the lower oesophageal sphincter and its response to various forms of physiological stress are the main determinants of gastro-oesophageal competence. Previous workers (Lind, Warrian, and Wankling, 1966; Cohen and Harris, 1971) have used physical stress in the form of Valsalva manœuvres and raised intra-abdominal pressure as a test of lower oesophageal sphincter function. Significantly reduced sphincteric responses to these stimuli were found in patients with gastro-oesophageal reflux. The response of the lower oesophageal sphincter to a test meal is also an appropriate stimulus since it produces the situation in which reflux is liable to occur over a longer period. The differences demonstrable between normal subjects and patients with reflux may therefore have more significance.

The patients presented in this study are by no means representative of the majority of patients with hiatus hernia since they all had symptoms severe enough to be referred for surgery. One group of these patients was found on investigation to have a lower oesophageal sphincter which was barely identifiable by manometric means and was associated with very severe oesophagitis and with early stricture or peptic ulceration. These patients with a poor sphincter tone had no increase in the pressure of the lower oesophageal sphincter on stimulation with the meat-extract test meal. It is uncertain whether this lack of response is attributable either to a primary defect of the lower oesophageal sphincter or to damage resulting from the gastro-oesophageal reflux.

The second group of patients was characterized by severe symptoms and a radiologically demonstrable hiatus hernia and had a lower oesophageal sphincter resting pressure not significantly different from that seen in normal subjects. The sphincteric response to meat extract in this group of patients was variable. Two of the patients had no response at all, but pressure increases were seen in the remaining 7 patients. The response seen in these patients differed from that in normal subjects in several respects. The mean amplitude of the pressure increase at 30 minutes was only 35 per cent above the resting tone compared with 86·7 per cent in the normal subjects. Thus, although the resting tone of the lower oesophageal sphincter in these patients was not abnormally low, an apparent defect in the response to a normal food stimulus was demonstrated. This defect might permit a gastro-oesophageal reflux to occur in response to food, both immediately after the meal and for several hours afterwards. The cause of this defective sphincteric response can only be conjectured since it might result from a failure of the gastric antrum to release gastrin on stimulation, or from a relative non-responsiveness of the lower oesophageal sphincter to gastrin in these patients, or be the direct result of anatomical displacement of the sphincter into the thoracic cavity.

It is not yet clear whether the meat extract sphincter test will be of additional diagnostic value in patients with gastro-oesophageal reflux, since a full spectrum of these patients has yet to be studied. However, the tests may provide some help in deciding upon the type of operative procedure to be employed in the surgical management of these patients. It may be possible to identify those patients in whom the lower oesophageal sphincter is completely defective and who require a procedure which creates a new valve at the gastro-oesophageal junction (Nissen, 1961; Skinner and Belsey, 1967). Conversely, patients with a lower oesophageal sphincter which is still responsive to meat extract might achieve equally satisfactory results with simpler operative procedures, such as simple repair of the hiatus or gastropexy. The test of this hypothesis will require a long-term clinical study.

Acknowledgement.—A. Roszkowski was supported by a grant from the West Riding Research Trust.

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THE EFFECT OF HYPOPHYSECTOMY ON THE CORTISOL SECRETION IN 4 PATIENTS WITH ADVANCED METASTATIC BREAST CANCER

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Summary

A raised cortisol production rate is found in patients with advanced breast cancer. The cortisol production rate was estimated before and after hypophysectomy in 4 patients with metastatic disease and was found to fall to one-sixth of the original level. It is concluded that the high preoperative cortisol production rate was dependent on pituitary function and was not due to the production of corticotrophin by the tumour cells.

It is now generally accepted that the estimation of the urinary metabolites of androgens and cortisol forms a useful measurement for predicting the response of a patient with advanced breast cancer to endocrine ablation (Bulbrook, 1965). Similar information can be obtained by measuring the plasma levels of these two groups of compounds (Deshpande, Hayward, and Bulbrook, 1965). The measurement of plasma titres of these steroids indicated that in metastatic breast cancer the plasma levels of cortisol are raised and this is mainly due to a higher production rate of the hormone as no other variables, such as the half-life of cortisol, its metabolic clearance or distribution, showed any differences when compared with those in normal control subjects (Jensen, Deshpande, Bulbrook, and Doouss, 1968a, b). It was felt that the raised cortisol production might be due to gross production of corticotrophin by tumour tissue such as that reported in patients with lung cancer and other neoplasms (Liddle, Givens, Nicholson, and Island, 1965). If so, the elimination of pituitary adrenocorticotrophic hormone (ACTH) by complete hypophysectomy would allow the effect of tumour corticotrophin to be demonstrated. The proposition was tested by estimating the production rate of cortisol in patients before and after hypophysectomy. The results obtained in 4 patients are reported.

METHODS AND RESULTS

The patients were admitted to hospital 3 weeks prior to surgery and all steroid therapy was terminated. Two weeks after admission the prehypophysectomy production rate was estimated from the specific activities of three urinary metabolites of cortisol, as described by Deshpande, Jensen, Carson, Bulbrook, and Lewis (1969). The patients were then treated by transfrontal hypophysectomy followed by the insertion of six 3·8-m.c. pure gold grains into the pituitary fossa. Following hypophysectomy the patients were stabilized on cortisone acetate, 25 mg. per day, and a further 2 weeks were allowed to elapse. Dexamethasone, 0·75 mg. per day, was then substituted for cortisone acetate. Five days later the production rate of cortisol was again determined. The results obtained for the production rate of cortisol are shown in *Table I*.

Table I.—PRE- AND POSTHYPOPHYSECTOMY PRODUCTION RATE OF CORTISOL IN PATIENTS WITH ADVANCED BREAST CANCER

PATIENT	AGE (yr.)	CORTISOL PRODUCTION RATE (mg per 24 hr)						TOTAL URINARY CORTICOIDS (mg. per 24 hr)	
		Cortisol		*Tetrahydrocortisone*		*Tetrahydrocortisol*			
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	53	16·0	—	28·5	2·6	22·7	3·0	6·9	—
2	68	24·2	—	26·2	2·1	27·4	1·6	8·3	0·6
3	63	21·6	—	23·5	3·0	23·3	2·7	6·9	—
4	50	20·3	—	18·6	3·7	16·8	4·0	10·6	0·13
Range in normal control subjects (Deshpande and others, 1969)	—	1·98–6·0	—	3·55–16·2	—	3·3–12·4	—	3·44–9·11	—

Cortisol, tetrahydrocortisone, and tetrahydrocortisol represent the production rate of cortisol based on the specific activities of urinary cortisol, tetrahydrocortisone, and tetrahydrocortisol.

CONCLUSIONS

Preoperatively the cortisol production rate in all 4 patients was raised to levels similar to those previously reported in cases of metastatic breast cancer (Jensen and others, 1968a). Although the number of cases studied is small the results clearly show that following hypophysectomy the cortisol production rate fell to one-sixth of the original rate. This indicates that the high prehypophysectomy cortisol production is not due to production of corticotrophin by tumour tissue, but depends on the presence of functioning pituitary cells. Abnormal prehypophysectomy cortisol production may be due to either excess pituitary ACTH or increased sensitivity of the adrenal cortex. Although the dependence of such abnormal cortisol production on the pituitary–adrenal feedback mechanism is not known, there is evidence that patients with advanced breast cancer respond normally to ACTH (Schubert, Bacigalupo, and Frankenberg, 1961).

The residual secretion of cortisol (approximately 3 mg. per 24 hours) is difficult to explain. The combination of open operation and local irradiation should completely destroy all the hypophysial tissue. Furthermore, the postoperative dexamethasone medication will suppress ACTH production from any residual hypophysial cells. It is unlikely, therefore, that the residual cortisol secretion is dependent on pituitary ACTH control, but may be the result of intrinsic adrenal production. There remains the possibility that the residual secretion of cortisol is due to the production of corticotrophins by tumour cells, and it is not possible to discount this on the basis of these figures. This small residual secretion is, nevertheless, quite inadequate to explain the raised cortisol production rate found before hypophysectomy.

Acknowledgements.—We are grateful to Mr. E. J. Radley-Smith for allowing us to study his patients, to Dr. R. D. Bulbrook for his support, and to Miss Pamela Carson and Miss Irene Mitchell for their skilled technical assistance.

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SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF EMPHYSEMATOUS PYELONEPHRITIS

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EMPHYSEMATOUS pyelonephritis is an unusual condition in which there is gas within the renal parenchyma, or sometimes within the pyelocaliceal collecting system. The diagnosis is made radiologically (Bliznak and Ramsey, 1972). Thirty-five cases have been reported in the literature, all of whom had diabetes mellitus or an obstruction to urinary outflow (Costas, 1972).

The present fatal case illustrates this condition and demonstrates the rapid way in which it may develop.

CASE REPORT

J. H., a 42-year-old woman, was admitted as an emergency in a semiconscious state. The relatives gave a history of several months' duration of malaise, urinary frequency, and intermittent burning pains in the feet. Five days prior to admission she had had rigors and nausea; she had become increasingly weak. Immediately before admission she had become disorientated and confused.

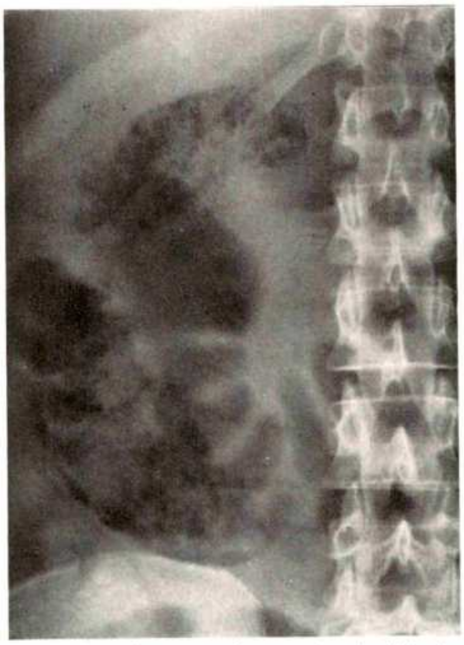

FIG. 1.—Right renal tomogram demonstrating air within the renal substance.

There was no family history of diabetes mellitus or renal disease. The patient had had an operation on the left kidney at the age of 7 years. She had been treated for syphilis when she was 26 years old.

The patient looked dehydrated and was drowsy and disorientated, though able to obey simple commands.

There was a left paramedian scar. A large tender mass was present in the right renal area. The oral temperature was 37·8° C., sinus tachycardia 140 per minute, and blood-pressure 70/50.

Laboratory data on admission included: blood-urea, 185 mg. per 100 ml.; serum sodium, 130 mEq./l.; serum potassium, 5·4 mEq./l.; serum chloride, 85 mEq./l.; blood-sugar, 650 mg. per 100 ml., with a metabolic acidosis; haemoglobin, 11·2 g. per 100 ml.; white-blood count, 10,000 per mm.^{3} Blood and urine cultures taken on admission both grew *Escherichia coli*. The patient was rehydrated and started on kanamycin at a reduced dosage in view of her renal failure (Mawer, Knowles, Lucas, Stirland, and Tooth, 1972; Mawer, Lucas, and McGough, 1972). The diabetes was controlled with soluble insulin.

The day after admission the patient remained severely hypotensive and had become anuric with a rapidly rising blood-urea, which was now 380 mg. per 100 ml. She had developed neck stiffness and a positive Kernig's sign. Cerebrospinal fluid obtained by lumbar puncture contained 180 polymorphonuclear cells per mm.^{3} Plain abdominal radiographs showed multiple gas shadows in the right renal area, and many small opacities in the gluteal region.

An abdominal tomogram 3 days after admission (*Fig.* 1) showed evidence of a considerable amount of gas within the right kidney.

Peritoneal dialysis was commenced to control the uraemia, and blood was transfused to maintain a central venous pressure of +4 cm. The haemoglobin had dropped to 9·3 g. per 100 ml., with a platelet count of 18,000 mm.^{3}, and coagulation studies demonstrated intravascular coagulation.

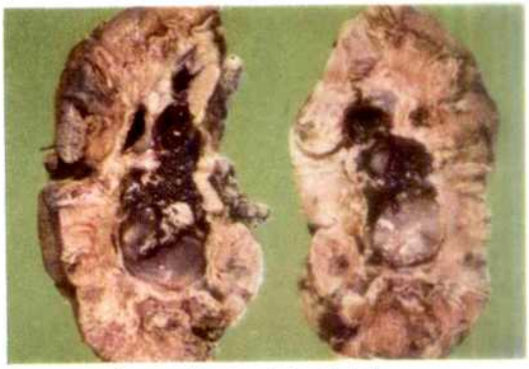

FIG. 2.—Interior of the right kidney.

The patient's general condition remained grave although the blood-sugar and blood-urea were satisfactorily controlled. The blood-pressure remained low (about 90 mm. Hg systolic pressure) and there was evidence of a continuing shock state. It was felt that surgery was essential if the patient was to survive. At operation a grossly necrotic right kidney was found and removed (*Fig.* 2). A swab from the right kidney at operation subsequently grew the same strain of *E. coli* that had been grown from the blood and urine. No left kidney was felt during the operation. The patient remained very ill and died 8 hours after the operation.

The resected right kidney was extensively destroyed by acute inflammation. Grossly, there was complete loss of the normal distinction between the cortex and the medulla. Microscopically, small ulcers were seen scattered throughout the kidney; in addition there was interstitial inflammatory infiltration and many of the tubules contained pus. There were extensive areas of coagulative necrosis in many of the small vessels. There were also areas of healthy renal parenchyma which showed no abnormality.

At post-mortem examination no left kidney was found and it was concluded that this had been resected at the earlier operation, when the patient was 7 years old.

DISCUSSION

There have been 35 reported cases of emphysematous pyelonephritis (Costas, 1972). Uncontrolled diabetes mellitus without urinary obstruction was the most common predisposing factor; in this group the mortality-rate was 40 per cent. All the patients with emphysematous pyelonephritis who did not have diabetes had an obstructing lesion in the urinary tract; in this group the mortality was 14 per cent.

In the group of patients with diabetes, the diabetes is usually out of control (Porter and Wright, 1961). Females are more frequently afflicted than males and the mean age of occurrence is 46 years (Schainuck, Foulty, and Culter, 1968). The left kidney is more often affected than the right (Stokes, 1966). *E. coli* is usually cultured (Olson, 1957; Costas, 1972), although other coliforms have been found occasionally (Schultz and Klorfein, 1962). Most coliform organisms are capable of metabolizing glucose to acid and carbon dioxide, and the raised blood-sugar and urinary sugar in diabetics may contribute to the aetiology (Gillies and Flocks, 1941). This is in contrast to the gas-producing infections of the gall-bladder, where clostridia are the usual causative organisms and only about 25 per cent of the patients have diabetes (Bigler, 1960; May and Strong, 1971).

Pathological findings are available in 11 diabetic patients. In the involved kidney a severe necrotizing pyelonephritis involving the cortex and medulla was present in every case and multiple abscesses were common (Schainuck and others, 1968).

Most authors feel that nephrectomy is not indicated (Stokes, 1966). In the present case, however, as the patient's condition continued to deteriorate in spite of antibiotic therapy it was felt that surgery was essential, and at operation the surgeon thought that nephrectomy offered the only means of a cure. Had the patient recovered she would have been placed on a long-term haemodialysis programme.

Acknowledgements.—I should like to thank Dr. N. P. Mallick for his permission to report this case and for his advice in the preparation of this paper, and Dr. H. Fox for the histological examination.

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MENINGIOMA FOLLOWING TRAUMA

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Summary

A case report is given of the development of an intracranial meningioma at the site of an authentic head injury incurred 21 years previously. The available literature on the subject is reviewed. The criteria satisfying the concept of trauma being a significant aetiological factor in the production of such tumours are stated and it is shown that the meningioma reported in this paper fulfils all these criteria. The aetiology of such tumours is discussed in further detail.

It is well recognized that there is a causal relationship between the irritative effects of prolonged trauma and the development of neoplastic changes in the affected tissue. Much more controversial is the question of whether a single non-recurrent traumatic episode can be aetiologically significant in the production of neoplasia. The criteria which must be satisfied before any malignant growth can be attributed to trauma have been summarized by Austen (1961).

1. The site of injury must correspond to the region in which the tumour develops.
2. The trauma must be authentic and of sufficient importance.
3. The previous integrity of the wounded part must not be in doubt and there must be proof that neither primary nor metastatic malignant disease was present before injury.
4. The time interval between injury and the development of the neoplasm must be significant.

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5. There must be continuity in the pathological changes or symptoms in the wounded part from the time of injury to the appearance of the tumour.

6. There must be microscopic proof of the existence of the tumour, its character, and structure.

The most plausible evidence of this type of trauma–neoplasia relationship is available in the study of intracranial meningiomas.

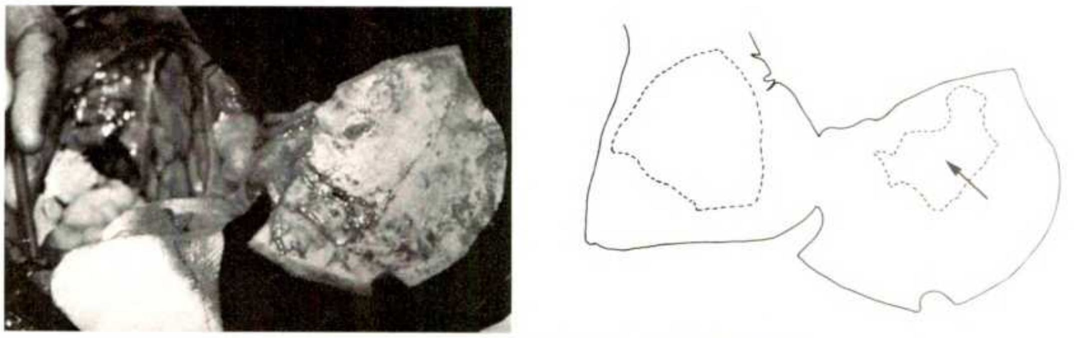
FIG. 1.—Hyperostosis of the bone-flap surrounding the old fracture site.

In his Cavendish lecture of 1922 Cushing, discussing his series of 85 verified meningiomas, stated: 'In so many of the cases in the series has a tumour been found at the exact situation where a stunning blow has been received on the skull years before, that this must represent something more than a mere coincidence.' In the large series described by Cushing and Eisenhardt in 1938, 20 out of 65 cases (31 per cent) of parasagittal meningioma had a previous history of local trauma.

Walshe (1961), in discussing head injuries as a factor in the aetiology of intracranial meningiomas, drew attention to Cushing's series and added a further 4 cases in support of the theory. He concluded: 'It is therefore submitted that the positive evidence available does not allow us to reject the existence of an aetiological relationship between a local skull injury and the subsequent development of a meningioma in a significant proportion of instances of this tumour, particularly when such an injury is related to a cranial suture and the trauma is found immediately subjacent to it.' More recently, Turner and Laird (1966) reviewed the literature and reported a case similar to the one described in this paper.

We believe that the tumour reported here, although not malignant, fulfils all Austen's (1961) criteria outlined above.

CASE REPORT

A 32-year-old, right-handed regular soldier suffered a right frontal to right parieto-occipital through-and-through machine-gun bullet wound on 8 Feb., 1945. He was admitted to the Brain Injuries Unit, Bangour Emergency Military Services Hospital, Edinburgh, and on 9 Feb. both entry and exit wounds were excised, and a craniotomy was performed with débridement and haemostasis of the missile track. Despite insufflation of penicillin and sulphamethazine powder he developed meningitis which ultimately responded to oral and intrathecal antibiotics. Postoperatively he retained a complete left homonymous hemianopia, hemiplegia, and hemianalgesia. By 8 Sept. he could walk 1 or 2 miles with the aid of a stick.

In the initial postoperative period the patient suffered six discrete left-sided motor fits associated with impairment of consciousness for which he received phenobarbitone until 1948. He had no further attacks until June, 1954, when he again suffered from left-sided motor fits. Anticonvulsants were resumed and continued up until the present time. Examination in 1954 revealed no new findings.

On 13 July, 1965, the patient complained of accentuation and persistence of the right frontal headaches from which he had suffered intermittently for 20 years. Examination at that time revealed no change. In February, 1966, his headache became so severe that he was forced to cease work. During the week prior to his readmission he became drowsy and confused and on 22 Feb. he was admitted to the Edinburgh Royal Infirmary with a history of vomiting and incontinence of urine of 1 day's duration. On examination he was conscious but confused and apathetic and only obeyed simple commands. His previous neurological deficits were more marked but he did not have papilloedema. An echo-encephalogram showed a marked shift of the midline structures from the right to the left, as did a right carotid angiogram, which also indicated the presence of a large frontal space-occupying lesion. Biopsy through the old entrance wound revealed a fine, gritty, vascular tumour instead of the cyst that had been suspected. A diagnosis of meningioma was made.

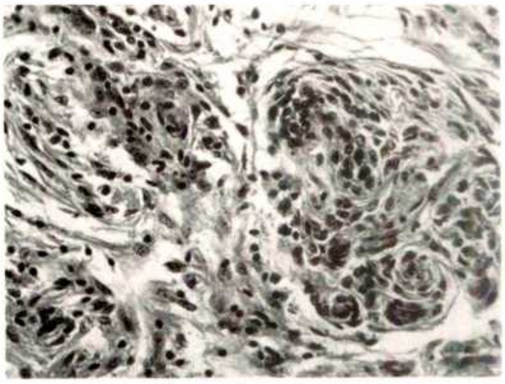
FIG. 2.—Section of the tumour. (× 116.)

The following day a large right frontal craniotomy was performed (E. R. H.). There was considerable vascularity of the diploë and on turning the bone-flap an area of hyperostosis was seen surrounding a portion of the old fracture line (*Fig.* 1). The dura below this was highly vascular with a large, middle meningeal blood-supply. On opening the dura a large meningioma was exposed, the origin of which was directly below the old fracture line and the hyperostosis. The tumour, which occupied most of the anterior half of the cranial cavity, was removed in its entirety. It measured 12·5 × 12·5 × 10 cm. and weighed 170 g. Pathological examination of the specimen confirmed the diagnosis of meningioma (*Fig.* 2).

Postoperatively the patient made good progress and was walking without help by March, 1966. He still, however, retains his left-sided deficits, which have persisted and were noted in his latest examination in March, 1972.

DISCUSSION

No one would deny that a penetrating gun-shot wound was authentic and significant and the subsequent tumour in this case developed directly beneath the old fracture site. As this future tumour site was inspected at the time of the original post-traumatic operation there is positive evidence that no tumour existed then. It is fortunate for the purposes of this case report that not only did the original and final surgery take place in the same neurosurgical unit but also that between these times the patient was reviewed in the unit as an out-patient. Thus by studying the complete case records it is apparent that there was continuity of symptoms and signs relating to the process of initial recovery from trauma and the subsequent development of new pathology. It is interesting to note that the original post-traumatic epilepsy, presumably related to the immediate effects of cortical damage, ceased without anticonvulsant drugs for 6 years from 1948 until 1954. The fits then recurred, requiring anticonvulsant suppression, and it seems likely that this recurrence was due to the new tumour growth attaining a significant size.

Cushing (1922) reviewed the evidence indicating that meningiomas originate from the islands of endothelial cells found between the layers of dura in close proximity to the arachnoid villi. In illustrating the intracranial areas of dural attachment of the meningiomas in his series he showed their frequent relationship to the dural sinuses and emphasized that these are the sites where arachnoid villi and the associated cell clusters abound. He stated that widespread occlusion of the arachnoid villi by either injury or disease will lead to stasis of the cerebrospinal fluid and hydrocephalus, and that with stimuli of this nature the cell clusters are prone to hypertrophy, a change which in turn may become permanent and lead to neoplastic tendencies.

The majority of patients with severe head injuries do not subsequently develop related meningiomas nor do the majority of patients suffering from intracranial meningiomas give a previous history of local trauma, and thus there must be other factors concerned in the aetiology of meningioma formation. Additional neoplastic agents may include infection, the irritative and occlusive effects of blood and tissue debris, the foreign-body effect of bone particles, and in the case of penetrated or explored wounds the contamination with extraneous matter or the introduction of antibiotic powder or sprays.

There is no evidence in the available literature of the development of meningiomas after surgical interference to the meninges or dural sinuses. It may be that the development of the meningioma in this case was precipitated by the gross trauma to these structures in much the same way as epithelial tumours of the skin arise from the scars subsequent to severe burns.

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ACUTE DIFFUSE PHLEGMONOUS GASTRITIS

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SUMMARY

Phlegmonous gastritis is a rare inflammatory disorder of the stomach and is thought to have first been described by Galen in 1600; its recognition as a bacterial cellulitis of the submucosa and muscularis is attributed to Cruveilhier in 1820. Three hundred and ninety cases were described in the world literature up to 1969. This case is of interest because the patient displayed a number of the typical features of the disease, and also because from a search of the literature of the past 12 years she appears to be only the second of the proven cases to have resolved with conservative management.

PHLEGMONOUS gastritis is a rare inflammatory disorder of the stomach and is thought to have first been described by Galen, although its recognition as a bacterial cellulitis of the submucosa and muscularis is attributed to Cruveilhier in 1820. Since the late 1950's a number of fairly comprehensive reviews of this condition have appeared in the American literature, based on the 390 cases described in the world literature up until 1969. These categorize predisposing causes and clinical and histological features, and indicate which form of management has been most effective.

The case described here is of interest because she displayed a number of the typical features of the disease, and also because from a search of the literature of the past 12 years she appears to be only the second of the proven cases to have resolved with conservative management.

CASE REPORT

A 67-year-old retired female factory worker from East London, who was holidaying on the South Coast under an old peoples' welfare scheme, was admitted to hospital on 1 March, 1972, with peritonitis. She had suffered from severe rheumatoid arthritis for many years and was currently on treatment with Brufen. She had never undergone steroid therapy. Apart from a recent severe upper respiratory infection which had necessitated hospital admission, there was no significant past history.

Her immediate history was of 48 hours' general malaise, abdominal discomfort, vomiting, and pyrexia. She had been seen by a general practitioner 24 hours before admission, and at that stage he had been unable to elicit any abnormal abdominal signs, except for a slight degree of hepatic enlargement. Cyclizine and Septrin were prescribed. In the course of the next 24 hours her condition had worsened, and she was admitted to hospital toxic and dehydrated. She then had a pyrexia of 37·3° C., a pulse of 110 per minute, and a blood-pressure of 100/60. Abdominally she had generalized tenderness and guarding, which appeared maximally in the lower quadrants. Bowel-sounds were absent. Radiography demonstrated two fluid levels in the right iliac fossa, but no other features of note in the abdomen. An incidental finding was of bone infarcts in the upper right humerus and upper left femur.

On admission her haemoglobin was 13·7 g. per cent and the white-cell count was 7000, being predominantly neutrophils with a shift to the left. The blood-urea and electrolyte estimations were compatible with a moderate degree of dehydration and salt depletion.

Intravenous rehydration and nasogastric aspiration were commenced, and laparotomy was undertaken through a right paramedian incision. The peritoneal cavity contained approximately 1 litre of dark-yellowish brown turbid

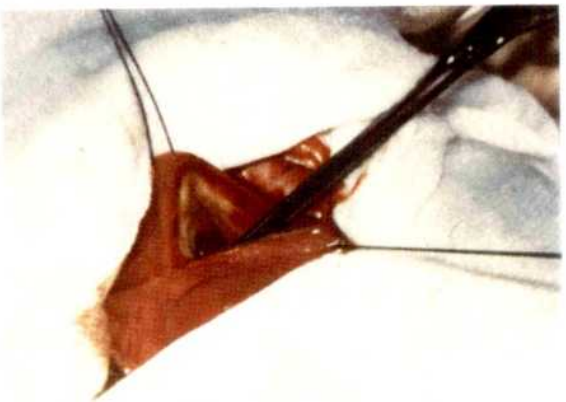

FIG. 1.—Opened stomach at operation.

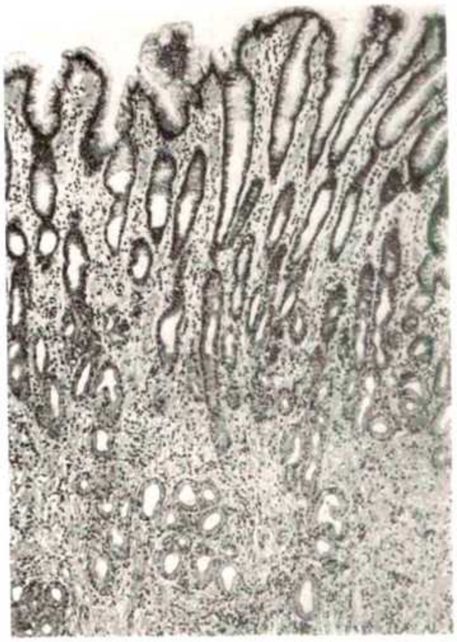

FIG. 2.—Gastric mucosa and submucosa.

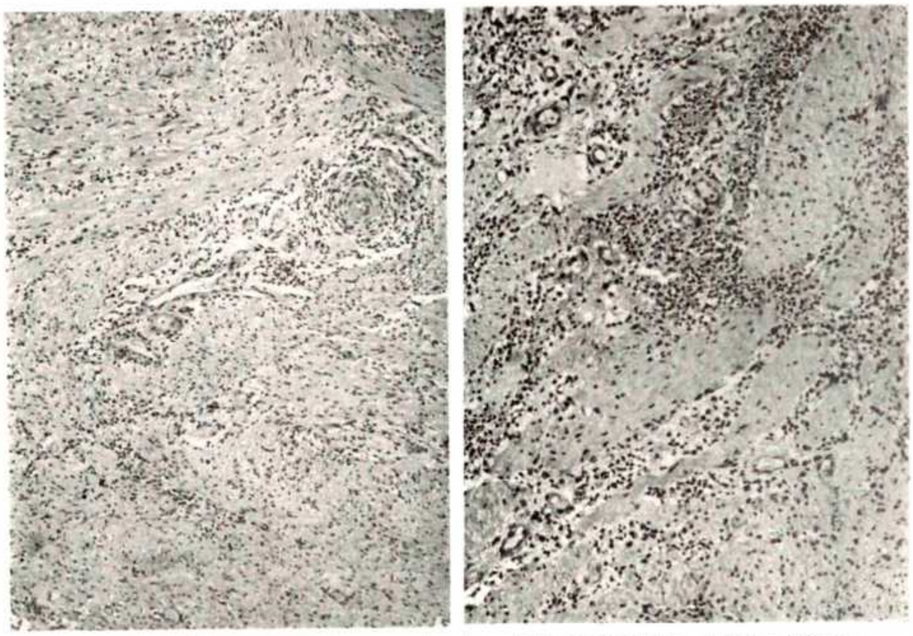

FIG. 3.—Muscularis externa showing separation of muscle bundles by polymorphonuclear infiltrate.

fluid, a specimen of which was sent for bacteriological investigation but with a negative result. The entire stomach was thick-walled and oedematous, and displayed serosal congestion from the cardia to the pylorus. In contrast the duodenum appeared relatively normal. The liver was uniformly pale and unusually firm in texture. The gall-bladder was oedematous but did not contain stones. The pancreas was exposed by opening the lesser sac through the gastrocolic omentum, and this also appeared mildly oedematous.

Anterior gastrostomy was performed as a means of obtaining clinical confirmation of the diagnosis and of providing a specimen for histological examination. On incision the appearances of the stomach wall were those of serosal and mucosal congestion, with considerable widening of the intervening layers by thick pus, as illustrated in *Fig.* 1. Inspection of the interior of the stomach revealed no additional pathology. Full-thickness biopsy was taken before closure of the gastrostomy. A wedge of liver tissue was also taken for histological purposes. No further procedure was undertaken, and after peritoneal toilet the abdomen was closed without drainage.

Histological examination of the stomach specimen showed an intact mucosa, which was oedematous and lightly infiltrated with inflammatory cells. There was heavy infiltration of the submucosa and muscle coats with acute and chronic inflammatory cells (*Figs.* 2, 3).

The liver biopsy showed slight oedema of the portal tracts which were heavily infiltrated with lymphocytes and plasma cells. There was mild fatty infiltration of periportal liver cells, which were normal elsewhere. Immediately postoperatively intensive antibiotic therapy was instituted, using an initial 5-day course of penicillin and streptomycin, followed by oral ampicillin.

Continuous gastric aspiration was maintained for 4 days postoperatively before graded oral fluids were permitted. The patient made a steady recovery, eventually being mobilized with difficulty owing to her extensive arthritis. She left hospital to finish her holiday on 12 April.

Other investigations were as follows:—

Repeat blood-counts indicated that she maintained her haemoglobin, although she had a persistent leucopenia in the region of 3000.

Serial biochemical profiles showed serum-albumin levels persistently between 2 and 2·5 mg. per cent, although her total protein levels remained within normal limits. All other estimations were normal except for a marginally raised lactic dehydrogenase.

The Wassermann reaction was anticomplementary, and the VDRL slide test was negative.

An auto-immune profile showed an atypical reaction by immunofluorescence with all tissues. This was thought to be due to the high rheumatoid titres.

The pentagastrin stimulation test yielded an 83-ml. specimen, with a *p*H of 4·3, and a free HCl content of 1·2 mEq. per specimen.

DISCUSSION

Eighty per cent of the reported cases of phlegmonous gastritis have been between the ages of 30 and 60 years. Earlier papers have suggested that the condition was commoner in females, but in the series of Stephenson, Yasrebi, Rhatigan, and Woodward (1970) the sex incidence was equal.

In over 70 per cent of cases in which organisms have been isolated from the pus a pure culture of a haemolytic streptococcus has been obtained. Other cases have yielded growths of pneumococci, staphylococci, proteus, and, rarely, gas-producing organisms which produce characteristic radiological appearances. Nevin, Eakins, Clarke, and Carson (1969) used Brown's stain to demonstrate bacteria in the submucosal layers of 3 cases. Smith, Garrett, and Herrick (1962) listed the predisposing causes as chronic gastritis, gastric trauma, alcoholism, hypo-acidity, infection elsewhere in the body, and hard work. Stephenson and others (1970) added malnutrition and low socio-economic status to this list.

Clinically, phlegmonous gastritis may be classified as localized or diffuse, and acute or chronic. In the diffuse form the entire stomach is involved, whilst in the localized variety infective changes are confined to a portion of the stomach—almost always the distal region.

Acute cases usually present with a short history of general malaise, vomiting, pyrexia, and abdominal pain. Characteristically the pain commences in the epigastrium and is completely relieved by sitting up (Deininger's sign).

The most common complication is rapidly developing peritonitis (70 per cent), but pericarditis, pleurisy, bronchopneumonia, and haemorrhage have also been recorded.

Starr and Wilson (1957) classified the condition as chronic if symptoms had been present for more than a few weeks. In these cases the clinical and radiological features often mimic linitis plastica or gastric outlet obstruction.

The macroscopic appearances of the stomach in phlegmonous gastritis are as described in this case, but occasionally there is a fibrinous exudate over the serosal surface, and rarely there is ulceration of the gastric mucosa.

Microscopically it is usual to see infiltration of all the layers of the gastric wall with inflammatory cells, but this is always maximal in, and may be confined to, the submucosa and muscularis.

The treatment of this condition has evolved over a period of many years into an aggressive surgical approach complemented by vigorous antibiotic therapy. In 1938 Eliason and Murray-Wright recorded a 16 per cent survival rate following gastrostomy and transmural drainage. By 1957 Starr and Wilson were able to record a 52 per cent survival rate and found that gastric resection with antibiotic therapy gave the best results. The recent analysis of the world literature by Stephenson and others (1970) provides a convincing testimonial for radical gastric resection, even in the diffuse type of phlegmonous gastritis. Of the 24 cases reviewed, there were 14 known survivors and the outcome in 3 cases was not known. Thirteen of the survivors had undergone either total or subtotal gastrectomy, and 8 of these had also received antibiotics. Of the 7 who died, 4 had received antibiotic therapy, 1 following subtotal gastric resection. The remaining 3 cases had neither received antibiotics nor undergone gastric resection.

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DEMONSTRATION OF SIMPLE URETEROCELE PROLAPSING INTO THE URETHRA OF AN ADULT MALE

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SUMMARY

A case is reported of a simple ureterocele descending into and obstructing the urethra during micturition in a 30-year-old male who had symptoms for only 6 months. This was demonstrated and recorded by a simple technique using conventional radiographic apparatus.

CASE REPORT

A 32-year-old pilot, who had previously enjoyed excellent health, presented with a 6-month history of dysuria. On starting to micturate he would pass 10–20 ml. of urine normally then the stream would stop abruptly. After a further minute, without straining, the stream would start again and continue until voiding was completed. The symptoms at first had only occurred during a diuresis, e.g., after alcohol, but more recently had become constant. The only other symptom was perineal discomfort during micturition.

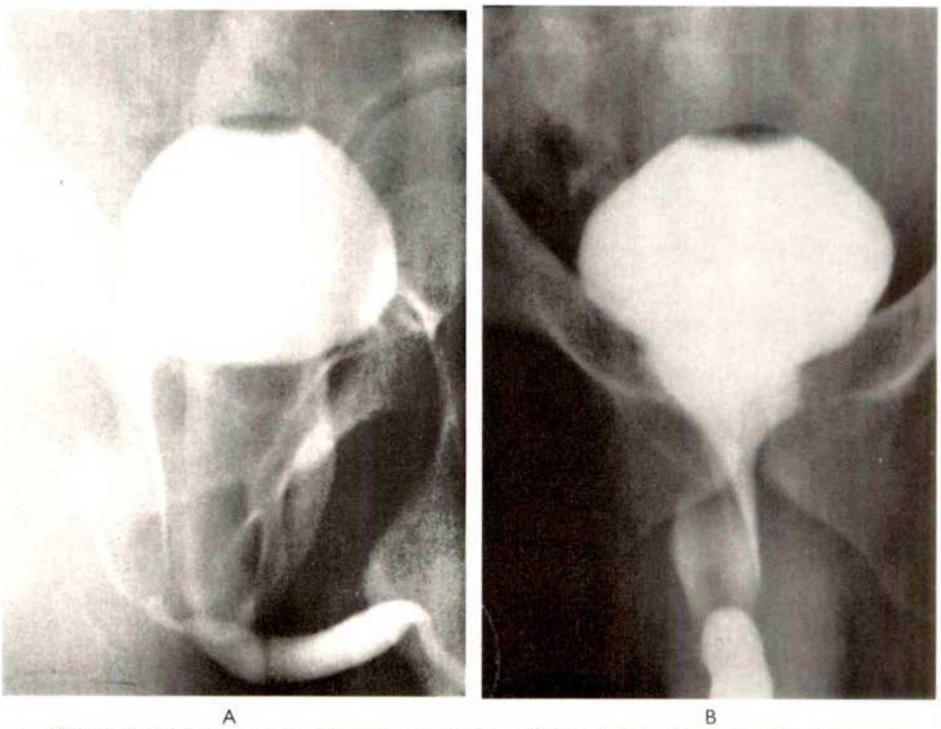

FIG. 1.—Oblique (A) and postero-anterior (B) cystograms showing widening of the bladder-neck and posterior urethra with a finger-shaped filling defect projecting downwards.

A micturating cystogram was carried out using conventional image-intensifier fluoroscopy and spot films. The bladder was filled retrogradely with 500 ml. of 17·5 per cent Diodone. The bladder was smooth in outline with a very faintly visible filling defect, 2·5 cm. in diameter, lying posteriorly on the left. Voiding was commenced and after 20 ml. of urine had been passed there was sudden cessation of the stream. The oblique view recorded at that stage (*Fig.* 1 A) showed widening of the bladder-neck and posterior urethra with a finger-shaped filling defect projecting downwards from the left and posteriorly. *Fig.* 1 B shows similar appearances on a postero-anterior film. These changes persisted throughout voiding and the filling defect appeared to remain in the urethra when the bladder was empty. With this investigation alone, differentiation could not be made from a prolapsing vesical polyp, urethral polyp, foreign body, non-opaque calculus, or ectopic ureterocele.

An intravenous pyelogram showed a moderately large ureterocele at a normally sited left ureteric orifice, with dilatation of the lower third of the left ureter. Otherwise the urinary tracts appeared normal, with no obstructive signs on the right (*Fig.* 2).

At cysto-urethroscopy a contracting ureterocele was found overlying the left side of the bladder base. The right ureteric orifice was normal and no other abnormality was found. A hole was made in the ureterocele by fulguration. Postoperatively the patient has been asymptomatic for 12 months.

DISCUSSION

Symptoms of bladder-neck obstruction are not uncommon in children with ureteroceles at normally sited ureteric orifices. Thompson and Kellalis (1964) reported interruption of the stream, overflow incontinence, or acute urinary obstruction in 20 of the 29 children with ureterocele who presented at the Mayo Clinic prior to 1963. Prolapse of a ureterocele along the female urethra and its presentation outside the external urinary meatus has been reported many times. Emmett and Logan (1944) found 37 recorded cases.

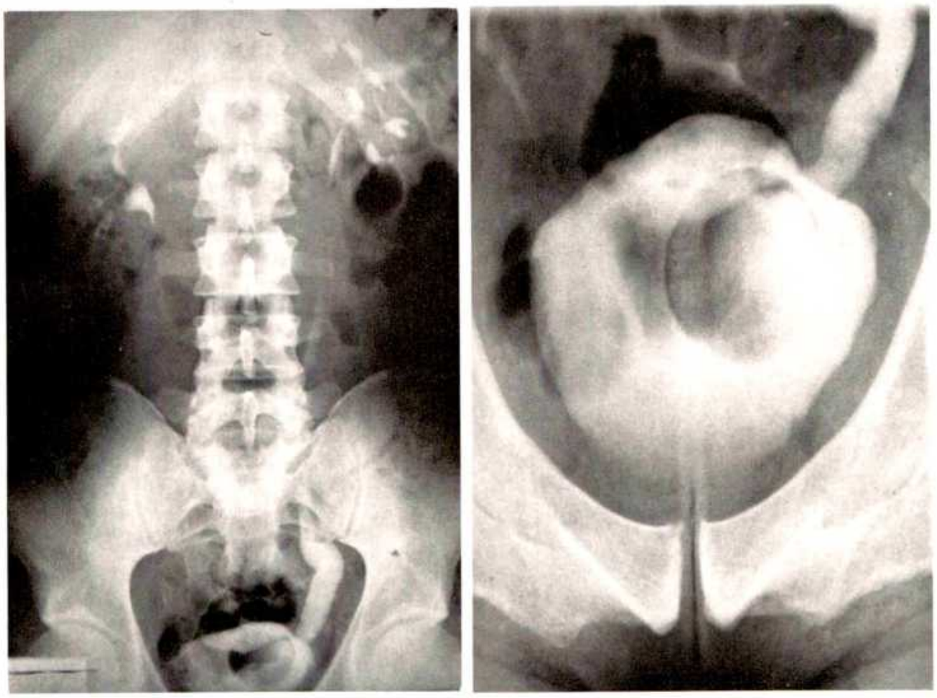

FIG. 2.—Intravenous pyelograms showing a moderately large ureterocele at a normally sited left ureteric orifice with dilatation of the lower third of the left ureter.

However, demonstration of a simple ureterocele prolapsing into the adult male urethra is extremely rare. We are aware of only 1 recorded case, that of Poznanski, Reynolds, and Johnson (1968). Their patient was aged 15 years and had a 2-year history of interruption of the urinary stream. Kinescopic cine-radiography, spot films from the image-intensifier phosphor, and videotape recording were used and the prolapsing ureterocele was recorded only on the cine-film.

In the present case we used conventional image-intensifier fluoroscopy and spot films. Using this simple technique the ability to record dynamic changes occurring during urine flow is lost. However, these can be observed on the television monitor and excellent detail can be recorded on spot films taken at appropriate intervals and angles. This technique is particularly suitable for a case such as this in which there is a slow rate of urine flow.

Acknowledgements.—We are indebted to Director-General of Medical Services, R.A.F., for permission to publish, and to Sir Peter Dixon, Group-Captain W. J. L. Harries, and Group-Captain P. D. Sutton for their encouragement and advice.

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REVIEWS AND NOTICES OF BOOKS

Pathology of Injury. Edited by A. C. HUNT, M.D., F.R.C.Path., Plymouth General Hospital. 9½ × 7 in. Pp. 129. 1972. London: Harvey Miller & Medcalf Ltd. £2.

THIS is a short, concise, and most inexpensive report from a working party of pathologists, describing 'current knowledge and future development'. The editor and his contributors have carried out an admirable and most valuable review of the pathology, biochemistry, metabolism, endocrinology, etc., of injury, including special subjects such as bacterial infection, uraemia, fat, and thrombotic embolism. However, the views of the obviously expert contributors about research and future development are not nearly so challenging. Even so, as a synopsis this should be background reading for all surgeons, especially those in training. This publication appears to have been written in order to highlight the recommendations of the working party of pathologists about numerous programmes on education and research for medical schools, colleges, Department of Health and Social Security, Medical Research Council, etc. One of the main recommendations is that major accident departments should be designated as centres of research in trauma and its pathology. This would be most acceptable to many surgeons and indeed has been recommended for a long time by the surgeons responsible for such accident departments. If more and more interested groups would press for support to develop research programmes this would help greatly in the battle against the 'modern devastation' of trauma.

Angiographie und ihre Fortschritte. Edited by Dr. K. E. LOOSE, Itzehre/Holst. 9½ × 6½ in. Pp. 308 + xx. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.98.

THIS book is an account of a congress which took place on 7–9 May, 1970, showing the progress of angiography, in which radiologists and vascular surgeons from Germany, Austria, Sweden, the Netherlands, and other countries took part. The scope of angiography has widened on such a scale that the book should be of universal interest.

This book includes contributions on many aspects of angiography. Angiography of the vessels of the limbs has been popular for many years, and the technical refinements such as cinematography and the use of amplifiers detailed in this book are interesting. Selective arteriography of the abdominal organs, for instance, in the case of suspected pancreatic carcinoma or abdominal haemorrhage, should prove to be one of the most important diagnostic aspects. Microradiography demonstrates calcification of the elastica and media of vessel walls, which are apparently different processes. Pharmaco-angiography is useful in showing vessels not visible by orthodox renal arteriography. It is doubtful whether phlebography should be performed in every case of uncomplicated varicose veins as argued by one of the participants. Lymphography has an important place in surgery and some surgeons do not perform rectal amputations without lymphography in order to determine the condition of the regional glands. Interesting communications deal with the vascularization of fractures (the periosteum is less important in this respect than was assumed previously) and the haemodynamics of venous grafts. One may express the hope that Professor Loose and his colleagues will continue to publish the results of future congresses.

Gynaecology Illustrated. By MATTHEW M. GARREY, M.B., D.P.H., F.R.C.O.G., Royal Samaritan Hospital for Women, Glasgow; A. D. T. GOVAN, M.D., Ph.D., F.R.C.P. (Glas.), F.R.C.Path., Royal Samaritan Hospital for Women, Glasgow; C. H. HODGE, M.B., F.R.C.S. (Edin.), F.R.C.O.G., Larkfield Hospital, Greenock; and ROBIN CALLANDER, F.F.Ph., M.M.A.A., A.I.M.B.I., Medical Illustration Unit, University of Glasgow. 9½ × 7½ in. Pp. 492 + xi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £3.

THIS book has been produced in a style similar to that of *Obstetrics Illustrated*, the immediate popularity of which has no doubt prompted the publication of this sister volume.

The emphasis is on simple line-drawings interspersed with a minimum of text. The result is an excellent summary of the essentials of gynaecology, giving a very friendly and readable effect.

There is little to criticize. The ubiquitous 'diverticulae' appears on p. 349 although it is correctly spelt 'diverticula' on p. 125. It is possible that in a book for undergraduates there is a slight imbalance between the information on diagnosis and that on operative and other techniques, for example, there are 6 whole pages devoted to the physics of radiotherapy as compared with a total of 4 pages on the diagnosis of fibroids, endometriosis, and tubal pregnancy.

This book is assured of a wide circulation, especially at its modest price.

The Neuropathology of the Alimentary Tract. By BARBARA SMITH, M.D., Ph.D., F.R.C.S., St. Bartholomew's Hospital, London. 9 × 6 in. Pp. 118 + ix. Illustrated. 1972. London: Edward Arnold (Publishers) Ltd. £4.

THIS is an important monograph describing the abnormalities of the myenteric plexus of the alimentary tract and is written by an acknowledged expert. The normal anatomy and the changes induced by pathological conditions are described in detail. The author points out that previous work has been hampered by inappropriate histological methods and she describes in detail her preparation of the specimens. The book maintains a balance between clinical abnormalities resulting from damage to the autonomic nerves and experimental work which has been done in this field, together with experimental work done by the author. The important feature common to all conditions in which there is myenteric plexus damage, whether congenital or acquired, is hypertrophy and probably hyperplasia of the smooth muscle. This thickening of the muscle is much more severe than that seen as a result of work hypertrophy behind an organic obstruction and is a macroscopic hall-mark of the condition.

There are chapters dealing with achalasia of the cardia, juvenile and adult hypertrophic pyloric stenosis, and Chagas's and Hirschsprung's diseases of the large bowel. Perhaps of particular interest is a discussion of the difficult problem of acquired megacolon and cathartic colon. There is also an important chapter on drugs which cause damage to the myenteric plexus. Although rather expensive, this book is well illustrated by photomicrographs and contains a bibliography of over 300 references. It should be read by everyone with an interest in gastroenterology.

Medical Care in the U.S.S.R. Report of the U.S. Delegation on Health Care Services and Planning. U.S. DEPARTMENT OF HEALTH EDUCATION AND WELFARE. NATIONAL INSTITUTE OF HEALTH. 1972. 50 cents.

IN May and June, 1970, a team of distinguished American doctors visited the Soviet Union to study health services and medical education. This was at the time of inception of a new health code legislation which at first sight would remind British readers of the reorganization of our own N.H.S. which is due to take place in 1974. However, the differences are considerable: the Soviet plan has as its stated aims the improvement of facilities, specialization, a more even standard of care in town and country, and an improvement in the first-line care offered by the polyclinic out-patients' system. Our own plan is for management and monitoring, perhaps with the same objectives as the U.S.S.R. but also, some suspect, motivated by the need for economy in an open-ended consumer demand for a necessary commodity which is free. The table of the organization plan on p. 7 of the U.S. booklet is reminiscent of the exhibits in our own Grey Book. The main part of the text concerns the powerful medical collectives that, like most things in Russia, do everything on a large and categorical scale, with less concern for individual needs except in so far as these fall under the procedural headings of the polyclinics, sanatoria, and hospitals. Emergency medical care, the 'Scoraya' (meaning = quick), has an overriding power of accident and emergency care and allocation with all the priority needed to carry this out. One can imagine the appeal to U.S. health workers in this. The service in Leningrad, Moscow, and Kiev was inspected and detailed information and examples are cited which are of great interest to Western readers. However, no judgement is passed on the standards. There are some amusing local cartoons and some interesting photographs of places visited. The Western medical tourist in the U.S.S.R., who may see little more than the sights and amusements of the lay visitor, will find this booklet of considerable interest, though like most such publications it still does not answer the basic question: 'What was it like?'

Bone Tumors. Fourth Edition By LOUIS LICHTENSTEIN, M.D., San Francisco. 9½ × 6¾ in. Pp. 441 + xviii, with 496 illustrations. 1972. London: Henry Kimpton. £11.

To those of us with a particular interest in bone tumours a new edition of Lichtenstein's book is quite an event, for it has for many years enjoyed a high reputation amongst the standard textbooks on the subject.

Knowing the author to be a clinical professor of pathology, one must expect this aspect to be stressed. Clinical features such as radiographs and treatment are, however, fully covered, although not in such detail. However, the reviewer must confess to some surprise at the very high standard of these purely clinical passages. Had they been written by a most experienced clinician in this field he could justifiably be proud of his work. This is not to say that one agrees with all that is written. The apparent trans-Atlantic bias against radiotherapy is evident and perhaps unjustified. Indeed, no reference could be found to the excellent work on osteosarcoma that has since come from Westminster Hospital by Sir Stanford Cade and others. In spite of this the bibliography is impressive and reasonably up to date.

Costing £11·00 in this country, this book is expensive Nevertheless, the reviewer considers it to be amongst the three best textbooks on the subject, being authoritative concise, and yet readable. Obviously most pathologist will wish to have access to it. I would also strongly recommend it to clinicians as one of the best reference books for them on the subject.

BOOK NOTICES

[*The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.*]

An Atlas of Surgical Anatomy and Techniques of the Temporal Bone. By RALPH J. CAPAROSA, M.D., Pittsburgh. 11 × 8½ in. Pp. 124 + xiii, with 111 illustrations. 1972. Springfield, Ill.: Charles C. Thomas. $18.

General Urology. By DONALD R. SMITH, M.D., San Francisco. 10¼ × 7¼ in. Pp. 436. Illustrated. 1972. London: Blackwell Scientific Publications. £4·15.

Die Behandlung der hämatogenen und der traumatischen Osteomyelitis. By STOJAN POPKIROV, Fruhjahr. 9½ × 6½ in. Pp. 408. Illustrated. 1971. Berlin: Veb. Verlag Volk und Gesundheit. DM.172.40.

A Nurse's Guide to the X-ray Department. By MYER GOLDMAN, M.B., Ch.B., D.M.R.D., Consultan Radiologist, North Merseyside, Ormskirk, and Southport Hospitals. 8½ × 5½ in. Pp. 87 + xv, with 47 illustrations. 1972. Edinburgh: Churchill Livingstone £1.

Unfall Begutachtung. By Dr. E. GUNTHER, Köln, and Assessor R. HYMMEN, Köln. 9½ × 6½ in. Pp. 158 + xi Illustrated. 1972. Berlin: Walter de Gruyter & Co DM.42.

Unfall Praxis. By Professor Dr. WALTHER EHALT 9 × 6 in. Pp. 233 + xviii, with 297 illustrations. 1972 Berlin: Walter de Gruyter & Co. DM.42.

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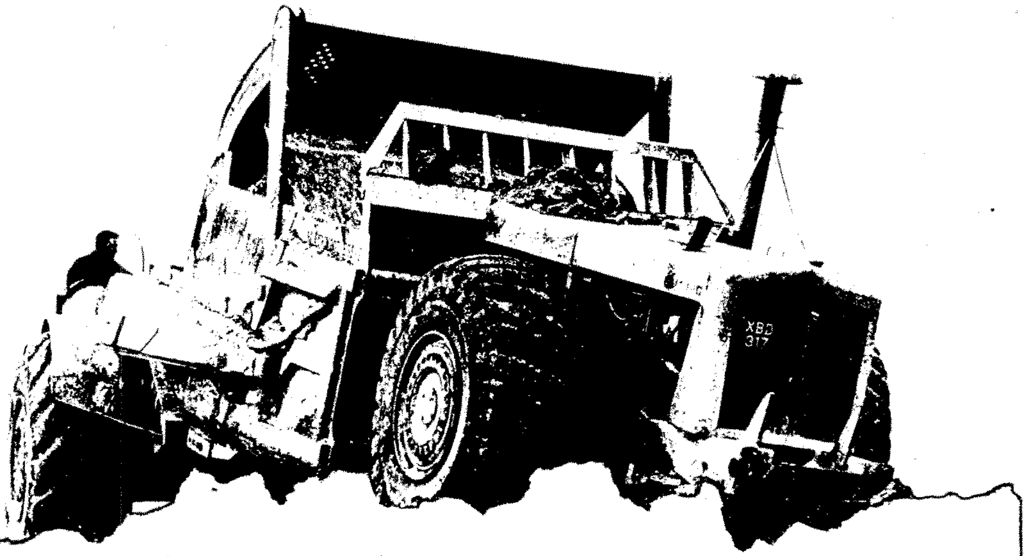

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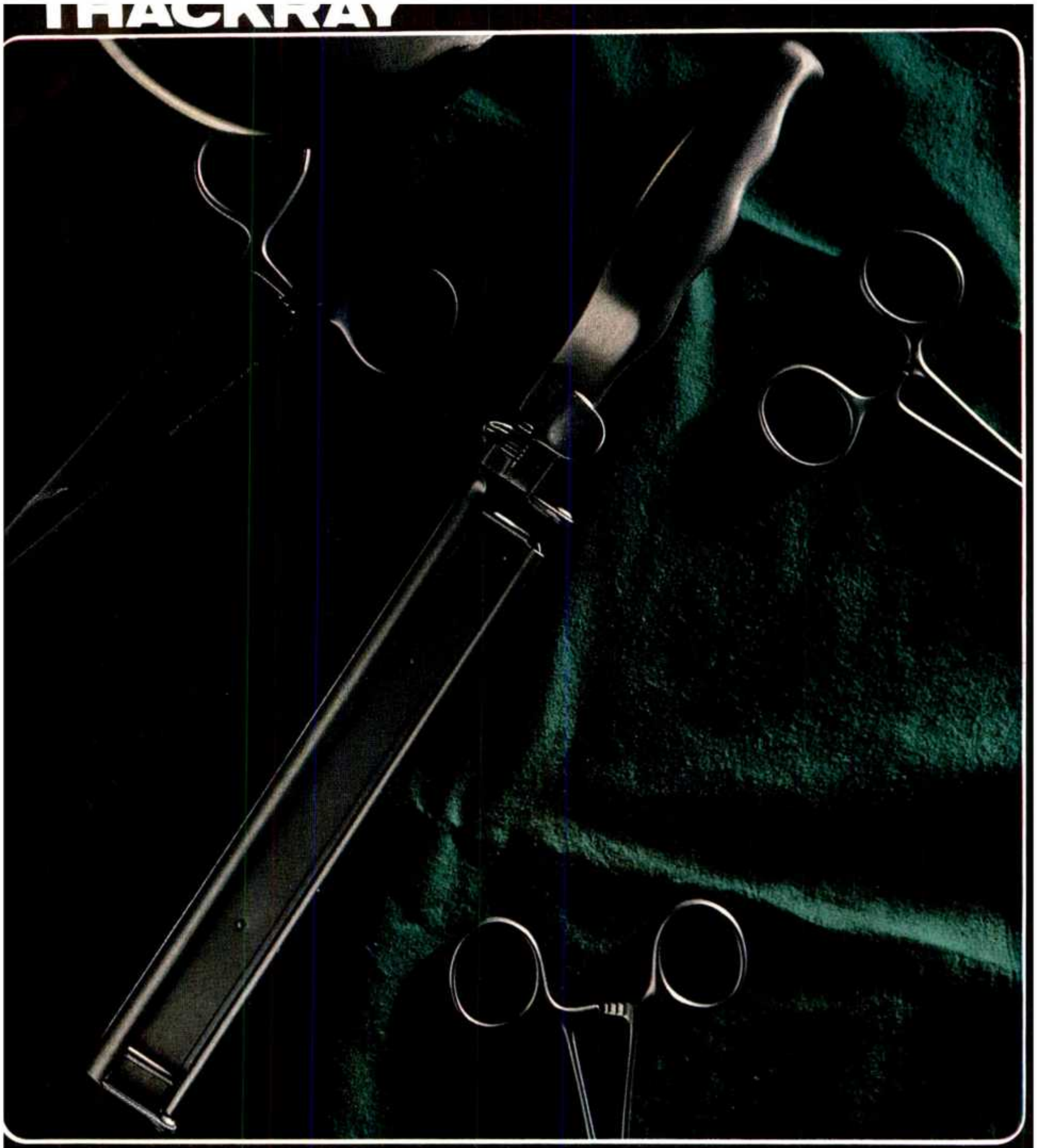

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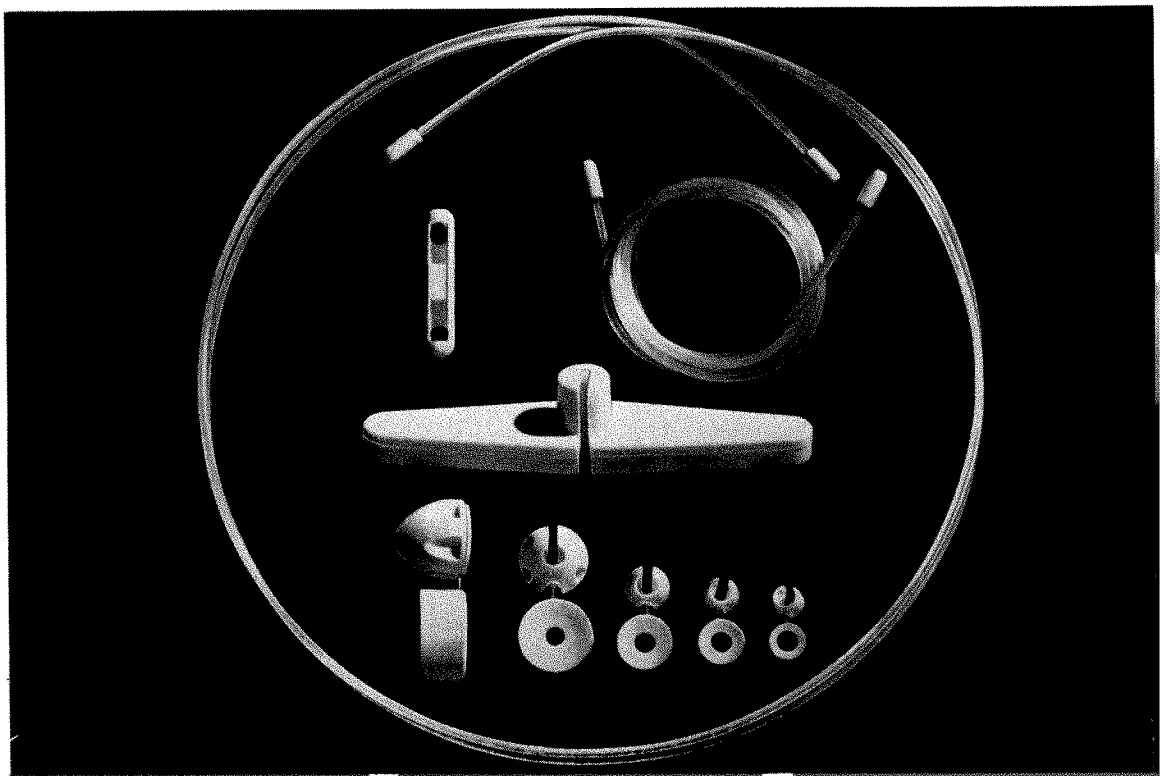

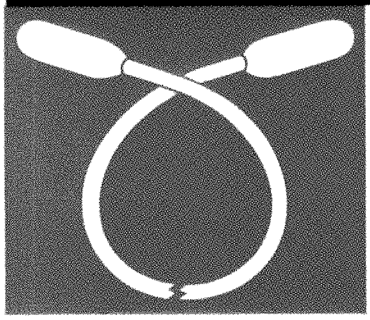

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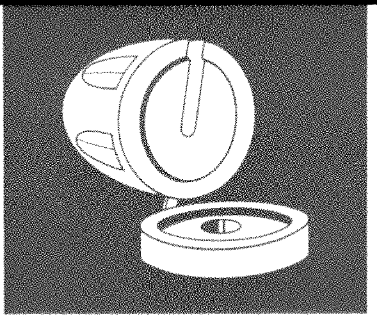

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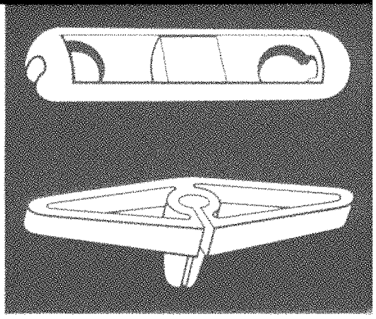

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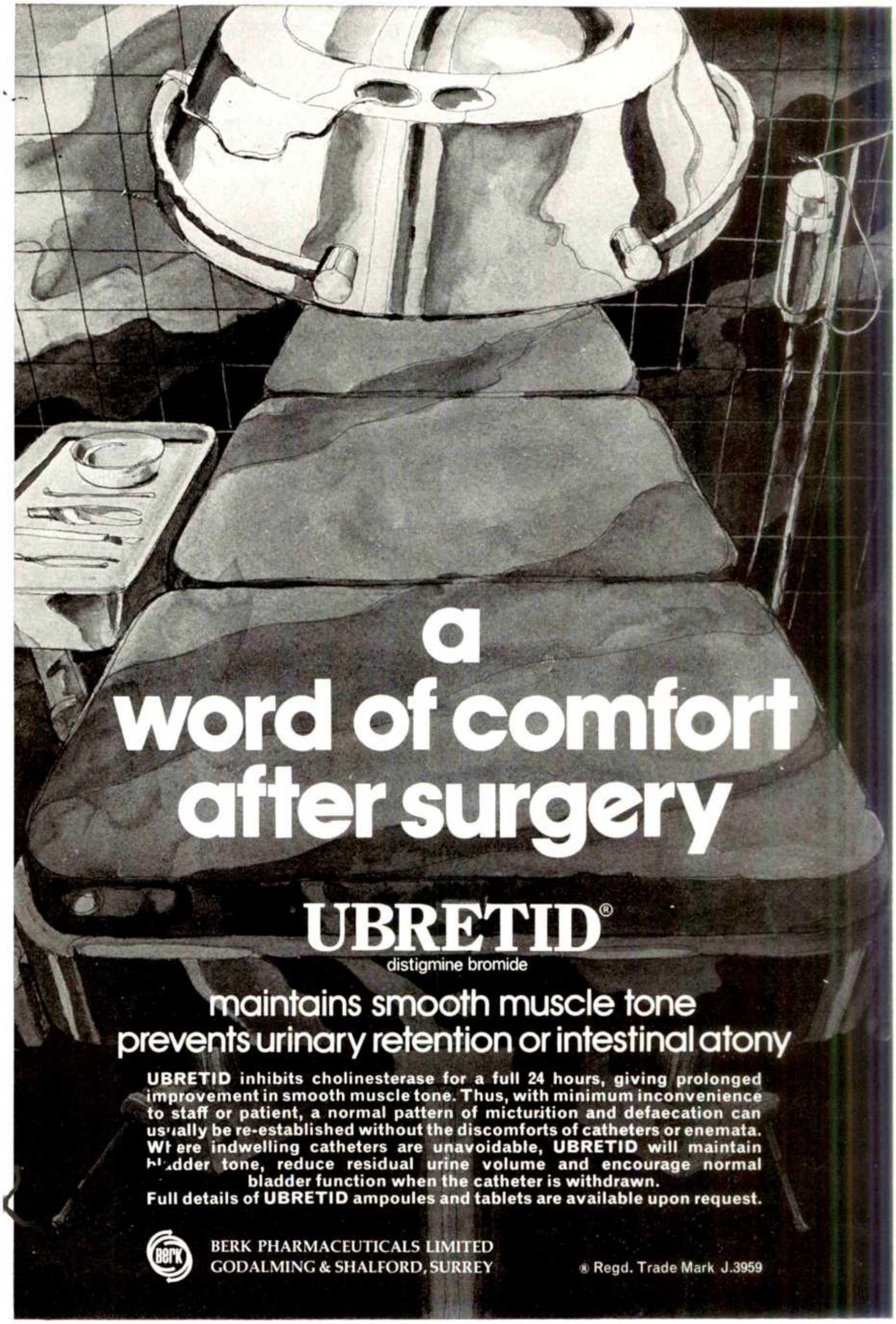

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1 *Brit med J*, (1969), **4**, 470
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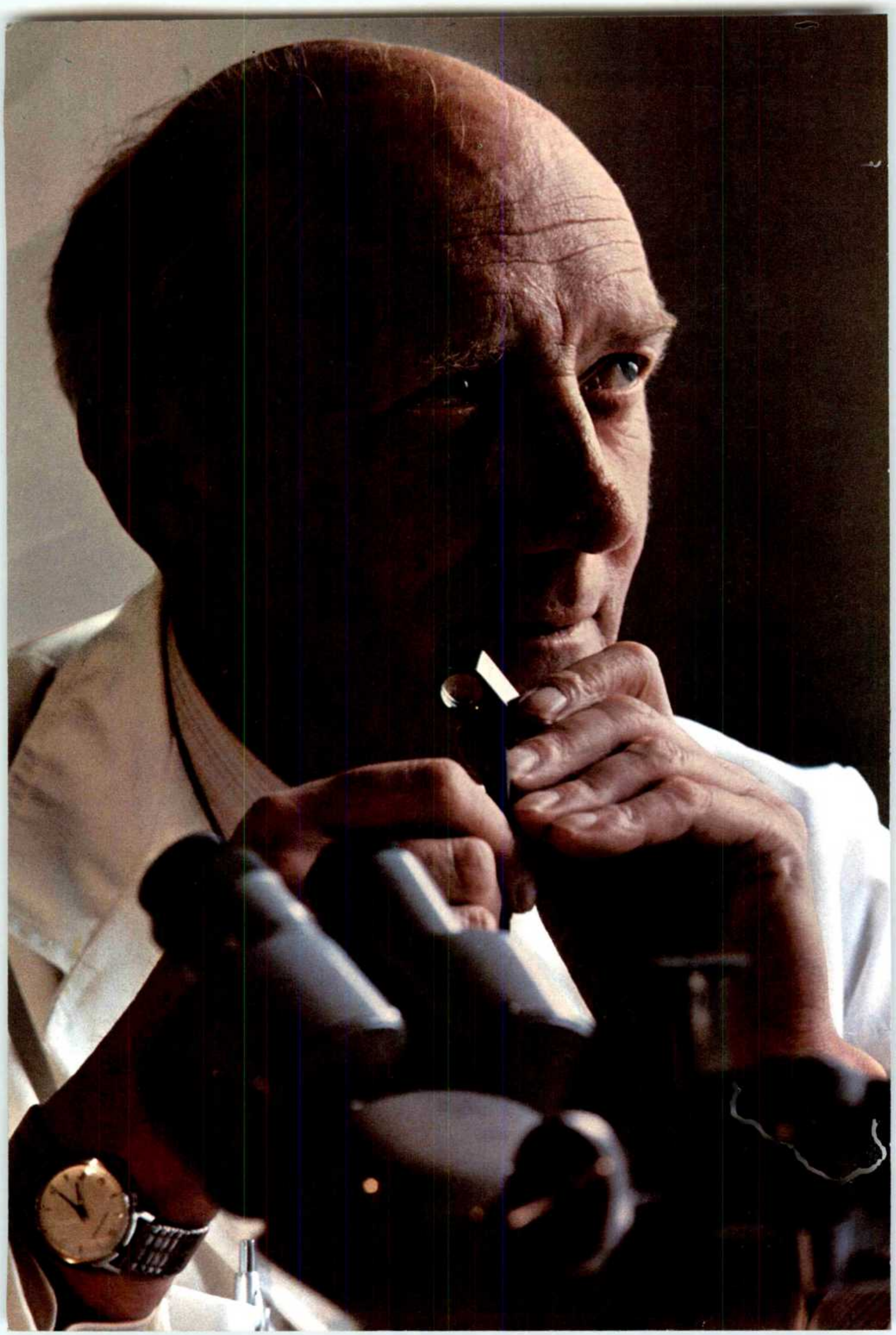

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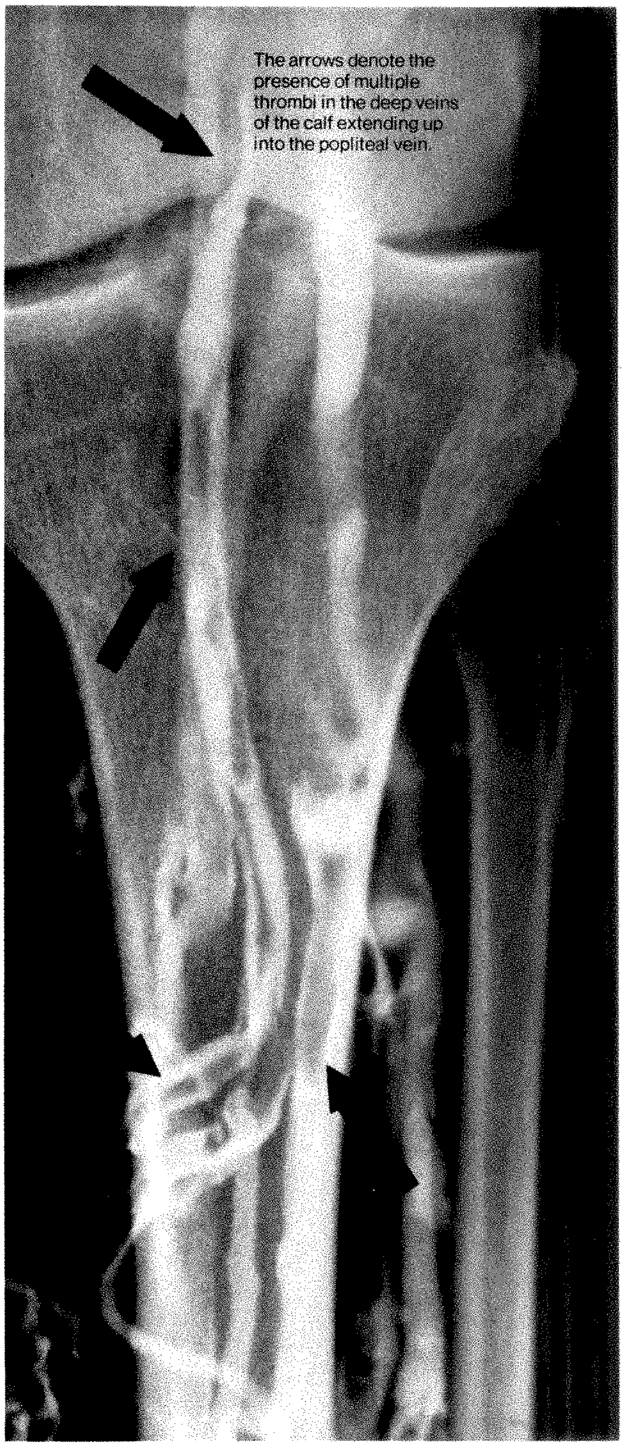

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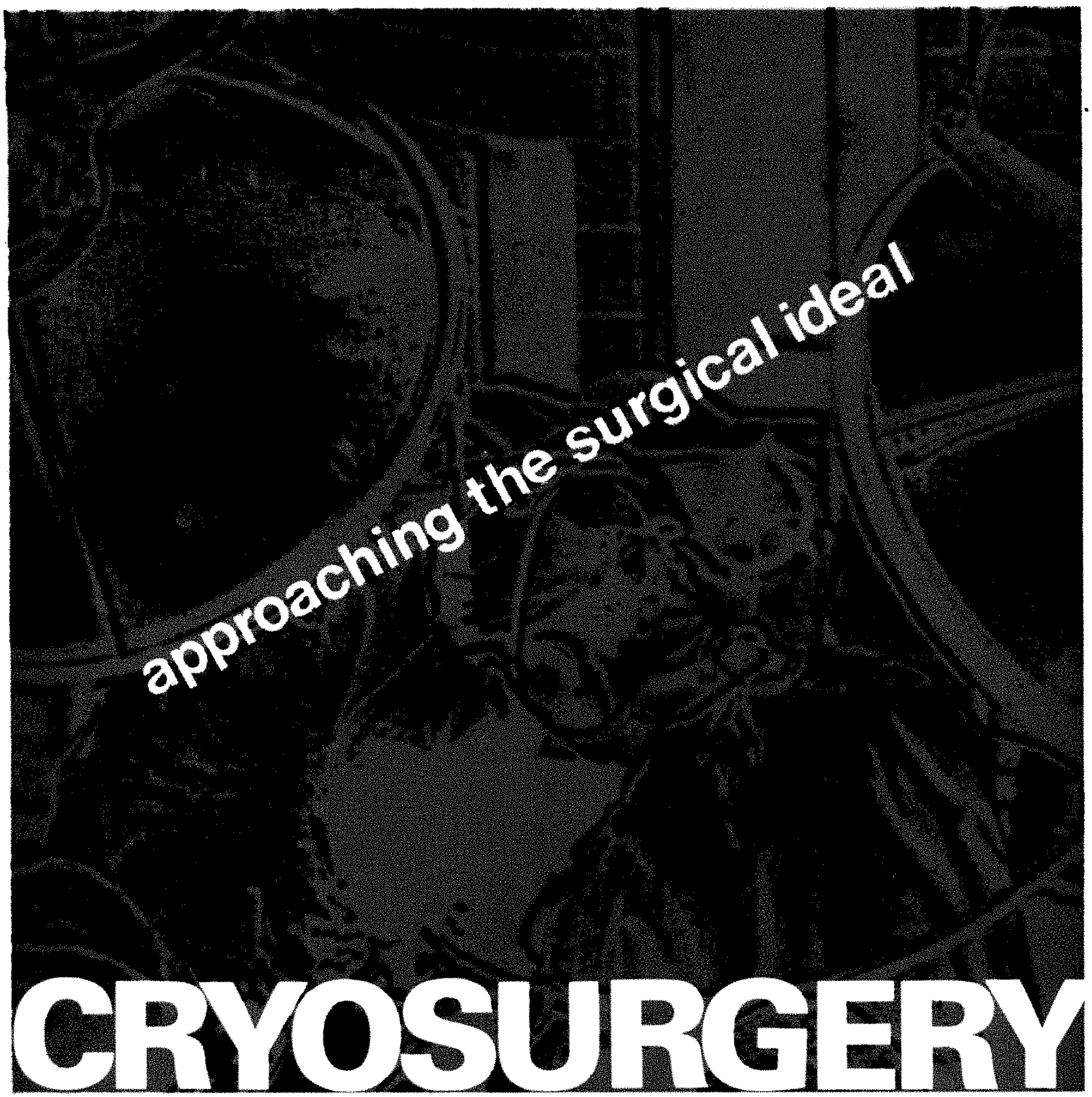

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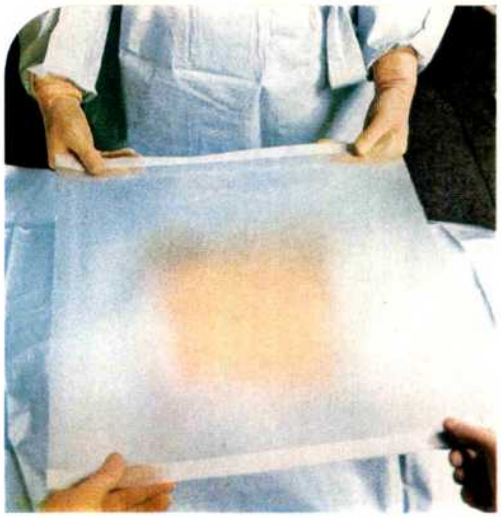

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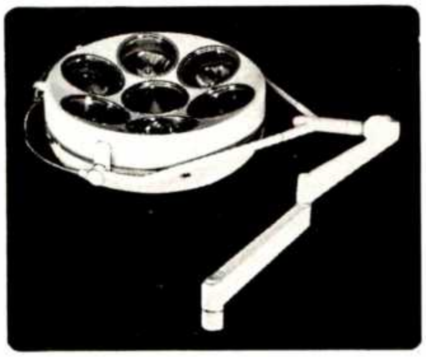

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ORIGINAL PAPERS

ARTERIAL EMBOLUS TO THE UPPER LIMB

BY H. R. CHAMPION* AND W. GILL*
DEPARTMENT OF CLINICAL SURGERY, THE ROYAL INFIRMARY, EDINBURGH

SUMMARY

Seven cases of arterial embolus to the upper limb are presented. The cases support the current trend to management by embolectomy and the restoration of normal hand function as an important feature.

ALTHOUGH early embolectomy is the accepted treatment of choice for emboli lodged in major arteries, traditional teaching had delayed its widespread application to upper-limb emboli. This may stem from the comparative infrequency (15 per cent) of upper-limb emboli (*Table I*), and the usual absence of gangrene whatever the therapy employed. With its abundant collateral blood-supply, occlusion of the upper-limb arteries has always been viewed with less concern than comparable lesions in the lower limb.

In 1963 Fogarty introduced his catheter (Fogarty, Cranley, Krause, Strasser, and Hofner, 1963), and this significantly reduced the amputation rate in patients with lower-limb emboli (Provan and Ransford, 1970; Thompson, Sigler, Rant, Austin, and Patman, 1970). The expedient application of this technique in the upper limb promotes the main objective of treatment, namely, the complete restoration of function in a previously ischaemic hand, where subsequent fine sensation and movement are all important.

Seven cases of upper-limb embolus which presented to the Professorial Surgical Ward in the Royal Infirmary of Edinburgh in a 7-year period are reported. *Table II* shows the case summaries.

CASE REPORTS

Case 1.—C. T., a 72-year-old woman who suffered from mitral stenosis, hypertension, exertional angina, and atrial fibrillation controlled on digoxin, was admitted in December, 1965, 90 minutes after she had first felt a sudden pain in her left arm. On examination the arm was white from mid-humeral level and was pulseless. Power was markedly diminished in the forearm and hand. She had an irregular pulse-rate of 100 per minute and a blood-pressure of 210/130 mm. Hg, and an electrocardiogram showed hypertrophy of both ventricles.

Table I.—FREQUENCY OF UPPER-LIMB EMBOLI COMPARED WITH THAT OF ALL EMBOLIC EPISODES REPORTED IN THE LITERATURE

Author	*All Embolic Episodes*	*Upper-limb Emboli*
Pearse (1933)	279	46
Key (1936)	380	46
Haimovici (1950)	312	53
Daley, Hattingley, Holt, Blend, and White (1951)	393	39
Warren, Linton, and Scannell (1954)	232	59
Shumaker and Jacobson (1957)	55	8
McGarity, Logan, and Cooper (1958)	86	16
Blum and Rosenthal (1960)	38	3
Young, Humphries, De Wolfe, and Lefevre (1963)	114	21
Stirling, Morris, Officer-Brown, and Barnett (1963)	41	7
Cranley, Krause, Strasser, Hofner, and Fogarty (1964)	214	29
Martin, King, and Stephenson (1969)	88	12
Thompson, Sigler, Rant, Austin, and Patman (1970)	188	25
	2420	364

Sixty minutes after admission a block of the brachial plexus was performed and resulted in the relief of pain but no return of the peripheral pulses. Reflex heating produced a slight improvement in the skin circulation. There was, however, no improvement in sensation or muscle power and 12 hours after admission (13½ hours after the onset) embolectomy was performed using a suction catheter through a mid-brachial arteriotomy incision.

Although the radial pulse was not palpable in the immediate postoperative period, the hand became warmer and the patient was placed on heparin (12,000 I.U. 6-hourly i.v.). Intensive physiotherapy resulted in little functional improvement of the hand and no sensory improvement or fine muscle movement was observed. The

---

*Present address: Center for the Study of Trauma, University of Maryland Hospital, 22 S. Greene Street, Baltimore, Maryland 21201.

Table II.—DETAILS OF THE 7 CASES OF UPPER-LIMB EMBOLUS IN THE PRESENT SERIES

CASE	AGE AND SEX	CONCOMITANT ILLNESS	DRUGS	CLINICAL LEVEL OF BLOCK	TREATMENT	TIME SINCE ONSET OF SYMPTOMS (hr.)	POST-OPERATIVE RADIAL PULSE	RESULT
1. C. T.	72 F	Rheumatic heart disease, mitral stenosis, atrial fibrillation, hypertension	Digoxin, chlorthiazide	Brachial	1. Brachial plexus block 2. Embolectomy, anticoagulants, physiotherapy	2½ 13½	No	Permanent loss of sensation and fine movement in the hand. Died of myocardial infarction 11 mth. later
2. C. F.	58 F.	Mitral valve disease, atrial fibrillation, previous embolus, intermittent claudication	Digoxin	Axillary	Embolectomy, heparinization, oral anticoagulants	6¾	No	Good
3 C H.	58 F.	Diabetic, and recent previous myocardial infarct	Nil	Brachial	Embolectomy, papaverine, heparinization, reflex heating, physiotherapy, oral anticoagulants	5	No	Power normal, hand cooler, sensation normal
4. M. F.	64 F.	Mitral stenosis, atrial fibrillation	Digoxin	Axillary	Embolectomy, heparin, physiotherapy, digoxin and frusemide	5	Yes	Good function
5. W. S.	65 M.	Aortic sclerosis, mitral incompetence, atrial fibrillation, chronic bronchitis, congestive heart failure, cirrhosis	Digoxin, frusemide, Aldactone-A	Brachial bifurcation	Heparinization for 1 wk., physiotherapy	6	Yes	Hand satisfactory Fatal cerebral embolus 3 mth. later
6. R. T	58 M	Previous myocardial infarct, intermittent claudication	Nil	Brachial bifurcation	Embolectomy, heparin, physiotherapy	9	Yes	Complicated by cerebrovascular accident. Good functional recovery but some fibrosis of thenar muscles
7. M. McM.	48 M.	Atrial fibrillation/flutter, myocardial infarction, ventricular tachycardia	Digoxin, practolol, Lasix, Warfarin, procainamide, lignocaine	Axillary	Heparin, embolectomy, physiotherapy	8	Yes	Good No loss of function

patient was followed up but there was no change in her upper-limb status and she eventually died 11 months later from a myocardial infarction.

Case 2.—C. F., a 58-year-old female with mitral valve disease and atrial fibrillation, experienced sudden left-arm pain accompanied by pallor 4¾ hours prior to her admission in April, 1967. The patient was obese, and had an irregular pulse of 65 per minute and a blood-pressure of 200/120 mm. Hg. On admission the arm was cyanosed beyond the elbow and sensation was absent from a point 5 cm. below the olecranon, with marked loss of power in the flexors of the wrist and in the hand muscles. No pulses were present beyond the left subclavian.

Axillary embolectomy was performed 2 hours after admission, using a suction catheter. A large amount of clot was removed both proximally and distally, which resulted in an acceptable proximal and retrograde flow of blood.

Heparin (12,000 I.U. 6-hourly i.v.) and oral anticoagulants (phenindione) were started postoperatively. The radial pulse did not return but there were good sensation and fine movement after a course of physiotherapy. Because of previous embolic episodes she was maintained on oral anticoagulants.

Case 3.—C. H., a 58-year-old female, had had angina pectoris 5 days previously with the sudden onset of pain, weakness, and numbness in her left arm 2 hours before her admission in January, 1971. She was a known diabetic controlled on dietary measures. There were no pulses distal to the axillary artery and sensation was diminished below the elbow. An electrocardiogram showed sinus rhythm and an old anteroseptal infarct with recent extension.

An embolectomy was carried out 3 hours after admission through a mid-brachial arteriotomy. Pulsation distal to the arteriotomy did not return despite bathing the vessel in 2·5 per cent papaverine. It was decided to close the wound and to reassess the arm in 6 hours, during which time reflex heating was used. The patient was heparinized using 1100 I.U. per hour by continuous infusion. The brachial pulse returned, and over the subsequent 2 days power and sensation in the hand and forearm returned to normal. Pulsation in the radial artery never returned and the left hand was always slightly colder than the right.

Case 4.—M. F., a 64-year-old female, presented in November, 1971, with a history of sudden severe pain in her right arm of 2 hours' duration. The arm became white and cold. She was known to have mitral stenosis and atrial fibrillation controlled by digoxin. On examination the right arm was cold and the hand cyanotic. There were no pulses palpable below the right subclavian. The patient was distressed and dyspnoeic, with an irregular pulse of 75 per minute and electrocardiographic evidence of left ventricular and atrial hypertrophy.

An arteriotomy in the mid-brachial artery with a No. 3 Fogarty catheter allowed much clot to be removed. The patient was heparinized postoperatively and stabilized on Warfarin by the fifth postoperative day. At the end of surgery the radial pulse was impalpable although it returned within 48 hours. Physiotherapy to the hand and forearm produced a satisfactory result with no residual disability.

Case 5.—W. S., a 65-year-old male, had a 15-year history of cirrhosis and ascites and was a known chronic bronchitic with congestive heart failure requiring digoxin, frusemide, and Aldactone-A. He developed sudden pain and loss of power and sensation in his left forearm 3 hours before his admission in December, 1971. He had atrial fibrillation and the left brachial pulse in the antecubital fossa was absent. The left forearm was cooler than the right but there was minimal loss of sensation and power.

The patient was heparinized for 5 days and given physiotherapy. At discharge 8 days later the radial pulse was palpable and the muscle power normal. Oral anticoagulants were discontinued because of cirrhosis and he died 3 months later from a cerebral embolus.

Case 6.—R. T., a 58-year-old male, was admitted in December, 1971, complaining of a gradual onset of numbness, weakness, pain, and coldness in his right forearm of 4 hours' duration. He had a history of myocardial infarction and intermittent claudication. On examination the brachial pulse was palpable in the antecubital fossa, but the radial and ulnar pulses were absent. Power and sensation in the hand were diminished. He was not fibrillating and had no evidence of cardiac failure.

Embolectomy using a Fogarty catheter was performed under general anaesthesia 9 hours after the onset of symptoms; the arteriotomy was sited just proximal to the elbow. The radial pulse returned the following day. Postoperative heparinization by constant infusion was discontinued on the second postoperative day when the patient suffered a cerebrovascular accident producing a left hemiparesis. Over the ensuing days, power and sensation in the right arm returned to normal apart from the infarcted thenar muscles which later fibrosed. Intensive physiotherapy later produced a satisfactory recovery from his cerebrovascular accident.

Case 7.—M. McM., a 48-year-old male, had atrial fibrillation of 5 years' standing controlled by digoxin. He was admitted to hospital in May, 1972, with an acute myocardial infarction and atrial fibrillation flutter, and he later developed runs of ventricular tachycardia. Anticoagulation with Warfarin was commenced.

Three days after admission it was noted that his right radial pulse was absent and then that the only palpable pulse in his right limb was the subclavian. The hand was cool, but had no loss of sensation or power. The patient had suffered no symptoms and at the time was adequately anticoagulated with a prothrombin ratio of 1·8 : 1.

Eight hours after detection a 1-cm. embolus was removed from the axillary artery using a No. 3 Fogarty catheter through a brachial arteriotomy. The radial pulse returned 10 minutes after surgery and at a later follow-up there was no functional deficit in the limbs.

DISCUSSION

The comparative infrequency of upper-limb emboli is probably due to anatomical factors. A large heavy embolus is less likely to leave the aortic stream and thus passes on to the legs. The emboli that do lodge in the upper extremity are likely to be small, 65 per cent lodging in the brachial, 30 per cent in the axillary, and 5 per cent in the subclavian arteries (Baird and Lajos, 1964). In this series four emboli lodged in the brachial artery, either at the origin of the profunda brachialis or at the terminal bifurcation of the brachial artery.

The diagnosis of upper-limb embolus presents no difficulty, though it must be emphasized that the onset is not always dramatic (Stirling, Morris, Officer-Brown, and Barnett, 1963; Young, Humphries, De Wolfe, and Lefevre, 1963; Baird and Lajos, 1964) and symptoms may develop over several hours if the embolus lodges distally, as in *Cases* 6 and 7, the latter patient being asymptomatic initially. A change in rhythm of the heart is important in the genesis of an embolus and this occurred prior to embolization in *Case* 7.

Arterial occlusion results in pain, numbness, pallor, and coldness, the degree and extent of which depend on the size and site of the embolus. Cutaneous sensation is diminished early, but some improvement may occur when the collateral flow becomes established (Deterling, 1966). Loss of motor power is a serious prognostic sign (Young and others, 1963). These symptoms and signs relate to the extent of distal and proximal propagation, and it is of interest to note the minimal upset present in *Case* 7 who was effectively anticoagulated at the time of presentation and in whom there was no evidence of propagation of the clot at operation.

The proximal extent of the embolus can frequently be identified by direct palpation, and this corresponds well with the pathological level of occlusion. Angiography is not usually necessary (Wheeler, 1968).

It has always been recognized that there is little risk to life or limb (i.e., amputation) from an embolus in the arm (Warren, Linton, and Scannell, 1954) and when death occurs it results from the primary cardiac disease (Warren and others, 1954; Stirling and others, 1963; Thompson and others, 1970). Conservative management was at one time frequently advocated (Frey and McGhee, 1957). Sympathetic blockade has been used to relieve pain and spasm (Veal and Duncan, 1951), as in the present *Case* 1. Dye, Olwin, Javid, and Julian (1955) were among the first to advocate strongly surgical treatment of upper-limb occlusion. Trumbull, Masashi, and Averbrook (1959) reported 9 cases of embolectomy, in all of which the radial pulse was restored, but early embolectomy for upper-limb emboli was not widely accepted until 1964 (Baird and Lajos, 1964; Cranley, Krause, Strasser, Hofner, and Fogarty, 1964). The procedure offers the advantage of mechanically removing the distal propagating thrombus and thus decreasing any dysfunction. Baird and Lajos (1964) analysed 102 upper-limb emboli in 95 patients; surgery produced good results in 88 per cent of the patients and conservative management in 75 per cent, but the poor results in those treated by conservative therapy were of a more serious nature than in the surgical group.

Of the 7 cases reported here, 5 were treated initially by embolectomy. Conservative treatment was used in 2 patients, failing in 1 (*Case* 1) and succeeding in the second patient who had a very distal embolus (*Case* 5). It is clear that those patients with minimal symptoms of gradual onset, absence of progressive cutaneous sensory loss, and a very distal embolus can be adequately managed on a conservative régime of anticoagulation and physiotherapy.

Late embolectomy was carried out in *Case* 1 after failure of a brachial plexus block. The hand remained viable with permanent loss of sensation and fine movement. The previously held concept that late embolectomy was of no value was challenged by Spencer and Eiseman (1964), who believed that embolectomy was worth while as long as severe muscle necrosis was absent. Cranley and others (1964) also emphasize that viability and not the duration of occlusion should determine operability. Darling (1969) suggests the use of late embolectomy in the non-viable limb to lower the level of amputation.

The brachial artery is easily exposed under local or regional anaesthesia, although this form of anaesthesia was only used in 1 of our patients (*Case* 7). Dissection of the vessels involved is relatively simple, but difficulty may be encountered negotiating the terminal bifurcation of the brachial artery and necessitates a second arteriotomy (Sachatello, 1968). 'Spasm' may prove troublesome during the operation, as in *Case* 3, and in this instance papaverine provided no help. Cranley and others (1964) stress the importance of maintaining patency at the arteriotomy site during closure and are prepared to reopen the artery as many as six times if necessary to ensure a good blood-flow. Clinical 'spasm' should alert the surgeon to the possibility of persisting debris within the artery or damage to the arterial wall. If pulsation is present 1–2 cm. distal to the site of the arteriotomy and the preoperative findings were favourable, then limb viability is guaranteed (Cranley and others 1964).

Prevention of further emboli is important and 80 per cent of the patients who have recurrent emboli are not receiving prophylactic therapy when they occur. Recurrent emboli appear to be associated with a greater mortality and morbidity (Darling, 1969). *Case* 5 in the present series who was not placed on long-term anticoagulants because of cirrhosis died of a fatal cerebral embolus within 3 months of the first embolus. Young and others (1963) advised mitral commissurotomy and auricular appendectomy in selected patients and carried out this operation in 24 of their 114 patients with peripheral emboli.

Most surgeons rely on long-term anticoagulants, and in the earlier patients in the present series simultaneous heparin and phenindione were given postoperatively. A more recent policy has been immediate heparinization on admission, continued by intravenous infusion into the postoperative 4–5 days, by which time oral anticoagulants have been started. The use of heparin preoperatively is strongly advocated by Cranley and others (1964) and Fogarty, Daily, Shumway, and Krippaene (1971).

The presence of the radial pulse after embolectomy is often regarded as important and some series report 100 per cent success in recovery of the radial pulse (Trumbull and others, 1959). This is not our experience. Moreover, it is possible to get good functional recovery without the return of radial pulsation (*Case* 3) and, conversely, for infarction of the small muscles of the hand to take place in the presence of a palpable radial pulse (*Case* 6).

With early surgical treatment, loss of the upper limb is a rarity (Rossi, Ehrenhaft, and Sensenig, 1965) but partial loss of function occurs in 10–15 per cent of cases (Baird and Lajos, 1964; Cranley and others, 1964). This is related to a delay in treatment or to atherosclerosis (Edwards, Tilney, and Lindquist, 1966). Death following embolectomy is most commonly due to concomitant cardiac disease, but whatever the physical state of the patient his condition is not improved by the presence of ischaemic muscle or a gangrenous limb (Kinmonth, Rob, and Simeone, 1962; Provan and Ransford, 1970).

The superiority of the Fogarty catheter over suction catheters for the procedure of embolectomy is well recognized. It does not require a direct approach to the site of the embolus, and can be carried out under local anaesthesia with little discomfort to the patient. Its early use to remove the embolus, and any distal and proximal propagating clot, together with preoperative heparinization to prevent such clot formation, should further reduce the incidence of disability that results from ischaemia of the small muscles and nerves of the hand.

Acknowledgements.—The authors wish to thank Professor Sir John Bruce, Professor A. P. M. Forrest, and Mr. I. B. Macleod for permission to report patients under their charge, and those colleagues contributing individual cases.

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GLUCAGON THERAPY IN ACUTE PANCREATITIS

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SUMMARY

Thirty patients with acute pancreatitis (10 classified as severe) were treated with glucagon at an initial dose of 1 mg. intravenously followed by 1–1·5 mg. every 4 hours.

Glucagon therapy was associated with the relief of pain and clinical improvement in all the patients including 2 subjects who eventually died. In all but 1 of the patients the plasma amylase fell during glucagon infusion. Two patients died, giving a mortality-rate of 7 per cent compared with 22 per cent and 26 per cent of most published series in Britain.

ADMINISTRATION of glucagon to patients with acute pancreatitis has been reported to result in clinical improvement and the relief of pain associated with a fall in the plasma amylase (Knight, Condon, and Smith, 1971). It was suggested that the main beneficial effect of glucagon in acute pancreatitis was due to the inhibition of pancreatic exocrine secretion, thus suppressing the activity of the acutely inflamed gland.

Further studies of the use of glucagon in patients with acute pancreatitis are reported here.

MATERIAL AND METHODS

Thirty patients at seven hospitals were studied. Acute pancreatitis was confirmed at operation in 13 cases. In 17 cases the diagnosis was made on the clinical picture and a high plasma amylase. One patient (*Case* 25) developed acute pancreatitis following an operative pancreatogram. This patient had no pancreatic pain but 3 days postoperatively developed a tachycardia with increased abdominal tenderness and a marked rise in the plasma amylase from 400 to 2000 Somogyi units per 100 ml.

An initial dose of glucagon, 1 mg. intravenously, was given in all the cases. This was immediately followed by an intravenous infusion of glucagon in either 5 per cent dextrose or normal saline. The dose of glucagon given by infusion varied from 1 to 1·5 mg. every 4 hours for 24–96 hours.

Plasma calcium was measured by atomic absorption spectrophotometry, plasma amylase by the method of Babson, Tenney, and Megraw (1970), and methaemalbumin by the method of Chong and Owen (1967).

The patients were assessed before and after glucagon therapy. The degree of abdominal pain, shock, and peritonism was recorded at intervals following the administration of glucagon. Plasma amylase, plasma calcium, and methaemalbumin were measured before and approximately 12 hours after glucagon had been started.

Ten of the patients treated (*Cases* 1–10) were classified as severe because of the presence of one or more of the following features: severe clinical shock, a plasma calcium of less than 7·0 mg. per 100 ml., and haemorrhagic pancreatitis diagnosed either at operation or by the detection of methaemalbuminaemia (Lipp and Hubbard, 1950; Kirby, Senior, Howard, and Rhoads, 1955; Winstone, 1965; Trapnell, 1966). The diagnosis in 5 of these patients (*Cases* 6–10) was confirmed at laparotomy.

Twenty patients (*Cases* 11–30) were classified as non-severe in the absence of all these features. The diagnosis was confirmed at laparotomy in 8 of these patients.

RESULTS

Severe Group.—

CASE REPORTS.—

Cases 6, 1, *and* 2.—These 3 patients, aged 47, 62, and 59 years, respectively, were extremely ill when first seen. All had severe epigastric pain with vomiting, abdominal tenderness, guarding, and rebound tenderness. They were hypotensive and had raised plasma-amylase values (*Fig.* 1). The severity of the pancreatitis was reflected by the low plasma-calcium levels of 7·1, 6·2, and 6·1 mg. per 100 ml., respectively. Following treatment with glucagon there was partial relief of abdominal pain at 30 minutes to 2 hours, with complete relief at 1, 12, and 3 hours respectively. Signs of peritonism subsided over 6–8 hours and this was associated with a marked clinical improvement and a rise in the blood-pressure. Plasma-amylase levels measured 12 hours after beginning glucagon therapy fell from the pre-glucagon values by 28, 54, and 43 per cent respectively (*Fig.* 1).

Case 3.—A female aged 70 years with epigastric pain had a plasma amylase of 2000 Somogyi units per 100 ml., a plasma calcium of 9·4 mg. per 100 ml., and methaemalbuminaemia (1 mg. per 100 ml.); she was not clinically shocked. Glucagon therapy resulted in the complete relief of pain within 8 hours and a fall in the plasma amylase of 62 per cent at 15 hours (*Fig.* 1).

Case 4.—A male aged 44 years with abdominal pain was shocked and had a plasma calcium of 8·4 mg. per 100 ml. and a plasma amylase of 1560 Somogyi units per 100 ml. Partial relief of epigastric pain occurred at 4 hours and complete relief at 12 hours. The plasma amylase fell by 10 per cent over 12 hours.

Cases 10 *and* 5.—These patients (a female aged 29 years and a male aged 78 years respectively) were not shocked but had plasma-calcium values of 6·2 and 6·9 mg. per 100 ml. respectively. In *Case* 5 the plasma amylase which was 533 Somogyi units on admission fell to 90 Somogyi units when glucagon was given for persistent abdominal pain. Relief of pain occurred 2 hours after starting glucagon. *Case* 10 had a pancreatic fistula and developed acute pancreatitis while awaiting surgery. Her plasma amylase fell from 857 to 608 Somogyi units per 100 ml. following glucagon.

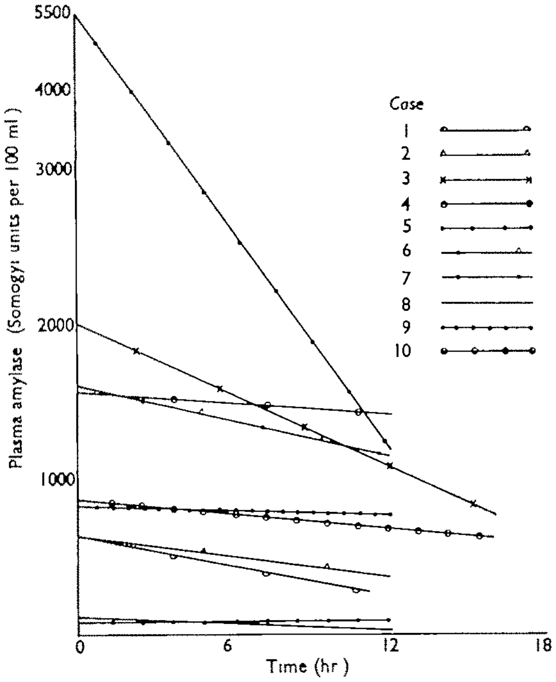

FIG. 1.—Decrease in the plasma amylase at 12 hours following the beginning of intravenous glucagon therapy in 10 patients with severe acute pancreatitis.

Case 7.—A 63-year-old female was found at laparotomy for generalized peritonitis to have acute haemorrhagic pancreatitis. Her plasma calcium was 9·2 mg. per 100 ml. and plasma amylase 115 Somogyi units per 100 ml. Glucagon resulted in the relief of the pancreatic pain at 6 hours and the plasma amylase fell to 58 Somogyi units per 100 ml. 12 hours after starting glucagon.

Case 9.—A 73-year-old female with cardiac failure and rheumatoid arthritis presented with a 5-day history of abdominal pain and vomiting. When seen she was shocked and had a rigid abdomen, and laparotomy confirmed acute haemorrhagic pancreatitis. The post-operative plasma amylase was 830 Somogyi units per 100 ml. and the plasma calcium was 6·2 mg. per 100 ml. Glucagon therapy which was started 11 hours post-operatively induced partial relief of the pancreatic pain within 6 hours. Following laparotomy the patient was anuric and she became hyperkalaemic and died. Post-mortem examination showed a necrotic area in the head of the pancreas with fat necrosis around the body and tail; the kidneys showed acute tubular necrosis.

Case 8.—A 69-year-old female presented with a 3-hour history of epigastric pain and vomiting. She was clinically shocked with a plasma amylase of 5000 Somogyi units per 100 ml. Operation confirmed the presence of acute pancreatitis. Glucagon therapy resulted in pain relief, clinical improvement, and a fall in the plasma amylase of 75 per cent. The patient appeared to be improving when 12 hours after beginning glucagon she suddenly became hypotensive and clinically ill. At this time she had no abdominal pain but rapid clinical deterioration occurred and she died. Post-mortem examination showed severe haemorrhagic pancreatitis.

Non-severe Group.—Twenty patients (11 males and 9 females, aged 23–83; average 46 years) had acute pancreatitis which was classified as non-severe.

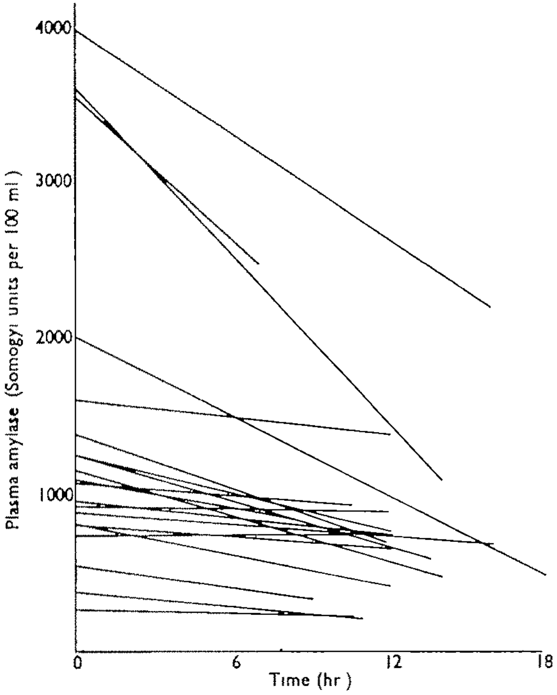

FIG. 2.—Decrease in the plasma amylase at 12 hours following the beginning of intravenous glucagon therapy in 20 patients with non-severe acute pancreatitis.

Table I.—PERCENTAGE OF PATIENTS WITH ACUTE PANCREATITIS CLAIMING PAIN RELIEF FOLLOWING GLUCAGON INFUSION

TIME (hr)	SEVERE GROUP (10 patients)	NON-SEVERE GROUP (20 patients)
0–3	30	50
3–6	60	55
6–12	90	95

All but 1 of these patients had abdominal pain, and glucagon infusion was associated with relief of pain within 1–12 hours (*Table I*) and a fall in the plasma amylase (*Fig.* 2).

DISCUSSION

Glucagon is known to suppress gastric secretion and motility (Stunkard, Van Itallie, and Reis, 1955; Dreiling and Janowitz, 1959; Quirarte, Woodward, and Dragstedt, 1966) and pancreatic exocrine secretion (Walker and Necheles, 1956; Necheles, 1957; Dyck, Texter, Lasater, and Hightower, 1970; Knight and others, 1971). These facts suggest that this hormone might be of benefit in treating patients with acute pancreatitis and our results lend some support to this concept.

In a series of 30 patients with acute pancreatitis treated with glucagon there were only 2 deaths, giving a mortality-rate of less than 7 per cent, in comparison with 22 and 26 per cent in published series in Britain (Pollock, 1959; Efron, 1966; Trapnell, 1966). Ten of the treated patients were classified as severe and in this group there were 2 deaths; a mortality-rate of 20 per cent. This compares with a mortality-rate in this country of over 40 per cent in patients with severe hypocalcaemia (Trapnell, 1966) and haemorrhagic pancreatitis (Sinclair, 1959; Northam, Winstone, and Banwell, 1965; Winstone, 1965; Trapnell, 1966). Glucagon therapy was associated with the relief of pain and clinical improvement in all the patients, including the 2 subjects who eventually died. In all but 1 patient the plasma-amylase values fell during glucagon infusion.

Glucagon is remarkably free of side-effects in man but nausea and vomiting may occur with large doses. Hypocalcaemia has been reported following its administration (Paloyan, Paloyan, and Harper, 1967; Birge and Avioli, 1969) and it is obviously important to monitor plasma-calcium levels in patients with acute pancreatitis receiving glucagon; if severe hypocalcaemia develops, intravenous calcium should be given. In our own series the maximum fall in plasma calcium did not exceed 1·1 mg. per 100 ml. following glucagon infusion and in some cases plasma calcium actually rose during glucagon therapy.

These findings are encouraging and indicate the need for a controlled trial in a large series of patients. This might well be organized on a multi-centre basis.

Acknowledgements.—We are grateful to the surgeons of St. George's Hospital and to Mr. A. Greening, Mr. K. H. Taylor, Mr. P. Lord, Mr. C. R. Anders, Mr. A. Eley, Mr. E. G. Lee, and Mr. L. R. J. de Jode for permission to report patients admitted under their care. We should also like to thank Mr. Rodney Smith for his encouragement and help. We are also indebted to Professor J. A. Owen, Mrs. P. Maitland, and the laboratory staff of St. George's Hospital.

M. Knight was supported by a research grant from the Board of Governors, St. George's Hospital, London.

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THE SURGICAL TREATMENT OF PEPTIC ULCER

A 15-YEAR REVIEW

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Summary

A 15-year retrospective study of 713 patients having surgical treatment for peptic ulcer was carried out. A comparison of gastrectomy with vagotomy and drainage was made. The ways in which other factors may affect the outcome were also studied.

The results are discussed and some conclusions drawn.

This paper reports a retrospective study of patients who had surgical treatment for peptic ulcer at the Harold Wood Hospital, Essex, during the 15-year period 1952–67. Elective and emergency operations for both duodenal and gastric ulcers are included.

The main objective was to compare the results of gastrectomy with those of vagotomy and drainage. Comparison was made of operative mortality and morbidity and late complications. In addition, how other factors affected the results were noted.

Although the greatest number of operations was performed by one of the consultants specializing in gastric surgery, all the operations for peptic ulcer, many of which were carried out by registrars, are included.

MATERIAL AND METHODS

The names of the patients were obtained from the theatre operations books. A form was designed which was filled in where possible at the follow-up clinic with the help of the patient. In a large number of cases where the notes were well kept until recently the form was filled in directly from the notes. Where the notes were inadequate, questionnaires were sent to the patients, and finally if the replies to the questionnaires were unsatisfactory, new appointments were made to see the patients again in the out-patients' department.

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The results were analysed on punch cards.

RESULTS

The initial number of patients was 967. We were unable to contact 217 and 37 had died of other diseases, so that the total number under review was 713 (*Table I*).

The total figures are shown in *Table I*.

Table I.—TYPE OF ULCER COMPARED WITH OPERATION PERFORMED IN 713 PATIENTS

TYPE OF ULCER	TOTAL NO OF PATIENTS	GASTRECTOMY			VAGOTOMY AND DRAINAGE			GASTRO-JEJUNOSTOMY ONLY
		Total	Polya	Billroth-I	Total	Vagotomy and Pyloroplasty	Vagotomy and Gastrojejunostomy	
Duodenal ulcer	527	228	204	24	275	146	129	24
Gastric ulcer	152	129	79	50	18	17	1	5
Duodenal and gastric ulcers	34	21	16	5	12	8	4	1
Total	713	378	299	79	305	171	134	30

Table II.—PERCENTAGE DISTRIBUTION OF THE DIFFERENT TYPES OF OPERATION PERFORMED DURING THE 15-YEAR PERIOD OF THE SURVEY

TYPE OF OPERATION	1952–7	1958–62	1963–7
Total No. of Cases	313	251	149
Polya gastrectomy	70·6	27·8	5·4
Billroth-I gastrectomy	21·1	4·0	2·0
Vagotomy and pyloroplasty	0·6	21·1	77·8
Vagotomy and gastrojejunostomy	1·0	44·7	12·8
Gastrojejunostomy only	6·7	2·4	2·0

Table III.—PERCENTAGE INCIDENCE OF EARLY POSTOPERATIVE MORBIDITY

MORBIDITY	GASTRECTOMY			VAGOTOMY AND DRAINAGE		
	Total	Polya	Billroth-I	Total	Vagotomy and Pyloroplasty	Vagotomy and Gastrojejunostomy
Total No. of cases	378	299	79	305	171	134
General complications	20	—	—	10·4	—	—
Specific complications	4·7	5·0	3·8	1·9	1·7	2·2

The type of operation performed varied over the 15-year period of the series, as is shown in *Table II*. The shortest follow-up period was 18 months, but it was much longer for the majority of cases.

Operative Mortality.—This includes patients dying during or following operation and before discharge from hospital. The longest period recorded for operative mortality was 17 days after operation.

Thirteen patients died (1·8 per cent for the whole series). Of these deaths, 10 were after emergency operation, 9 of which had been for bleeding and 1 for perforation. The mortality for elective gastrectomy was 3 out of 309 cases (1·1 per cent).

Ten of the patients who died were over the age of 60 years, their operation being performed before 1958. The mortality between 1952 and 1957 was 3·8 per cent. This dropped to 0·5 per cent from 1958 to 1962, and there were no deaths in the last 5 years of the series. However, only 11 partial gastrectomies were performed for benign peptic ulcer in the last 5-year period.

There were no deaths in any of the 305 patients who had vagotomy and drainage procedures.

Table IV.—PERCENTAGE INCIDENCE OF RECURRENT ULCERATION AFTER OPERATION FOR DUODENAL ULCER

CRITERION FOR RECURRENCE	GASTRECTOMY		VAGOTOMY AND DRAINAGE		GASTRO-JEJUNOSTOMY ONLY
	Polya	Billroth-I	Vagotomy and Pyloroplasty	Vagotomy and Gastrojejunostomy	
Total No. of cases	204	24	146	129	24
Recurrence on barium-meal examination	1·5	16·7	2·7	3·9	4·2
Further operation for recurrent ulcer	2·0	29·2	2·7	2·3	16·7

Early Postoperative Morbidity.—This has been divided into general complications that occur after any operation, and those specific to gastric surgery (*Table III*). The general complications include chest infection, deep venous thrombosis and pulmonary embolism, wound infection, burst abdomen, and coronary thrombosis. The specific complications are bleeding, stomal obstruction, and anastomotic or duodenal stump leakage.

Recurrent Ulceration.—It is not easy to diagnose a recurrent ulcer with certainty. The most reliable way is at further operation, although even then it may sometimes be difficult. A barium-meal examination should be reliable, but some patients found to have an ulcer at operation had equivocal barium-meal findings. Further criteria are epigastric pain and bleeding, but these are not definite evidence of a recurrence of ulceration.

For the purpose of this review recurrence was recorded from the barium-meal examination and from reoperations (*Tables IV, V*).

Postcibal Symptoms.—In order to assess dumping, patients were asked if they suffered from attacks of sweating, dizziness, or fainting after meals. Those who had were asked whether these attacks came on soon after meals and were relieved by rest, or whether they came on 2 hours or more after meals and were relieved by taking more food.

Table V.—PERCENTAGE INCIDENCE OF RECURRENT ULCERATION AFTER OPERATION FOR GASTRIC ULCER

CRITERION FOR RECURRENCE	POLYA GASTRECTOMY	BILLROTH-I GASTRECTOMY	VAGOTOMY AND DRAINAGE
Total No. of cases	79	50	18
Recurrence on barium-meal examination	2·5	4·0	—
Further operation for recurrent ulcer	—	4·0	—

Table VI.—PERCENTAGE INCIDENCE OF POSTCIBAL SYMPTOMS

SYMPTOM	GASTRECTOMY			VAGOTOMY AND DRAINAGE		
	Total	Polya	Billroth-I	Total	Vagotomy and Pyloroplasty	Vagotomy and Gastro-jejunostomy
Total No of cases	378	299	79	305	171	134
Early dumping	10·8	12·6	5·1	4·9	2·8	8·2
Late dumping	1·1	1·3	—	1·6	2·3	0·75
Epigastric fullness	3·4	3·6	2·5	1·3	2·3	—
Vomiting	7·6	10·6	1·2	3·8	5·2	2·9
Further operations for symptoms other than recurrent ulcer	2·1	2·7	—	3·9	4·1	3·7

Table VII.—PERCENTAGE INCIDENCE OF NUTRITIONAL PROBLEMS

NUTRITIONAL PROBLEM	GASTRECTOMY			VAGOTOMY AND DRAINAGE		
	Total	Polya	Billroth-I	Total	Vagotomy and Pyloroplasty	Vagotomy and Gastro-jejunostomy
Total No. of cases	378	299	79	305	171	134
Loss of appetite	7·4	8·0	5·0	2·3	2·3	2·2
Weight-loss of more than 6·4 kg.	7·4	7·3	7·6	4·6	4·6	4·4
Iron-deficiency anaemia	11·9	12·6	8·8	4·6	1·1	10·4
Vitamin-B_{12}-deficiency anaemia	4·7	6·0	—	—	—	—

Patients were also asked if they noticed any undue feeling of fullness in the stomach after meals since their operation, and if they had suffered from vomiting which was more than mild and occasional. Initially it was attempted to divide the vomiting into biliary and food types, but later this was felt to be too inaccurate and was discontinued.

Operations considered here are for symptoms other than those of recurrent ulcer; for example, afferent-loop symptoms after Polya gastrectomies or gastro-jejunostomies, and late obstruction after pyloroplasty. The results are shown in *Table VI.* (In *Table VI* and in *Tables VII* and *VIII*, which consider nutritional factors and bowel habits, the results for all peptic ulcers are given together. Separate analysis showed virtually no difference in these factors between duodenal and gastric ulcers.)

Table VIII.—PERCENTAGE INCIDENCE OF ALTERATION IN BOWEL HABIT

BOWEL HABIT	GASTRECTOMY	VAGOTOMY AND DRAINAGE	TRUNCAL VAGOTOMY	SELECTIVE VAGOTOMY
Total No. of cases	378	305	280	25
Bowels improved	5·5	15·7	15·8	12·0
Moderate diarrhoea	1·6	3·6	3·9	—
Severe diarrhoea	0·3	1·3	1·4	—

Nutritional Problems.—The nutritional aspects examined were loss of appetite, where this was sufficient for the patient to complain about it; loss of weight, where this was more than 6·4 kg. compared with the preoperative weight; and anaemia, where the haemoglobin was 75 per cent or below. Only anaemia developing or persisting for more than 1 year after operation has been included. The results are shown in *Table VII.*

In addition there was 1 case of folic-acid-deficiency anaemia which occurred as part of a generalized malabsorption syndrome following a Billroth-I gastrectomy.

Diarrhoea.—Patients were asked whether their bowel habit had altered since their operation, and if so whether it had improved or whether they had suffered from diarrhoea. If they had suffered from diarrhoea they were asked whether they considered this to be mild, moderate, or severe. The results are shown in *Table VIII.* Results were obtained for the different types of gastrectomy, and different types of drainage, but they were similar to those for the whole group.

General Assessment.—At the end of reviewing each patient a general assessment was made on a modification of Visick's classification (Visick, 1948), into the following categories:—

Excellent: Perfect result; absolutely no symptoms.

Very good: No symptoms complained of, but on questioning specifically there were mild symptoms which did not bother the patient.

Good: Mild symptoms complained of, but which did not interfere with work or enjoyment of life and were easily kept under control.

Unsatisfactory: Moderate or severe symptoms, or complications which interfered considerably with work or enjoyment of life; all recurrent ulcers and second operations, further bleeding, etc., even if subsequently perfect.

The results are shown in *Table IX.*

Other Factors affecting the Results of Operation.—

1. *The Indication for and the Urgency of the Operation.*—The mortality for emergency operations was approximately twenty times that for elective operations, as would be expected. For duodenal ulcer the figures were 9·5 and 0·4 per cent and for gastric ulcer 11·4 and 0·6 per cent respectively. The mortality was highest for emergency gastrectomies for bleeding, being 15·5 per cent (9 out of 58 cases; 5 with duodenal ulcer and 4 with gastric ulcer). The lowest mortality occurred after operation for failed medical treatment, being approximately 0·5 per cent for both duodenal and gastric ulcers. There was 1 death after operation for each of the following indications: perforation (total, 81 patients), pyloric stenosis (total, 84 patients), and suspected malignancy (total, 34 patients). Of the 81 patients with perforation, 10 had gastric ulcer and 71 had duodenal ulcer, and the patient who died had a gastric ulcer.

Table IX.—PERCENTAGE DISTRIBUTION OF THE DIFFERENT CATEGORIES USED TO ASSESS THE RESULTS OF OPERATION

CATEGORY	DUODENAL ULCER		GASTRIC ULCER	
	Partial Gastrectomy	Vagotomy and Drainage	Partial Gastrectomy	Vagotomy and Drainage
Total No. of cases	228	275	129	18
Excellent	33·8	38·9	30·2	38·9
Very good	32·5	31·7	31·1	44·4
Good	23·6	18·9	27·1	11·1
Unsatisfactory	10·1	10·5	11·6	5·6

The operative morbidity was the same for elective and emergency operations and for the various indications.

The rate of recurrent ulceration was about the same for elective and emergency operations, and for each of the indications (i.e., between 2 and 3 per cent).

The incidence of patients requiring further operation for symptoms other than recurrent ulceration was similar for all the groups of patients, with one exception: 4 out of 13 patients who had had vagotomy and pyloroplasty for duodenal ulcer with pyloric stenosis subsequently developed a late stenosis of the pyloroplasty, requiring further surgery.

Out of the 81 patients who had a perforation, 51 had a simple suture followed by a definitive operation a few weeks or months later, and 21 had definitive procedures at the initial operation.

2. *Age.*—The patients were divided into three age-groups: under 30 years, 30–60 years, and over 60 years old. Gastric and duodenal ulcer cases were considered separately.

As would be expected, mortality increased with age. The mortality-rate for the over-60 age-group was 5·5 per cent for duodenal ulcer and 8·5 per cent for gastric ulcer as opposed to 0·5 per cent and none respectively for the under-60 age-groups. Postoperative morbidity was markedly lower in the under-30 group, being 10 per cent compared with about 20 per cent in the two older groups.

The recurrent ulcer rate was highest in patients under 30 with duodenal ulcer, being 7·7 per cent, whereas in the older age-groups it varied from 2 to 2·8 per cent for both duodenal and gastric ulcers.

The incidence of unsatisfactory results fell with age, being 15 per cent in the under-30 age-group, about 10 per cent in the 30–60 age-group, and about 7 per cent in the patients over 60.

The other factor worth noting is the incidence of emergency operations, which rose steadily with age, being 5 per cent in the under-30 group and 25–30 per cent in the over-60 group.

Table X.—PERCENTAGE DISTRIBUTION OF DIFFERENT RESULTS OF OPERATION COMPARED WITH THE SEX OF THE PATIENTS

RESULT	DUODENAL ULCER		GASTRIC ULCER	
	Males	Females	Males	Females
Total No. of cases	454	73	107	45
Recurrent ulcer on barium-meal examination	3·5	1·4	1·9	4·4
Further operation for recurrent ulcer	3·5	2·7	0·9	2·2
Unsatisfactory result	9·9	16·4	9·3	15·6

Table XI.—PERCENTAGE DISTRIBUTION OF DIFFERENT RESULTS OF OPERATION COMPARED WITH THE BLOOD GROUP IN PATIENTS WITH DUODENAL ULCER

RESULT	BLOOD GROUP				RHESUS FACTOR		AVERAGE FOR SERIES
	A	B	AB	O	+ve	−ve	
Incidence of this blood group in the general population	42·4	8·3	1·4	47·9	85	15	—
Total No. of patients with duodenal ulcers	36·6 (177)	7·9 (38)	4·6 (22)	50·9 (246)	83 (401)	17 (82)	483
Recurrence of ulcer on barium-meal examination	2·8	2·6	4·5 (1)	3·6	3·7	1·2	3·3
Further operation for recurrent ulcer	3·9	—	4·5 (1)	3·3	3·2	3·7	3·3
Unsatisfactory results	10·1	13·1 (5)	18·1 (4)	10·6	11·7	7·3	11·0

Table XII.—PERCENTAGE DISTRIBUTION OF DIFFERENT RESULTS OF OPERATION COMPARED WITH THE BLOOD GROUP IN PATIENTS WITH GASTRIC ULCER

RESULT	BLOOD GROUP				RHESUS FACTOR		AVERAGE FOR SERIES
	A	B	AB	O	+ve	−ve	
Incidence of this blood group in the general population	42·4	8·3	1·4	47·9	85·0	15·0	—
Total No. of patients with gastric ulcers	39·9 (57)	8·4 (12)	2·1 (3)	49·6 (71)	76·9 (110)	23·1 (33)	143
Recurrence of ulcer on barium-meal examination	—	—	—	4·2	1·8	3	2·1
Further operation for recurrent ulcer	1·8	—	—	—	0·9	—	0·7
Unsatisfactory result	12·3	—	—	14	12·7	9·0	11·9

3. *Length of Follow-up.*—The variation in the type of operation performed over the period of the study has already been shown (*Table II*).

The recurrent ulcer rate increased with the passage of time, being 1·8 per cent in the patients whose operation had been less than 5 years earlier, 2·7 per cent in patients operated on 5–10 years earlier, and 3·2 per cent in cases in whom the operation had been more than 10 years previously.

4. *Sex.*—The results of surgery for male and female patients are shown in *Table X*. The higher percentage of unsatisfactory results in females was due to an increased incidence of weight-loss, anaemia, vomiting, and diarrhoea.

5. *The Presence of Combined Gastric and Duodenal Ulcers.*—There were 34 patients with both duodenal and gastric ulcers, of whom 20 had gastrectomy, 12 had vagotomy and drainage, and 2 had gastrojejunostomy alone.

There were no deaths and no specific postoperative complications. Six patients had general complications (17·6 per cent), which is in keeping with the rest of the series. There were no episodes of bleeding, no symptoms of recurrent ulcer, and no reoperations. The result of operation in 1 patient was assessed as unsatisfactory owing to severe regurgitation after a Billroth-I gastrectomy.

6. *Blood Group.*—The blood groups of the patients are shown in *Tables XI* and *XII*. In some cases the blood group was not known, which accounts for the numbers shown being less than the total number of patients.

DISCUSSION

In 1968 the results of the Leeds/York trial (Goligher, Pulvertaft, de Dombal, and others, 1968) were published which showed that patients with duodenal ulcer who had a gastrectomy did marginally better than those having vagotomy and drainage. We were surprised by this and therefore decided to review our own results.

This is a retrospective study and we included both elective and emergency operations for both duodenal and gastric ulcers. We acknowledge the problems and discrepancies that can arise from retrospective surveys and in particular the large number of patients who cannot be traced. However, despite this, we feel some useful conclusions can be drawn as there still remains a large number of patients in the present review.

An ideal operation for peptic ulcer is one which is safe, simple, effective in curing the ulcer, and has a minimum of unwanted effects. The choice varies with the type of ulcer and to some extent with the degree of urgency.

Elective Operations for Duodenal Ulcers.—Billroth-I gastrectomy had a 29 per cent incidence of recurrent ulceration in our series. Other series have shown recurrence rates of 10 per cent (Mathieson, 1962) and 12·1 per cent (Newton and Judd, 1963), and it is widely accepted that this operation has a very high recurrent ulcer rate for duodenal ulcer. Simple gastrojejunostomy without vagotomy had a 16 per cent recurrent ulcer rate. Other series have shown recurrent ulcer rates of 34 per cent (Lewisohn, 1925) and 50 per cent (Swynnerton, 1955). We have therefore stopped performing gastrojejunostomy as a routine operation.

Polya gastrectomy was the most effective method of curing the ulcer, but had a mortality of 3·7 per cent. However, for elective operations the mortality was 1·1 per cent, and there were no deaths in the last 5 years of the survey.

The morbidity, both general and specific, was twice as high after gastrectomy as after vagotomy. The recurrent ulcer rate and incidence of diarrhoea were lower, but the other long-term complications were more frequent.

There were no deaths following vagotomy in this series. The recurrent ulcer rate was only slightly higher than that after gastrectomy, but the incidence of recurrent ulceration increases with time, and all the vagotomies were performed more recently than the gastrectomies. It is therefore likely that the incidence will increase slightly. The incidence of diarrhoea was slightly higher after vagotomy than that after gastrectomy, but severe diarrhoea only occurred in 1·4 per cent of cases. It should be remembered that the assessment used was the purely subjective view of the patient, but this is surely what matters.

The main criticism of vagotomy is knowing whether complete denervation has been obtained, whereas with gastrectomy it is easy to tell that an adequate amount of stomach has been resected. A postoperative insulin test is useful to the surgeon in training, but it does not help the individual patient. Burge's electrical stimulation test (Burge and Vane, 1958) is more immediately useful and we feel that it should be used more, particularly by surgeons learning the technique of vagotomy.

Selective vagotomy looks promising from the point of view of diarrhoea, and the extra dissection may well be a better guarantee of complete vagotomy (Burge and Frohn, 1969). It certainly warrants further investigations with larger series.

Pyloroplasty generally gave better results than gastrojejunostomy. However, we feel that it is wiser to do a gastrojejunostomy where pyloric stenosis is an indication for surgery because of the risk of recurrent stenosis of the pylorus. It is worth noting that late stenosis of the pylorus may be due to recurrent ulceration, and an insulin test should be done in these patients.

On general assessment the number of unsatisfactory results was the same for vagotomy and drainage as for gastrectomy, but the number of excellent results was better after vagotomy. Taking everything into consideration we feel that vagotomy and drainage is preferable for routine treatment of duodenal ulcer.

Elective Operations for Gastric Ulcer.—Comparing the types of gastrectomy, the recurrent ulcer rate was slightly higher after Billroth-I gastrectomy. Morbidity, postcibal symptoms, and nutritional problems were greater after Polya operations.

Vagotomy and drainage gave very good results for gastric ulcer in the present series, but there were only 30 patients. Other series have also shown favourable results (Hendry and Al Bahrani, 1965; Burge, 1966) and have rationalized this operation (Burge, 1966). Another series (Duthie and Smith, 1968) showed similar results for Billroth-I gastrectomy and vagotomy and pyloroplasty, but pointed out the danger of missing a carcinomatous ulcer. They recommended excising all the ulcer edge for biopsy. We feel that it is wiser to do a gastrectomy for all antral and greater curve ulcers, even if they appear benign, and to biopsy all lesser-curve ulcers, preferably by frozen section.

Other Factors.—The highest rate of recurrence occurred where the indication was suspected malignancy. We were unable to account for this.

As far as emergencies are concerned, it is important to differentiate between a definitive ulcer-curing operation and a life-saving operation which does nothing to stop the ulcer tendency. This applies to operations for bleeding or perforation, where the important thing is to tide the patient over the immediate emergency. However, if the patient is fit enough, and particularly if there have been previous symptoms, then a definitive operation can be done in the first instance.

Until fairly recently gastrectomy was the commonest operation for bleeding peptic ulcer. However, the mortality-rate is high, being 15·5 per cent of 58 patients in our series, whereas there were no deaths among the 21 patients who had emergency vagotomy and drainage for bleeding. A series from Oxford (Schiller, Truelove, and Gwyn Williams, 1970) showed a mortality-rate in operations for bleeding of 21 1 per cent for Polya gastrectomy, 13·2 per cent for Billroth-I gastrectomy, and 8 per cent for vagotomy and drainage.

Perforation has a lower mortality than bleeding, although it may be particularly dangerous in the elderly. The safest operation is simple suture, but there is a growing tendency towards definitive operation at the time of perforation.

In our series most of the patients had a definitive procedure subsequently as a matter of routine policy. In a series of 57 patients treated by simple suture (Hofkin, 1966) 52 per cent subsequently needed definitive surgery. We believe that patients with a perforation and previous ulcer history should have a vagotomy and drainage if they are fit enough and those with no previous symptoms whatever should have simple suture. However, the latter should be followed up for many years, and at the slightest suggestion of further ulceration, definitive surgery should be advised.

We are unable to account for the increased proportion of unsatisfactory results in females.

CONCLUSIONS

The mortality, morbidity, and the long-term complications, with the exception of diarrhoea, are greater after gastrectomy than after vagotomy and drainage. The recurrent ulceration rate is higher after vagotomy, but taking everything into account this is now preferred for duodenal ulcers.

Vagotomy does appear to give good results for gastric ulcers, but where there is a suspicion of malignancy gastrectomy is preferred, and in all cases the ulcer should be adequately biopsied.

Emergency operation for bleeding carries by far the highest mortality. The long-term results are similar for all the various indications for operation.

A pyloroplasty should be avoided where pyloric stenosis is an indication for operation.

The older age-group had a higher proportion of emergency operations, a higher mortality, but a better long-term result if they survived. Patients under 30 years had a higher incidence of recurrent ulceration.

Peptic ulcers are much less common in females but their outcome after surgery appears to be less favourable.

The occurrence of gastric and duodenal ulcers in the same patient does not affect the outcome adversely.

We found no correlation between blood group and the incidence or recurrence of ulcers.

Acknowledgements.—We would like to thank the following people for their kind help and co-operation: Mr. A. D. Messent and Mr. E. C. B. Butler for allowing us to study patients who were under their care; Mrs. Alison Spira who worked so hard as secretary for the project while the results were being obtained; the Brentwood Punch Card Bureau for analysing the data; Professor N. L. Browse and many other colleagues who gave advice and criticism.

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ACID SECRETION IN RELATION TO RECURRENCE OF DUODENAL ULCER AFTER VAGOTOMY AND DRAINAGE

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SUMMARY

The acid secretory responses of patients with recurrent ulcer after vagotomy and drainage have been compared retrospectively with those of patients with a positive insulin test but no recurrent ulcer and with those of patients with a negative insulin test. Patients with recurrent ulcer were on average 10 years younger than patients with an incomplete vagotomy but no recurrence, although their pre- and postoperative acid secretory responses were similar.

Insulin tests were unreliable when performed less than 3 months after vagotomy. The only possible criterion by which recurrent ulceration could be predicted was a postoperative reduction in the peak acid output after pentagastrin of less than 60 per cent. Equal numbers of patients with 'early' and 'late' positive responses to insulin developed a recurrent ulcer.

Routine postoperative insulin tests may be helpful in assessing the efficiency of the vagotomist but are of limited prognostic value.

The chief value of postoperative insulin tests appears to be in the diagnostic evaluation of post-vagotomy dyspepsia.

It is still not clear whether tests of acid secretion are of any value to clinicians in predicting which patients are liable to develop recurrent duodenal ulcer after vagotomy and drainage procedures. Although recurrent ulcers are almost always associated with incomplete vagotomy, the incidence of incomplete vagotomy evaluated by the insulin test is very much higher than the incidence of recurrent ulcer. Different authors, using the criteria of Hollander (1948) or multiple criteria, have found an incidence of incomplete vagotomy ranging from 15 per cent (Johnston and Goligher, 1971) to 50 per cent (Jordan and Condon, 1970). On the other hand, the reported incidence of recurrent ulcer ranged from 1·5 per cent (Burge, Stedeford, and Hollanders, 1970) to 27 per cent (Stempien, Dagradi, Lee, and Simonton, 1971) but has usually been less than 10 per cent.

It is thus apparent that many patients with an incomplete vagotomy will not develop recurrent ulcer and attempts have been made by various investigators to find criteria based upon acid-secretion tests which would predict which patients are prone to recurrent ulceration (Ross and Kay, 1964; Kronborg, 1972). No clear-cut discriminant functions have been found and the present study is a further attempt to seek such functions.

Three groups of similar size have been studied. Two groups had incomplete vagotomy by Hollander's criteria; all the patients in one of these groups had recurrent ulcer whereas those in the other group had remained symptom-free for at least 3 years after operation. The third group had undergone a complete vagotomy by the same criteria.

PATIENTS AND METHODS

The patients had all been treated by vagotomy and drainage for chronic duodenal ulcer during the decade 1960–9. Each patient had a postoperative insulin test. Some patients had undergone tests of maximum acid output before operation. The following three groups of patients were studied:—

1. **Recurrent Ulcer.**—Twenty-four patients had developed a recurrent duodenal ulcer (excluding one with Zollinger-Ellison syndrome). Sixteen of the patients (13 males and 3 females) had a definite recurrent ulcer which was confirmed by inspection at a second operation, and 8 (6 males and 2 females) had a probable recurrent ulcer which was diagnosed on the basis of recurrent symptoms with radiological demonstration of an ulcer.

2. **No Recurrence.**—Twenty-five patients (23 males, 2 females) had an incomplete vagotomy by the criteria of Hollander (1948) and were followed up for at least 3 years without developing symptoms of recurrent ulcer. These were a consecutive series, excluding the patients who had been lost to follow-up.

3. **Complete Vagotomy.**—Twenty-five patients (23 males, 2 females) had undergone complete vagotomy as judged by Hollander's criteria. These were a consecutive series of such patients chosen at random from our records.

Gastric Secretion Tests.—These were performed after an overnight fast. A size 14 French gauge nasogastric tube was passed into the stomach, the position was checked fluoroscopically, and the resting contents were aspirated and discarded. Fifteen-minute collections of gastric juice were then made by continuous pump and intermittent hand suction. After a basal hour insulin, 0·2 U. per kg., was injected rapidly intravenously and a further eight 15-minute collections were made. In some patients this was followed by the intramuscular injection of pentagastrin, 6 μg. per kg., and a further four 15-minute collections. Preoperative tests were performed in some patients with either histamine acid phosphate, 0·04 μg. per kg. subcutaneously (Kay, 1953), or pentagastrin, 6 μg. per kg. intramuscularly.

Analyses.—The volume of each specimen was recorded and the titratable acidity was determined by titrating to *p*H 7 with *N*/50 NaOH using a glass electrode and autoburette.

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Peak acid output (mEq./hr.) in response to insulin, histamine, or pentagastrin was calculated by adding the two highest consecutive 15-minute outputs and multiplying by two. Blood-glucose was determined by the Autoanalyzer method of Wincey and Marks, (1961).

Statistical Methods.—Student's *t*-test for paired and unpaired data was used where appropriate. Data for males and females have been pooled because there were so few females, even though our previous study (Spencer, Burns, Cheng, Cox, and Welbourn, 1969) had shown significant differences between the sexes in their response to insulin.

RESULTS

1. Timing of the Postoperative Test.—Before November, 1969, all postoperative insulin tests were performed before the patient was discharged from hospital. Since November, 1969, insulin tests have been performed 3 months after the operation. *Table I* shows the mean intervals after operation at which postoperative insulin tests were performed in patients in each of the three groups. Twelve (50 per cent) of the patients with recurrent ulcer were Hollander negative at their first test, but when they were re-tested on a second occasion because of recurrent symptoms all had become Hollander positive. The other 12 patients were Hollander positive at the first test and were no re-tested. Nine of the 12 patients with false-negativ results to their first test had this test less than 4 week after operation.

Table I.—INTERVAL AFTER OPERATION AT WHICH THE INSULIN TESTS WERE PERFORMED IN PATIENTS IN THE THREE GROUPS

INTERVAL AFTER OPERATION	HOLLANDER RESPONSE			
	Positive with Recurrence		*Positive without Recurrence*	*Negative 'Complete'*
	Positive First Test	Positive Second Test		
1–4 wk.	9	–	19	10
1–3 mth	1	2	4	14
3 mth.+	2	10	2	1

Table II.—MEAN DURATION OF FOLLOW-UP AFTER THE INITIAL OPERATION OF PATIENTS IN THE THREE GROUPS

GROUP	TIME (yr.)	
	Mean ± S.E.M.	Range
1 Recurrence		
Reoperated*	2·6 ± 0·42	0·2–6·5
Probable	3·0 ± 0·66	1 –6
2. No recurrence	4·1 ± 0·33	3 –10
3. Complete vagotomy	2·2 ± 0·10	1·4–2·6

* Interval between operations

Table III.—PREOPERATIVE BASAL AND PEAK ACID OUTPUTS (TO HISTAMINE OR PENTAGASTRIN) OF PATIENTS WHO SUBSEQUENTLY HAD AN INCOMPLETE VAGOTOMY

TEST	ACID OUTPUT (mEq./hr.)		*P*
	Recurrence ($n = 20$)	No recurrence ($n = 22$)	
Basal	5·2 ± 1·8	4·5 ± 0·8	0·6
Peak acid output	39·8 ± 4·7	38·9 ± 3·6	0·8

Patients who were Hollander positive at the firs test but have not developed symptoms of a recurren ulcer have not been tested again. Twenty-three o the 25 patients were tested less than 3 months postoperatively. Twenty-four of the 25 patients in th complete vagotomy group were tested either at months or at a shorter interval after the operation None of these patients has been tested again.

2. Duration of Follow-up after Initial Operation.—It can be seen from *Table II* that the mea interval between operations in patients who wer reoperated on for recurrent ulcer was 2·6 years whilst patients with probable recurrence had bee followed up for a mean of 3·0 years. On the othe hand, patients with an incomplete vagotomy but n recurrence have so far been followed up for a mean o 4·1 years with a minimum follow-up period of 3 years

3. Age at Time of First Operation.—The ag distribution of patients with a positive insulin tes who developed a recurrent ulcer and of those wh have remained symptom-free is shown in *Fig.* 1. Th mean age of the recurrent ulcer group was 9·7 year lower than that of the no-recurrence group; this is highly significant difference ($P < 0·01$). There wa no difference in age between patients with confirme recurrence and those with probable recurrence.

4. Gastric Acid Secretion.—

a. Preoperative Acid Secretion.—There was n significant difference between the mean basal aci output or the peak acid output of the patients wit recurrent ulcer and those with no recurrence (*Tabl III*).

Table IV.—POSTOPERATIVE BASAL ACID SECRETION O PATIENTS IN THE THREE GROUPS

GROUP	PEAK ACIDITY (mEq./l.)	*P*	ACID OUTPUT (mEq./hr.)	*P*
1 Recurrence	40·8 ± 4·9	0·003	2·99 ± 0·6	0·02
2 No recurrence	21·3 ± 4·1	0·2	1·36 ± 0·3	0·7
3. Complete vagotomy	29·0 ± 4·2		1·50 ± 0·3	

Table V.—POSTOPERATIVE ACID RESPONSE TO INSULI (0·2 U. per kg.) OF PATIENTS IN THE THREE GROUP

GROUP	PEAK ACIDITY (mEq./l.)	*P*	P.A.O. (I) (mEq./hr.)	*P*
1. Recurrence	100 ± 5·0	0·03	11·25 ± 1·43	0·4
2 No recurrence	83·2 ± 6·4	<0·001	9·42 ± 1·26	<0·001
3. Complete vagotomy	26·5 ± 4·4		1·64 ± 0·35	

P.A.O. (I), Peak acid output to insulin.

b. Postoperative Acid Secretion.—

i. *Basal secretion* (*Table IV*, *Figs.* 2, 3): The mea peak basal acidity and the mean basal acid outpu were significantly higher in patients with recurren ulcer than in patients with incomplete vagotomy bu no recurrence. The corresponding results fo patients with complete vagotomy were intermediat between these two groups. There was almost complete overlap between the three groups.

ii. *Insulin-stimulated secretion*: Mean changes in titratable acidity from basal levels after intravenous insulin are shown in *Fig.* 4. In general, patients with recurrent ulcer attained a significantly higher level of acidity than patients with incomplete vagotomy but no recurrence. However, the increase of acidity above the basal levels was almost identical in each group as the patients with recurrent ulcer started from a higher basal level of acidity. Peak acidity and acid output after insulin are shown in *Table V*. There was no significant difference in peak acid output after insulin between patients with and without recurrence.

The blood-glucose values of the different groups were examined and no differences were found between the groups with regard to fasting, or lowest or maximum fall in blood-glucose.

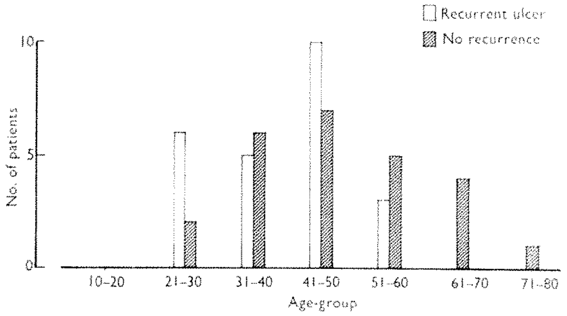

FIG. 1.—Age at the time of the initial vagotomy operation in the patients with an incomplete vagotomy.

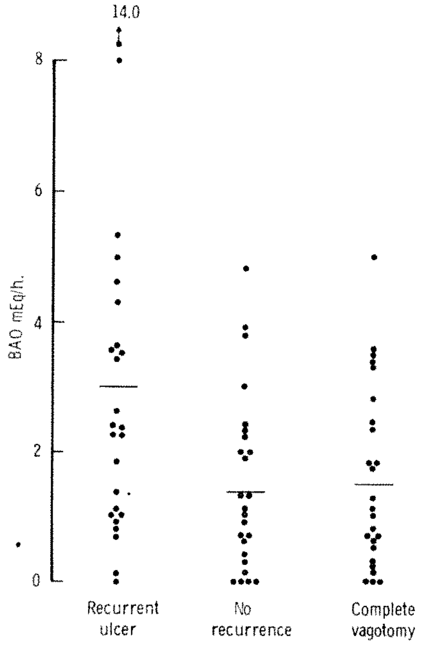

FIG. 3.—Basal acid output (mEq./hr.) during the postoperative secretion test of individuals in the three groups.

iii. *Timing of the Hollander response to insulin* (*Table VI*): The patients with a positive Hollander response have been divided into those whose response was achieved during the first hour (early responders) and those who responded in the second hour (late responders). The numbers of early and late responders were about equal in each group, suggesting that the distribution was completely random. This finding also applied when the patients with recurrent ulcer whose insulin test was positive at either the first or the second test were studied separately. On the other hand, there were quantitative differences; the peak acid output after insulin in both groups was greater in early responders than in late responders, a difference which is significant only when both groups were combined. It can be seen from *Fig.* 5 that the titratable acidity was also greater in the early

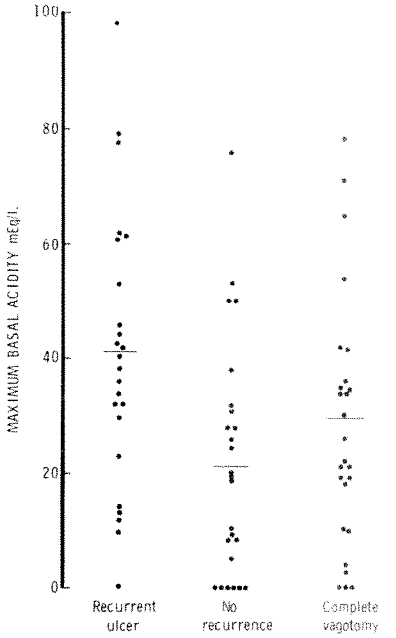

FIG. 2.—Maximum basal acidity (mEq./l.) during the postoperative secretion test of individuals in the three groups.

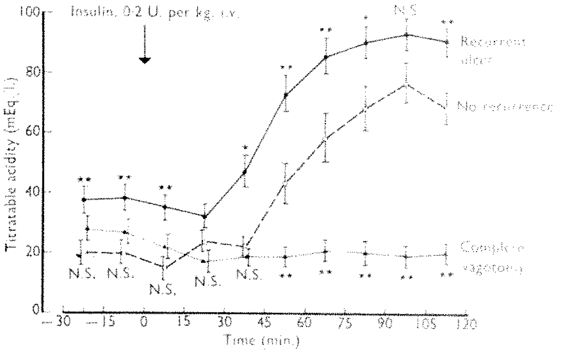

FIG. 4.—Mean titratable acidity (mEq./l.) at the end of each 15-minute period in patients with a positive Hollander response before and after insulin, 0·2 U. per kg. N.S., Not significant. *, $P < 0·05$. **, $P < 0·01$.

responders in both groups. No difference was found in the peak acid output to pentagastrin between early and late responders.

c. Pentagastrin or Histamine-stimulated Secretion.—The peak acid outputs in the three groups are plotted in *Fig.* 6. The scattergram shows considerable overlapping of the groups, and the differences between the mean values of the three groups were of borderline significance. No level of peak acid output could be set which would separate most of the patients with recurrent ulcer from those with no recurrence. The percentage reduction of peak acid output in the smaller number of patients in each group who were tested both before and after operation is shown in *Table VII*. The difference between the mean reduction in patients with recurrent ulcer and in those with no recurrence was not significant at the 5 per cent level, but there was a significant difference between patients with recurrence and those with complete vagotomy ($P < 0{\cdot}05$). Individual results are plotted in *Fig.* 7. Maximum discrimination was achieved between the groups by drawing an arbitrary line at a reduction of 60 per cent. Thirteen out of 17 patients with complete vagotomy and 7 out of 11 patients with no recurrence had a reduction of at least 60 per cent, whereas only 2 of the 19 patients with recurrent ulcer achieved this percentage reduction of peak acid output.

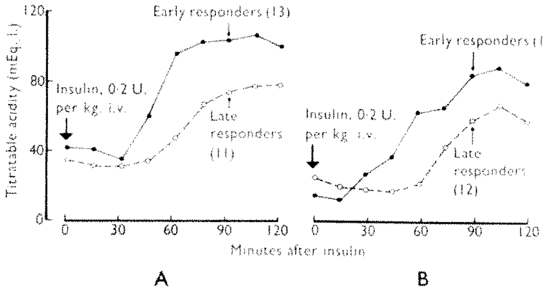

FIG. 5.—Mean titratable acidity at the end of each 15-minute period after insulin, 0·2 U. per kg., in (A) patients with a positive Hollander response who developed a recurrent ulcer, and (B) patients with a positive Hollander response with no recurrent ulcer.

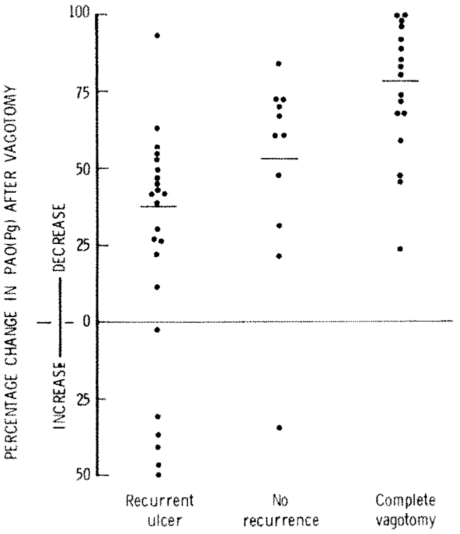

FIG. 7.—Percentage change in peak acid output to pentagastrin after vagotomy in individuals in the three groups pre- and postoperatively.

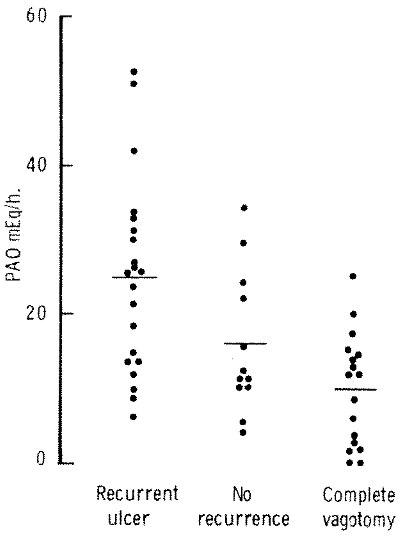

FIG. 6.—Postoperative peak acid output of individuals in the three groups. The difference between the means in the recurrent ulcer and the complete vagotomy groups was significant ($P < 0{\cdot}01$).

Table VI.—TIMING OF THE HOLLANDER RESPONSE IN PATIENTS WITH AND WITHOUT RECURRENT ULCER

GROUP	EARLY RESPONDERS		LATE RESPONDERS		P
	No. of Patients	P.A.O. (I) (mEq./hr.)	No. of Patients	P.A.O. (I) (mEq./hr.)	
1. Recurrence					
Confirmed	9		7		
Probable	4		4		
All	13	13·60	11	8·47	0·07
2. No recurrence	13	11·03	12	7·67	0·2

Mean P.A.O. (I) was significantly higher in patients with an early response ($P < 0{\cdot}05$), although there was no significant difference in P.A.O. (Pg) (pentagastrin) between the two groups.

DISCUSSION

The patients in this series who developed a recurrent ulcer were on average 10 years younger at the time of the first operation than those who have not so far developed a recurrence, although their pre- and postoperative acid secretory responses were very similar at all ages. Thus, vagotomy and drainage appears in this regard to be an acceptable procedure in older patients, but its use in young patients seems to require a more considered evaluation in the future. If vagotomy is used, no effort should be spared in seeking to achieve a complete nerve section.

Our findings are in agreement with those of Watkin and Duthie (1971), who found that the results of insulin tests performed less than 1 month postoperatively were unreliable but that the results of tests at 6 months seemed to represent the final pattern of secretion. Half of the present patients who developed recurrent ulceration had a negative response to an early test and were reported as having had a complete vagotomy. However, once recurrent symptoms had developed all these patients had become Hollander positive, suggesting incomplete vagotomy, when re-tested. We therefore agree with the proposition that postoperative insulin tests should be delayed for several months.

Table VII.—Percentage Reduction of Peak Acid Output to Pentagastrin or Histamine (P.A.O. (Pg or H)) after Vagotomy in Patients in the Three Groups Pre- and Postoperatively

Group	No. of Patients	P.A.O. (Pg or H) (mEq./hr.)		Reduction (per cent)	*P*
		Pre-operatively	Post-operatively		
1. Recurrence	19	40·3	23·4	37*	0·09
2. No recurrence	11	35·2	16·5	53	0·02
3. Complete vagotomy	17	43·5	9·8	78*	

* For groups 1 and 3, $P < 0{\cdot}05$.

One patient with recurrent ulcer after vagotomy and pyloroplasty was excluded from the study because he was found to have a gastrinoma. Two insulin tests carried out at least 6 months after the first operation showed no increase in titratable acidity above the basal levels and it may be assumed that he had had a complete vagotomy. The arbitrary criteria of Hollander (1948) appeared to be useful in that they demonstrated an 'incomplete vagotomy' in patients with recurrent ulcer. On the other hand, the finding of a positive Hollander response is of little value in helping to predict the patients who are liable to develop a recurrent ulcer. In the present study the patients in the no-recurrence group who were followed up for 1½ years longer than the interval between operations in the recurrent ulcer group had a positive Hollander response less than 1 month after the operation. We agree with Kronborg (1971) that insulin tests, however analysed, provide no quantitative data which allow discrimination between groups of patients.

Many investigators have sought criteria which would allow acid-secretion tests to help in predicting which patients are at risk of developing a recurrent ulcer. Kronborg (1972) studied large numbers of patients and found that the following criteria provided the best discrimination: patients were more liable to develop a recurrent ulcer if they had (1) a preoperative maximum acid output (M.A.O.) to histamine or pentagastrin greater than 46 mEq./hr.; (2) a postoperative M.A.O. of more than 20 mEq./hr.; (3) a postoperative reduction of less than 70 per cent in the M.A.O.

The peak acid outputs of our three groups of patients were very similar (*Tables VI, VII*), and Kronborg's first two criteria would have been of little discriminatory value. On the other hand, the percentage decreases in peak acid output did differ between the groups (*Fig.* 7). Patients with a complete vagotomy had the greatest reduction and patients with recurrence the smallest one. A reduction of less than 70 per cent gave some discrimination, but the best discrimination (far from complete) was achieved by a reduction of less than 60 per cent.

In this study of the effects of vagotomy the peak acid output before and after vagotomy has been studied as conventionally described. We appreciate, however, that there is evidence that the dose of pentagastrin required to achieve peak acid output may increase after vagotomy (Konturek, Wysock, and Olesky, 1968; Aubrey and Forrest, 1970; Rosato, Rosato, and MacFadyen, 1971), and in this sense our postoperative dose of pentagastrin may have been 'submaximal'.

Ross and Kay (1964) believed that there were two types of positive response to insulin after vagotomy: an 'early' response, which occurred within the first 45 minutes after insulin, and a 'late' response, which occurred during the 45–120-minute period. Subsequent workers have taken 60 minutes as the dividing time between early and late responders (Johnston, Thomas, Checketts, and Duthie, 1967). The latter group of workers found that the incidence of recurrent ulcer was higher in patients with an early positive Hollander response (36 per cent) compared with 7 per cent in the late positive group. We have failed to confirm this finding in the present study and have found that equal numbers of patients with an early and late response developed a recurrent ulcer. Furthermore, patients who have not developed a recurrent ulcer despite a positive Hollander response were also distributed equally between the two groups of responders. This finding is in accordance with that of Burns, Cheng, Cox, Payne, Spencer, and Welbourn (1969), who studied 100 patients with unoperated duodenal ulcer, found 37 per cent with a 'late positive' response, and concluded that the division into 'early' and 'late' responders was artificial. It must be emphasized, however, that the peak acid output to pentagastrin of early responders in the present study was greater than that of late responders, a finding which is in agreement with that of Giles, Mason, and Clark (1968).

We therefore believe that although the insulin test, when carried out several months after operation and with Hollander's criteria applied, may be helpful in assessing the completeness of vagotomy, basal secretion, preoperative peak acid output, and the insulin test, as judged by any criteria, are not of any value in predicting which patients are liable to develop a recurrent ulcer. The sole criterion we have found of possible value in the prediction of recurrent ulcer is a postoperative reduction of peak acid output after pentagastrin of less than 60 per cent.

We therefore consider that the chief role of gastric acid tests after vagotomy operations (apart from the diagnosis of the Zollinger-Ellison syndrome) is the evaluation of residual vagal innervation in patients with recurrent dyspepsia. We doubt if there is at present a place for routine insulin tests after vagotomy except as part of the systematic assessment of the vagotomist (Kay, 1969; Johnston and Goligher, 1971).

Acknowledgements.—We wish to thank Staff Nurses Shearman, Pope, and King for assistance in carrying out the tests. The support of the Wellcome and Peel Trusts to J. H. B. is gratefully acknowledged.

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TEN YEARS' EXPERIENCE IN THE SURGICAL TREATMENT OF BASAL-CELL CARCINOMA

A STUDY OF FACTORS ASSOCIATED WITH RECURRENCE*

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SUMMARY

A retrospective review of 817 basal-cell carcinomas which were treated surgically and confirmed by histological examination is presented.

Slightly more than half of the 590 patients were men. Eighty per cent of the lesions occurred in patients over the age of 50 years.

Ninety-four per cent of the lesions occurred in the head and neck with the highest density in the nasal and periorbital regions.

One lesion in 4 had been unsuccessfully irradiated prior to referral.

Less than one-half of the pathology reports gave any indication of completeness of removal. Nineteen per cent of these reported tumour in the margin of resection, indicating incomplete removal.

Over half of the lesions were kept under observation for more than 2 years.

The overall recurrence rate for the series was 9·8 per cent, but for the 535 lesions treated primarily by us the recurrence rate was 5·2 per cent.

Factors producing an increased risk of recurrence probably operate in combination making it difficult to evaluate them individually. Such factors are: (*a*) the anatomical site, the nasal and periorbital regions carrying the highest risk; (*b*) previous treatment before referral, including irradiation; (*c*) free skin-grafting as a method of repairing the defect; (*d*) the presence of tumour histologically in the margin of resection.

Fifty-nine lesions did not recur in spite of pathology reports which indicated incomplete removal. This was not related to either a shorter length of follow-up or the type of repair used in these cases.

THE basal-cell carcinoma which is the commonest of the malignant skin tumours is currently treated in several different ways. The method chosen usually depends on the clinical orientation or discipline of the physician or surgeon involved. Accordingly, surgeons excise these lesions and repair the defects surgically, dermatologists curette or electrofulgurate them, and radiotherapists irradiate them. Each applies his own method more or less unselectively to most of the lesions that he sees, referring certain ones to a colleague when his own form of treatment seems unsuitable. The surgeon is in a unique position in this respect, since his method alone has no limitation to its application. Surgical removal and repair are rarely or never contra-indicated by the size, location, or number of the lesions, or by their clinical subtype (Lever, 1967). Furthermore, the surgeon, unlike his colleagues in dermatology and radiotherapy, is rarely obliged to abandon recurrent lesions. Indeed, he is often consulted in cases of multiple recurrence when the anatomical extent of the lesion or the total dose of ionizing radiation required makes these other forms of treatment unsuitable. Since few, if any, of these tumours are rejected as unsuitable for surgical removal, case selection cannot be expected to play a significant part in improving the results of surgery in any large series. On the contrary, the results might be adversely affected by the inclusion of a large proportion of recurrences, i.e., failures of one of the other methods of treatment.

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[*] Presented at the annual meeting of the Canadian Society of Plastic Surgeons, Montreal, in May, 1969.

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MATERIAL AND METHODS

Odstock Hospital is the regional Plastic Surgery Centre for southern England, serving a population of approximately 2·5 million people. Skin tumours of all types, including basal-cell carcinomas, are referred to the centre from general practitioners and consultant specialists in the region. The centre has been operating for 20 years and most patients are referred directly by their own family doctor. A significant but lesser number are sent by dermatologists and radiotherapists. These patients have either new lesions which are considered to be unsuitable for non-surgical treatment or recurrent lesions.

The authors felt that such a large and broadly based clinical experience would offer a unique opportunity to study the results of surgery in an unselected series. With this aim in mind a 10-year retrospective study was undertaken based on all the pathology reports of basal-cell carcinoma submitted during the years 1956 to 1965 inclusive. The study was divided into two parts. In the first part the composition and various statistical features of the series will be described. In the second part our interest will focus on the lesions which recurred following surgical treatment. Knowing that a significant number of the lesions that were referred were failures of other forms of treatment, we were particularly interested in determining whether they carried a higher risk of further recurrence after surgical treatment.

COMPOSITION AND STATISTICAL FEATURES OF THE SERIES

1. Age and Sex.—Five hundred and ninety patients made up the series and this included 341 males and 249 females. They presented with a total of 817 lesions. The age distribution is shown in *Fig.* 1. It should be noted that 80 per cent of the patients were over 50 years of age, but also that these lesions may infrequently be encountered in the second and third decades of life.

2. Multiple Lesions.—Eighty per cent of the patients were treated for solitary lesions. In the remaining 20 per cent multiple lesions were present up to a maximum of seventeen in 1 patient. Patients with more than three lesions comprised less than 4 per cent of the series.

Table I.—ANATOMICAL DISTRIBUTION OF 817 LESIONS

Anatomical Site	*No. of Lesions*	*Per cent*	
Scalp, frontotemporal	158	20	Head and neck 94 per cent
Periorbital	158	20	
Nose	212	26	
Cheek	92	11	
Ear	70	9	
Lower face	48	6	
Neck	16	2	
Trunk	41		Body and limbs 6 per cent
Upper limb	16		
Lower limb	6		

3. Anatomical Site.—*Table I* shows the distribution of the 817 lesions by anatomical site. Ninety-four per cent were removed from the head and neck region. Two-thirds of the lesions were located in the upper face and scalp, with by far the highest density being found in the nasal and periorbital regions.

4. Previously Treated Lesions.—More than one-third of the 817 lesions had been unsuccessfully treated elsewhere prior to referral. *Table II* shows the types of treatment used in this group before we received them. Such methods were designated as either 'surgery', 'radiotherapy', or 'other', the latter including electrical and chemical cautery, curettage, etc. Two hundred and eighty-two of the 817 lesions had received one or more of these forms of treatment unsuccessfully before we saw them. Radiotherapy, with or without other methods, had been used in just over three-quarters of the previously treated group (218 lesions).

Table II.—TYPES OF PREVIOUS TREATMENT IN 282 CASES

Nature of Previous Treatment	*No. of Cases*
Irradiation	184
Surgery	36
Other (chemical and electrocautery, curettage, CO_2 snow)	26
Irradiation plus surgery	25
Irradiation plus other	9
Surgery plus other	2

Table III.—TYPES OF REPAIR AFTER REMOVAL OF 817 LESIONS

Method of Repair	*No. of Cases*	*Per cent*
Direct closure	438	54
Free skin-graft	207	25
Local flap	162	20
Distant flap	10	1

5. Lesion Size.—Knowing the importance of lesion size in determining recurrence rate, we were very disappointed to find that clinical records were not detailed enough to enable us to record it in any significant number of the total. We felt that some indirect indication of size is given by the method of repair used in each case.

6. Method of Surgical Repair.—*Table III* shows the various methods used to repair the defects. More than one-half of them required simple approximation of wound edges. Free skin-grafts or flaps were required for the remainder in roughly equal proportion.

7. Histology of Margin of Resection.—In 429 or just over one-half of the pathology reports no indication was given of the completeness of removal. Eighty per cent of the reports which did give this information stated that the margins of resection were histologically free of tumour.

8. Duration of Follow-up.—Various factors contributed to the wide variation in the duration of follow-up observation of the patients in the series. Age and general health, together with certain geographical limitations, were the commonest factors. Many patients were sent back to the referring physician for follow-up soon after suture removal. These patients were obviously followed up for a longer time than our records could show. Despite these limitations, 55 per cent of the patients were followed up for more than 2 years postoperatively, and only 17 per cent for less than 6 months.

RECURRENT LESIONS

What is a recurrence? Many factors influenced our decision in each instance, but often there was great difficulty in deciding whether a lesion which reappeared in the same site was a true recurrence or a new lesion. First, lesions appearing many months or years after removal can hardly be called 'recurrent', but it is difficult to establish an arbitrary time after which recurrence is unlikely. Secondly, only by examining serial sections cut in three planes can the pathologist accurately comment on completeness of removal. Very few of the specimens in this series were so examined. We feel that this approach is justified in a busy pathology department dealing with a tumour of such low-grade malignancy. Thirdly, reports which do indicate incomplete removal should localize the residual tumour to either a deep or peripheral margin of resection so that the location of a future recurrence with respect to the scar of removal can be correlated with this information. Such an approach is neither possible nor practical in the majority of centres. Our records were certainly not detailed enough to enable us to take all these factors into account; therefore, we designated lesions as 'recurrent' when suspicion of recurrence was queried by the surgeon on the clinical notes or pathology requisition. Thus, the referring physician, the patient, or the surgeon himself noted the presence of some abnormality in or immediately adjacent to the scar of previous removal or repair.

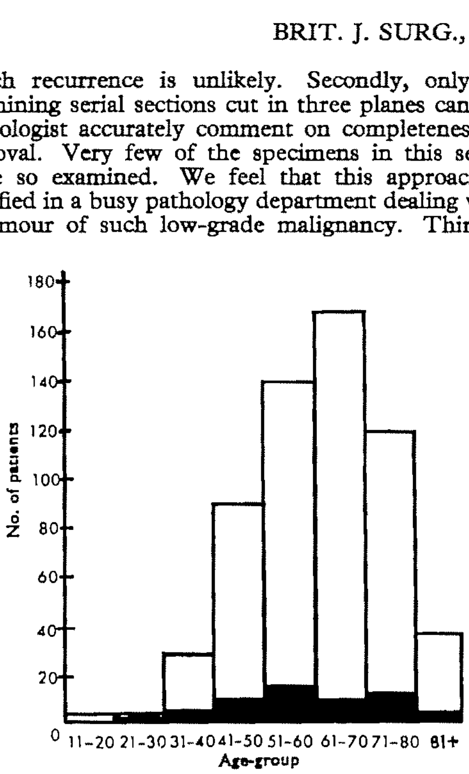

FIG. 1.—Age distribution of 590 patients with basal-cell carcinoma. ■, Recurrences.

There were 59 recurrent lesions found in 52 patients. Several of the 59 lesions recurred more than once, so that the total number of tumours in this group was 82. This represents an overall recurrence rate for the series of 9·8 per cent. We were interested to note that in many instances where recurrence was suspected clinically and a biopsy was carried out, there was no evidence of tumour histologically. It is regretted that exact numbers were not recorded to support this observation.

1. Age and Sex.—The age distribution of recurrent lesions, as shown in *Fig.* 1, is similar to that for the whole series. There were a few more males than females in the recurrent group.

2. Anatomical Site.—*Table IV* shows the distribution of the recurrences by anatomical site. The recurrence rate in the nasal and periorbital regions was significantly higher then in the rest of the head and neck. The higher risk in these areas may be more apparent than real because of the very high incidence of lesions in these relatively small areas. The greater technical difficulties encountered in removing lesions and repairing the defects around the eyelids and nose may also account for the greater incidence to some extent.

3. Previous Treatment.—There were 31 recurrences amongst the 282 lesions which had been treated previously elsewhere (a rate of 11 per cent). The recurrence rate for the 558 lesions treated primarily by us was 5·2 per cent, which seems to be significant. Lesions which had previously been treated surgically had a recurrence rate of 8·7 per cent compared with 17 per cent for those treated by 'other' methods prior to referral.

4. Recurrence Interval.—*Table V* shows the length of time between the removal of the lesion and the detection of a recurrence. Recurrences continue to appear at a fairly constant rate over 3 years in our experience. Only one-third appeared within a year of excision, while one-fifth had still not become apparent by the end of the third year.

Table IV.—ANATOMICAL DISTRIBUTION OF 82 RECURRENCES

Anatomical Site	*No. of Recurrences*	*Recurrence Rate* (per cent)
Scalp, frontotemporal	11	6·9
Periorbital	25	15·8
Nose	28	13·2
Cheek	8	8·7
Ear	3	4·3
Lower face	3	6·3
Neck	0	—
Trunk	4	9·7

Table V.—RECURRENCE INTERVAL OF 82 RECURRENT LESIONS

Time from Removal until Recurrence	*No. of Cases*	
0–6 mth.	11	36 per cent in first year
7–12 mth.	19	
13–24 mth.	18	22 per cent in second year
25–36 mth.	17	21 per cent in third year
36 mth	17	21 per cent after 3 years

Table VI.—TYPES OF REPAIR USED IN 82 RECURRENT LESIONS

Method of Repair	*No. of Cases*	*Recurrence Rate* (per cent)
Direct closure	27	6
Free skin-graft	37	17
Local flap	16	10
Distant flap	2	20

5. Method of Repair.—The relationship between recurrence and the type of repair used is shown in *Table VI.* Not unexpectedly, the use of either a free graft or flap carried a higher risk of recurrence. As stated previously, this is an indirect measurement of the size of the lesion. Of greater interest to us was the fact that the use of a free graft seemed to carry a higher risk of recurrence than a local flap. In order to exclude the possibility that free grafts enable a potential recurrence to be detected sooner owing to the thin coverage, we compared the recurrence interval in grafted defects with that in ones closed with bulkier tissue. No significant difference was found. It has also been suggested that thick coverage over residual tumour may inhibit or even prevent its growth. To test this theory we examined the method of repair used in 59 lesions which did *not* recur clinically in spite of pathology reports indicating the presence of tumour in the margins of resection. A flap type of repair was not found to have been used more frequently in these lesions.

The higher recurrence rate which appears to be associated with the use of a free graft repair is probably related to several other factors which are selectively introduced when this method is chosen by the surgeon. The anatomical site of the lesion is an obvious factor. Periorbital and nasal lesions, with their intrinsically higher recurrence rate, are also places where free skin-grafts are used more frequently because of local technical considerations. Also, free grafts are frequently used when removal is known to be incomplete and in extremely large lesions.

Table VII.—Margins of Resection in 840 Lesions and 82 Recurrences

Pathologist's Report	No. of Cases	No. of Recurrences	Recurrence Rate (per cent)
Margin of resection clear of tumour	333	19	5·7
Tumour present in margin of resection	78	19	24·4
No indication given	429	44	9·7

6. Histology of Margins of Resection.—The correlation between clinical recurrence and the pathologist's report as to the completeness of removal is shown in *Table VII*. Lesions reported as being incompletely removed were more than four times as likely to recur as those said to be completely removed. Of particular interest also is the fact that only 1 in 4 lesions removed incompletely according to the pathologist actually gave rise to a clinical recurrence. This was not due to a shorter length of follow-up since over one-half of this group of patients was followed for more than 2 years.

CONCLUSIONS

Because of an anticipated increase in the risk of recurrence, basal-cell carcinomas in the following categories probably require observation over a period of approximately 3 years: (*a*) lesions in the nasal and periorbital regions; (*b*) lesions which have already recurred following any form of treatment; (*c*) lesions in which residual tumour is reported in the margin of resection.

As noted earlier, cold-knife surgical removal and repair are rarely contra-indicated. The recurrence rate of 5·2 per cent for an unselected group of 535 lesions treated primarily in this series is significantly better than that reported in two similar series (Shanoff, Spira, and Hardy, 1967; Monballiu, 1968) where other forms of treatment were selectively applied. Although lower recurrence rates have been reported in series treated by electro-desiccation and curettage, such series rejected lesions over a certain size or in certain locations, or those which had previously recurred. We feel that our findings strongly support surgical excision and repair as the ideal method for primary treatment of basal-cell carcinomas.

Acknowledgements.—The authors wish to thank Mr. John Barron and Mr. J. E. Laing for access to the clinical records of their patients at Odstock Hospital. We are also grateful to Dr. J. R. H. Pinkerton for his co-operation in obtaining the pathology reports upon which all the clinical material in this paper is based.

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OBSTRUCTIVE UROPATHY IN GRANULOMATOUS BOWEL DISEASE

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SUMMARY

Ureteral obstruction is a seldom recognized complication of Crohn's disease and its incidence and natural history are unknown. The intravenous pyelogram findings in 5 cases of Crohn's disease are discussed and it is suggested that ureteral involvement signifies severe disease necessitating operation. The operative treatment of 1 of the cases by ureterolysis plus bowel excision is presented and discussed. Routine intravenous urography is recommended as part of the assessment of cases of Crohn's disease.

Among the urological complications of granulomatous bowel (Crohn's) disease, ureteral obstruction is an uncommon but increasingly frequently diagnosed complication (Present, Rabinowitz, Banks, and Janowitz, 1969). Up to 1970, 28 cases of ureteral obstruction developing as a consequence of Crohn's disease were reported in the American literature (Enker and Block, 1970). No similar reports have appeared in the British literature. This paper reports a case of Crohn's disease presenting as obstructive hydronephrosis and discusses the intravenous pyelogram findings in this patient and 4 other cases of Crohn's disease.

CASE REPORT

Case 1.—N. O'M., a 22-year-old male, was referred to the Meath Hospital Urological Department in August, 1971, for investigation of a right-sided hydronephrosis. He presented with an 8-month history of weight-loss (19 kg.), abdominal pain (especially in the right flank and right thigh), loss of energy, and constipation. He had a past history of appendicitis complicated by peritonitis in 1968, for which he had had an operation in another hospital. Examination revealed a thin, sick-looking young man. His weight was 47·2 kg.; haemoglobin, 12·4 g. per cent; leucocytes, 13,900 per c. mm.; erythrocyte sedimentation rate, 116 mm. per hour; urea, 38 mg. per cent; serum protein, 7·5, with albumin 2·8. A vague mass was palpable in the hypogastrium and there was a small, fluctuant swelling in the left gluteal region.

Intravenous urography on 10 Aug., 1971, revealed a grade III dilated right pelvis, and a grade II–III dilated right ureter (*Fig.* 1). Radiographs of the chest and hips were negative. Rectal examination revealed a large stenosing rectal mass of 10 cm. Biopsy showed non-specific inflammation with focal mucosal ulceration. The gluteal abscess was aspirated and the aspirate grew *Streptococcus faecalis* and *Escherichia coli*. Tubercle bacillus culture was negative. Repeated urine cultures were sterile, as were blood cultures.

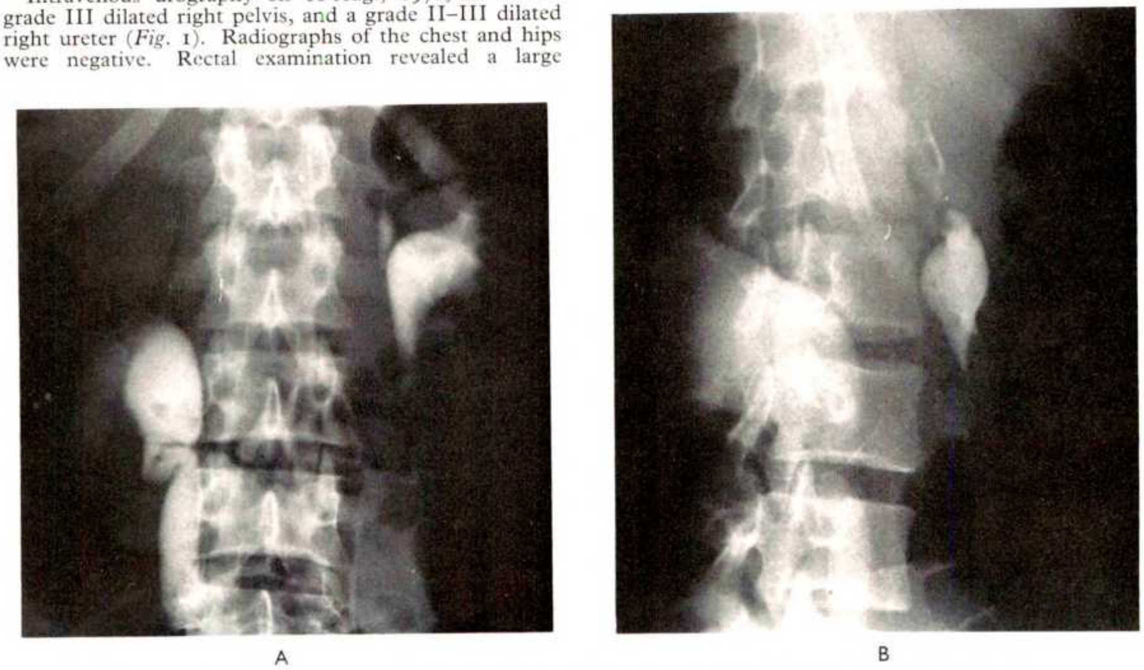

FIG. 1.—*Case* 1. A, Intravenous urogram, showing the dilated right ureter (grade II–III) and pelvis (grade III). B, Oblique view of A showing the grossly dilated right pelvis.

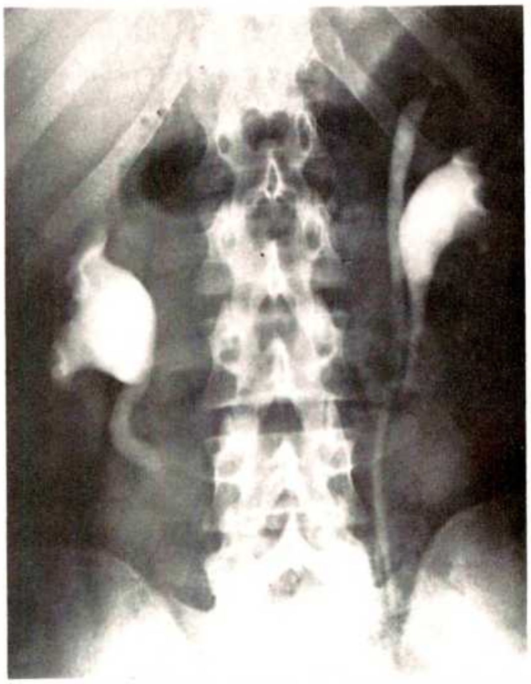

FIG. 2.—*Case* 1. Intravenous urogram 2 weeks postoperatively showing marked reduction in the ureteral and pelvic dilatation.

At laparotomy on 23 Aug. the terminal ileum and caecum were found to be thickened and adherent to the large bowel and a large rectal mass was adherent to the sacrum. The right ureter was dilated by approximately 2 cm. down to the pelvic brim, where it was involved by the inflammatory mass. The ureter was dissected free from the mass and an anterior resection of the rectum was performed together with a transverse colostomy.

The pathology report was as follows: the excised rectum was diffusely thickened and the overlying mucosa showed a cobble-stone appearance. There were foci of mucosal ulceration, subserosal fibrosis, and granulomas, with occasional giant cells.

Repeat urograms 2 weeks postoperatively prior to discharge showed a reduction in the ureteral and pelvic dilatation (*Fig.* 2). A barium-enema examination revealed an irregular mucosal pattern in the caecum and terminal ileum consistent with Crohn's disease.

The colostomy was closed on 24 Feb., 1972, following a course of cortenemas through the proximal loop. Intravenous urograms on 18 Feb. revealed grade I–II ureteral dilatation and grade I pelvic dilatation. The patient's weight was 66·2 kg.; haemoglobin, 16 g. per cent; erythrocyte-sedimentation rate, 4 mm. per hour. At a follow-up examination on 28 March the patient weighed 71·7 kg. and had returned to work after an absence of 14 months.

UROGRAPHY FINDINGS IN 4 CASES OF CROHN'S DISEASE

Case 2.—E. F., a 21-year-old female, was investigated for pyrexia of unknown origin and found to have severe Crohn's disease of the large bowel with enteric fistulation.

The erythrocyte-sedimentation rate was 120 mm. per hour and an intravenous pyelogram showed a grade I–II dilatation of the right pelvis and ureter.

Case 3.—E. O'D., a 22-year-old female, developed reactivation of Crohn's disease after an ileotransverse anastomosis 5 months previously. A barium-enema examination showed an abnormal mucosal pattern in the caecum and fistula formation. The erythrocyte-sedimentation rate was 70 mm. per hour and an intravenous pyelogram revealed grade I dilatation of the right pelvis.

Case 4.—T. M., a 55-year-old male, had been followed up for 2 years after a right hemicolectomy for Crohn's disease of the terminal ileum and caecum. A barium-enema examination showed normal mucosa in the terminal ileum. The erythrocyte-sedimentation rate was 5 mm. per hour and an intravenous pyelogram showed normal appearances.

Case 5.—M. H., a 50-year-old female, had been asymptomatic after an ileotransverse anastomosis for Crohn's ileitis 18 months previously. The erythrocyte-sedimentation rate was 10 mm. per hour and an intravenous pyelogram showed no ureteral or pelvic dilatation.

DISCUSSION

Hyams, Weinberg, and Alley (1943) were the first to report ureteral obstruction as a complication of Crohn's disease. Since then it has been increasingly recognized and reported.

The true incidence of ureteral involvement in Crohn's disease is not known. Schofield, Staff, and Moore (1968), using radioactive renography, demonstrated ureteral stasis in 50 per cent of patients with regional enteritis. The intravenous urographic findings in the 5 cases reported here would seem to indicate that ureteral involvement occurs in cases of severe, active Crohn's disease (i.e., with fistulation, elevated erythrocyte-sedimentation rates, perianal complications, etc.). Present and others (1969), in a report from New York, found obstructive hydronephrosis in 7 per cent of patients affected by Crohn's disease. They attributed this high incidence to the fact that most of their patients were referred from other centres because of severe complicated disease.

The reasons for ureteral involvement in Crohn's disease are not clear. Redish (1952) regards it as a reflex disturbance of ureteral tone resulting from the adjacent intestinal inflammation. However, Schofield and others (1968) favour the view that it results from the direct involvement of the peri-ureteral tissue by intestinal microperforation and resulting inflammation.

Prior to the report of Enker and Block (1970) the treatment of this complication of Crohn's disease was centred exclusively on the involved intestine, and surgical intervention to liberate the involved ureter was considered unwarranted by Present and others (1969). However, results of this approach to treatment have been unsatisfactory. Of the 21 cases in the literature which were not treated by ureterolysis, 50 per cent achieved ureteral decompression at a cost of at least two operative procedures (including two nephrectomies).

CONCLUSION

1. A case of Crohn's disease presenting as a right-sided ureteral obstruction is presented. The best treatment is probably directed simultaneously at both the intestinal and urological disorders.

2. From our small experience obstructive uropathy must be considered a sign of advanced inflammatory bowel disease and, as such, constitutes an indication for operative intervention.

3. The literature on the subject of ureteral involvement in Crohn's disease is briefly reviewed. Routine intravenous urography is recommended as part of the investigations of all cases of Crohn's disease in order (*a*) to ascertain the true incidence of obstructive uropathy and (*b*) to assess the activity of the disease and the need for operation.

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LOBULAR CARCINOMA IN SITU OF THE BREAST

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SUMMARY

Ten patients with lobular carcinoma in situ of the breast have been seen in 2½ years in Cambridge. Within that period of time 8 of these patients also had infiltrating carcinoma. Four out of 5 cases had bilateral lobular carcinoma in situ and 2 patients had bilateral infiltrating carcinomas. The pre-malignant nature of lobular carcinoma in situ is not proven but is likely. It is suggested that the evidence supports previously expressed views that a histological diagnosis of lobular carcinoma in situ merits mastectomy and a large contralateral biopsy in the first instance.

IT is only in recent years that most pathologists have become fully aware of lobular carcinoma in situ of the breast and its apparent dangers, although it

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was first described 32 years ago (Foote and Stewart, 1941; Muir, 1941). Increased interest in the subject has been stimulated by studies in the U.S.A. which suggest that the disease may be multifocal, bilateral, and premalignant in a high proportion of cases (McDivitt, Hutter, Foote, and Stewart, 1967; Hutter and Foote, 1969; Urban, 1969; Farrow, 1970). The lack of published accounts in this country prompts us to record our experience with this condition.

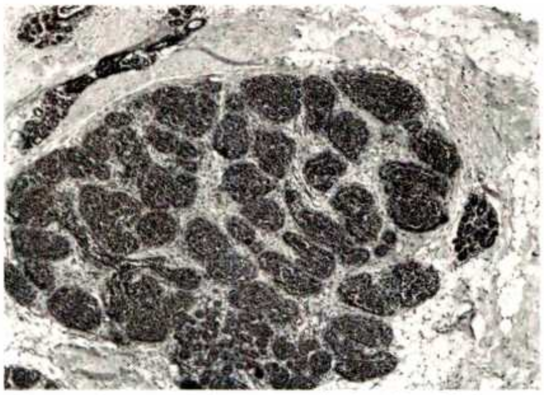

FIG. 1.—*Case* 4.—Lobular carcinoma in situ. H. and E. (× 33.)

The histological diagnosis of lobular carcinoma in situ has been made in 10 patients in the Department of Pathology, University of Cambridge, over a period of 2½ years. During this time approximately 850 breast biopsy and mastectomy specimens have been examined. In each of the 10 cases of lobular carcinoma in situ the diagnosis was made independently by at least two observers. All the mastectomies described were simple.

CASE REPORTS

Case 1.—In late 1971 a biopsy of a right breast lump in a 51-year-old woman showed lobular carcinoma in situ. A right mastectomy was performed and a blind biopsy of the left breast was taken. Both specimens showed only dysplasia. The patient then developed a lump in the left breast. A larger biopsy was taken which showed lobular carcinoma in situ. A left mastectomy was performed, and examination of the specimen revealed multifocal lobular carcinoma in situ with no evidence of an infiltrating carcinoma.

Case 2.—In early 1971 a right breast lump in a 32-year-old woman proved on biopsy to be an infiltrating lobular carcinoma. The right mastectomy specimen showed residual infiltrating carcinoma. One year later a biopsy of a lump in the left breast also showed an infiltrating carcinoma, and, in addition, lobular carcinoma in situ. Re-examination of sections of the right mastectomy specimen revealed lobular carcinoma in situ which had not been reported originally.

Case 3.—In late 1971 a large biopsy of a right breast lump in a 49-year-old woman showed extensive lobular carcinoma in situ with a tiny focus of infiltration in one area. A right mastectomy revealed neither residual infiltrating carcinoma nor lobular carcinoma in situ. The left breast has not yet been biopsied.

Case 4.—A 51-year-old woman complained in mid-1971 of a lump in the left breast; an unnoticed ill-defined nodular area was also found in the right breast. The left biopsy showed only dysplasia but that of the right breast demonstrated lobular carcinoma in situ. A right mastectomy revealed extensive lobular carcinoma in situ (*Fig.* 1) with a tiny focus of infiltration (*Fig.* 2). A larger biopsy of the left breast then revealed lobular carcinoma in situ; the left mastectomy specimen showed multifocal lobular carcinoma in situ but no infiltrating carcinoma.

Case 5.—In 1968 a 48-year-old woman complained of a discharge from the right nipple. No mass was palpable but a biopsy of the mammary ducts was reported as showing dysplasia. In 1969 a recurrent lump in the same region proved on biopsy to be an infiltrating carcinoma. The right mastectomy specimen showed residual infiltrating carcinoma. In 1971 a lump was found in the left breast and proved to be an infiltrating carcinoma. The left mastectomy specimen showed no residual infiltrating carcinoma but extensive lobular carcinoma in situ. The sections of the biopsy of the right mammary ducts taken 3 years previously were then reviewed and showed unequivocal lobular carcinoma in situ. This patient is now (mid-1972) dying from carcinomatosis.

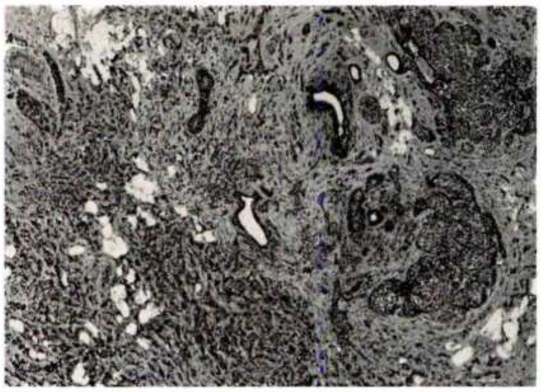

FIG. 2.—*Case* 4. Early infiltrating carcinoma in the area of lobular carcinoma in situ. H. and E. (× 33.)

Case 6.—In mid-1971 an infiltrating carcinoma was found in the biopsy of a right breast lump in a 27-year-old woman. The mastectomy specimen showed residual infiltrating carcinoma and multifocal lobular carcinoma in situ. Biopsy of the other breast has not been performed.

Case 7.—In early 1971 a biopsy of a left breast lump in a 72-year-old woman showed an infiltrating carcinoma. The mastectomy specimen showed no residual carcinoma but a few foci of lobular carcinoma in situ. Biopsy of the other breast has not been performed.

Case 8.—In late 1970 a biopsy of a right breast lump in a 72-year-old woman showed an infiltrating carcinoma and lobular carcinoma in situ. Sections of the mastectomy specimen showed only dysplasia. No contralateral biopsy has been performed.

Case 9.—In 1970 a biopsy of a left breast lump in a 47-year-old woman showed an infiltrating carcinoma. The mastectomy specimen revealed some residual infiltrating carcinoma and lobular carcinoma in situ. The other breast has not been biopsied.

Case 10.—In mid-1970 a biopsy of the right mammary ducts was performed in a 51-year-old woman complaining of a persistent discharge. This showed infiltrating carcinoma as well as lobular carcinoma in situ. A right mastectomy showed another area of lobular carcinoma in situ. Two subsequent blind biopsies of the left breast have shown only dysplasia.

DISCUSSION

In all except 1 of the 10 patients diagnosed as having lobular carcinoma in situ there was an infiltrating carcinoma on one or both sides. It would, however, be grossly incorrect to conclude that lobular carcinoma in situ gives rise to infiltrating carcinoma in 9 out of 10 cases, because in 6 of the current series the lobular carcinoma in situ only came to light when an infiltrating carcinoma was palpated. The majority of cases of lobular carcinoma in situ are probably clinically silent. However, 2 of the 9 infiltrating carcinomas were small and found in the centre of large expanses of lobular carcinoma in situ. The appearances suggested that at least in these 2 patients lobular carcinoma in situ may have developed into an infiltrating carcinoma. Of the 5 cases in which both breasts have been examined histologically, 4 have so far shown evidence of bilateral lobular carcinoma in situ with 2 bilateral infiltrating carcinomas. There is also abundant evidence from the present 10 patients that lobular carcinoma in situ is a multifocal disease.

Clearly such small numbers add nothing to the overall statistical study of the disease and the evidence presented here is purely anecdotal. Nevertheless, some of these case reports present striking sequences of events. For instance, it is likely that the impalpable tiny infiltrating carcinoma in the mastectomy specimen in *Case* 4 would have remained undetected if lobular carcinoma in situ had not been seen on the biopsy and mastectomy advised. It is also possible that the unfavourable outcome in *Case* 5 might have been prevented by the recognition and treatment of lobular carcinoma in situ at the time of the first breast biopsy.

In view of these observations we have attempted to find examples of lobular carcinoma in situ in sections seen in this department in the years 1946–61 in the hope of providing a retrospective study of patients followed for 10 years or more. This has proved somewhat frustrating because of the small numbers and inadequate follow-up. Two hundred and eighteen specimens were re-examined because they had been indexed as showing dysplasia with epithelial proliferation. Only 4 examples of lobular carcinoma in situ which had been treated by biopsy only were found. Three of these 4 patients have been followed for 10 or more years, with no clinical recurrence of breast disease. Eight examples of lobular carcinoma in situ were found in sections of breasts removed because of infiltrating carcinoma (6 cases) or persistent nipple discharge. Clinical follow-up data are available for these 8 patients at 0, 3, 4, 6, 9, 9, 14, and 18 years after mastectomy respectively. None has had clinical contralateral disease. Clearly this retrospective study, admittedly of very limited value, would not lead one to suppose that lobular carcinoma in situ is a dangerous disease, in contrast to the findings in our more recent patients.

The histological diagnosis of lobular carcinoma in situ is not difficult. In several of the present cases it was made on cryostat sections. The appearances have been reviewed elsewhere (McDivitt, Stewart, and Berg, 1968). The pathological differential diagnosis includes benign epithelial proliferation as well as direct lobular invasion by a ductal carcinoma (Feckner, 1971).

Lobular carcinoma in situ appears to be clinically silent in most cases. Out of 14 breasts with the disease in this series of 10 patients, 4 were palpable lumps, 1 was found after a nipple discharge, and the others were apparently silent until a carcinoma was palpated or a blind biopsy was performed.

The management of a patient with lobular carcinoma in situ is often a problem. To judge from the American retrospective studies quoted above if lobular carcinoma in situ alone is found on biopsy the risk of another focus of carcinoma in situ in the same breast giving rise to infiltrating carcinoma is high (up to 35 per cent in 20 years) and merits immediate mastectomy. From the same studies it appears that the incidence of bilateral lobular carcinoma in situ is also high (up to 54 per cent) and held to justify a large contralateral biopsy even if the other breast is clinically normal. Clearly if this biopsy also shows carcinoma in situ then another mastectomy would be indicated.

Comment on this advice seems unjustified after our small experience of the condition, but at least we have seen nothing in our study to contradict this suggested management. The only exceptions might be the elderly or those in whom the operative risk is high. Lobular carcinoma in situ has received insufficient attention in this country; further retrospective and prospective studies are justified in centres where large numbers of patients with breast disease are seen.

We do not feel qualified to judge the merits of introducing expensive screening procedures such as mammography in the hope of detecting the 'silent' cases of lobular carcinoma in situ. It does, however, seem that the evidence that lobular carcinoma in situ is a premalignant condition is not dissimilar from that suggesting that carcinoma in situ of the cervix leads to invasive carcinoma. In both these relationships the pathological and statistical evidence is suggestive but not conclusive. It is safer to regard lobular carcinoma in situ seriously than to ignore it.

Acknowledgements.—We are grateful to surgeons at Addenbrooke's Hospital, Cambridge, for permission to publish data on their patients, to Dr. G. A. Gresham for the pathological material, and to Mr. Peter Haslam of the Department of Medical Photography, Addenbrooke's Hospital, for the illustrations.

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TRAUMATIC ANEURYSMS OF THE SUPERFICIAL TEMPORAL ARTERY

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SUMMARY

Six patients with aneurysm of the superficial temporal artery are reported from Africa. The presenting symptom was a pulsating swelling in the temporal region, and blunt trauma to the side of the head was the aetiological agent in every case. Treatment by surgical excision is advocated. It is suggested that aneurysms of the superficial temporal artery occur more frequently than reports in the literature suggest.

THE earliest reported case of superficial temporal aneurysm appears to have been that of Bartholin in 1740 which is included in a group of 37 cases in De Santis's book of 1884 (Brown and Mehnert, 1942). Up to 1970 a total of 131 cases had been reported in the literature (Schecter and Gutstein, 1970). It would seem, therefore, that these aneurysms are infrequently encountered and are for the most part overlooked by the authors of standard textbooks on head injury. It is our belief that the paucity of the case reports belies the real incidence of this complication of head trauma. The 6 patients presented here are the first cases reported from Africa and are used to emphasize the fact that post-traumatic aneurysms of the superficial temporal artery occur more commonly than is generally supposed.

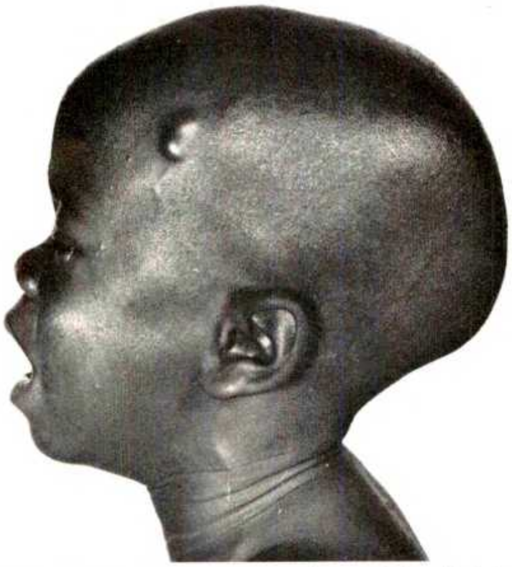

FIG. 1.—*Case* 1. Bilocular aneurysm on the anterior branch of the superficial temporal artery.

CASE REPORTS

Case 1.—A 3-year-old boy knocked his head against a chair after which a large haematoma developed in the left temporal area. When this resolved there remained a small swelling which gradually became larger.

On examination there was a bilocular swelling in the left anterior temporal region on the line of the anterior branch of the superficial temporal artery (*Fig.* 1). The lower part of the swelling was pulsatile and the upper part solid. No bruit was audible over the mass. Compression of the superficial temporal artery below the swelling abolished the pulsation and a diagnosis of an aneurysm was made.

At operation the superficial temporal artery was ligated above and below the aneurysm and the mass was excised *in toto*. Microscopic examination confirmed that the aneurysm contained some organized blood-clot in its lumen (*Fig.* 2).

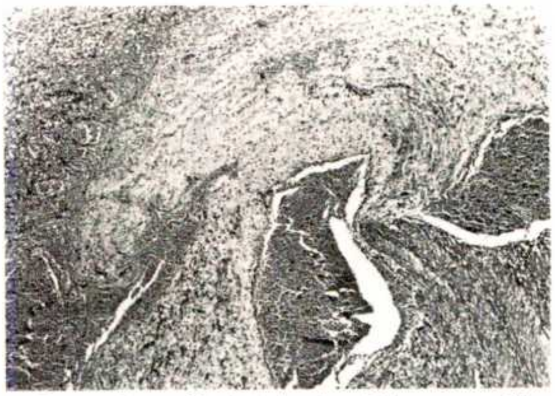

FIG. 2.—*Case* 1. Histological section of the aneurysm. The lumen (upper left) contains some solid blood-clot. There is some intramural haemorrhage in the aneurysm wall. H. and E. (× 28.)

Case 2.—A 36-year-old man presented with a swelling in the left temple which had progressively increased in size since it had first been noticed a month previously. It had appeared 4 days after he had been assaulted about the head.

On examination there was a pulsatile swelling 2·0 cm. in diameter situated just above the zygomatic arch (*Fig.* 3). A thrill was palpable but there was no audible bruit over the mass. The swelling was completely excised together with a small length of the adjacent superficial temporal artery. Histological examination showed that this was a false aneurysm.

Case 3.—A 28-year-old man tripped and fell, striking his head against the floor. He immediately developed a painful swelling of the right forehead. After this had subsided there remained two small pulsatile swellings in the right temporal area which were reducible by direct pressure.

At operation these swellings were found to be two small aneurysms on the anterior branch of the superficial temporal artery.

Case 4.—A 42-year-old man sustained a laceration on the right side of his forehead as the result of a motor accident. One week later he noticed two small 'tumours' in the right temporal region.

On examination there were two small pulsatile dilatations on the anterior branch of the superficial temporal artery but these were not directly related to the adjacent forehead wound (*Fig*. 4). The swellings were compressible and non-tender, and were diagnosed as aneurysms. They were excised after proximal and distal ligation of the parent artery.

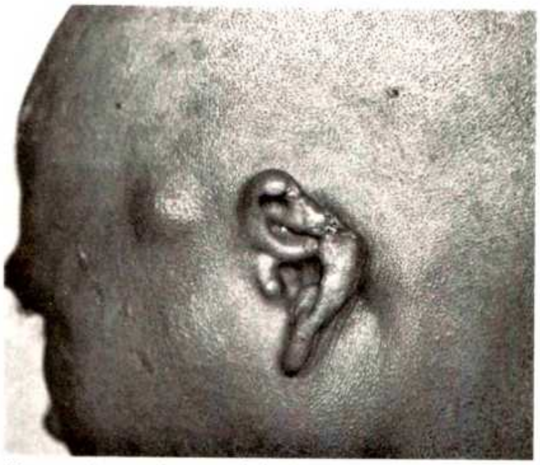

FIG. 3.—*Case* 2. Aneurysm lying just above the left zygomatic arch.

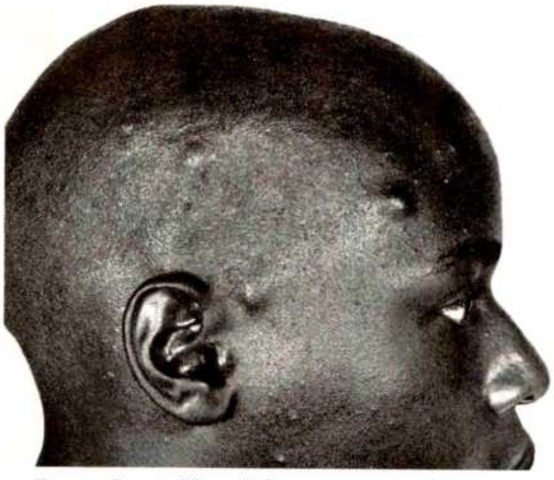

FIG. 5.—*Case* 6. Three distinct aneurysms on the superficial temporal artery; one over the zygomatic arch, one on the anterior branch, and the third on the posterior branch.

Case 5.—A 25-year-old man was involved in a fight and sustained multiple small lacerations and bruises about the head. Four weeks later he presented complaining of a pulsating mass in the left temple. This was an aneurysm on the anterior branch of the superficial temporal artery. Operation was not carried out as the patient failed to appear for admission and efforts to trace him were unsuccessful.

Case 6.—A 26-year-old man presented with three distinct swellings in the right temple, all of which had developed a few weeks after a closed head injury (*Fig*. 5). One was located over the zygomatic arch, another on the anterior branch of the superficial temporal artery, and the third was on the posterior branch. They were soft, pulsatile, and compressible. A palpable thrill over each swelling was abolished by proximal compression of the superficial temporal artery as it crossed the zygomatic arch.

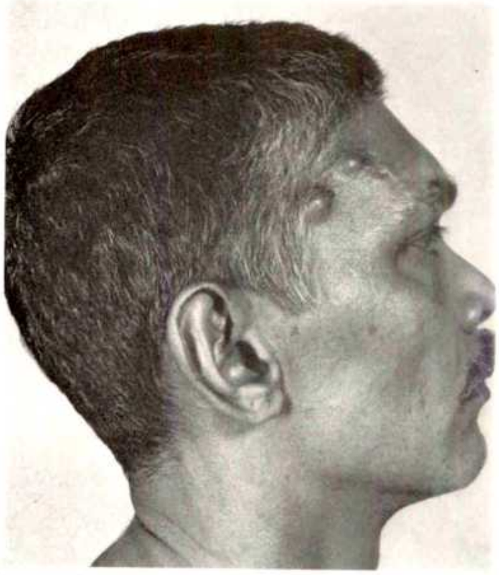

FIG. 4.—*Case* 4.—Two distinct aneurysms on the forehead adjacent to a previous scar.

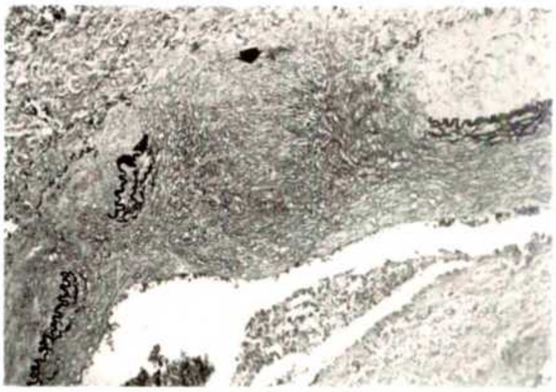

FIG. 6.—*Case* 6. Photomicrograph illustrating the disruption of the tunica elastica at the site of origin of the aneurysm (arrow). Weigert. (× 70.)

Having demonstrated by angiography that each swelling was a small aneurysm, they were excised after ligation of the parent artery above and below each swelling. Histological examination showed that they were all false aneurysms with disruption of the tunica elastica (*Fig*. 6).

DISCUSSION

All 6 patients in this series were males whose ages ranged from 3½ to 42 years (average age 26 years). Five were Ugandan Africans and 1 was an Asian. The aneurysms were equally distributed on each side of the head. In 2 instances (*Cases* 2, 5) there was a single aneurysm, 1 was bilocular (*Case* 1), while in the remaining 3 cases there were multiple distinct aneurysms.

Fig. 7 is a composite drawing showing the sites of the aneurysms in this series. It can be seen that they most commonly occurred either where the superficial temporal artery crossed the zygomatic arch or at the attachment of the temporalis fascia to the superior temporal line. More aneurysms were found on the anterior branch of the artery than on the posterior one.

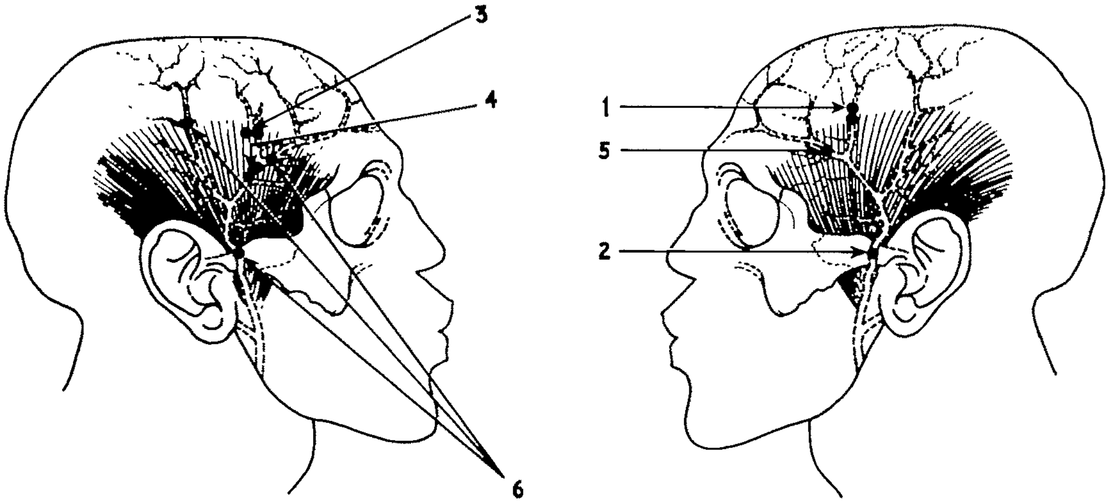

FIG. 7.—Composite diagram indicating the sites of the aneurysms in the present series

Blunt trauma to the side of the head is the commonest cause of this aneurysm nowadays and was the aetiological agent in all the cases in this series. The superior temporal line is often salient anteriorly but fades away posteriorly (*Gray's Anatomy*, 1969). It is postulated that the anterior branch of the artery, which is unprotected by overlying muscles, may be crushed against this prominent ridge by a blow to the side of the head.

Aneurysms of the superficial temporal artery have also been reported following open wounds, especially in the nineteenth century when sword duelling was common practice and temporal arteriotomy was in vogue for the treatment of epilepsy and apoplexy (Davies, 1961). Spontaneous development of this type of aneurysm is rare and only 11 cases have been reported (Schecter and Gutstein, 1970). These were either congenital or arteriosclerotic in origin. No luetic or mycotic aneurysms have been reported.

The usual presenting symptom is a pulsating swelling in the temporal region or a throbbing headache. The presence of a bruit or a palpable thrill over the aneurysm is dependent on the amount of thrombus in the swelling. A continuous bruit implies that an arteriovenous fistula has developed between the artery and its accompanying vein.

These aneurysms can usually be obliterated by direct pressure, while proximal arterial compression will maintain the collapsed state. Angiography can be used to confirm that the pulsation is caused by an aneurysm but this is not usually necessary to make the diagnosis.

Histologically, these are false aneurysms, part of the wall being formed by intimal lined fibrous tissue. It is assumed that the blow causes local necrosis of the arterial wall with subsequent saccular dilatation. Spontaneous complete thrombosis of the aneurysm may theoretically occur although this has never been documented.

Surgical excision is the usual mode of treatment because these aneurysms progressively enlarge and there is a risk of profuse haemorrhage from a subsequent head injury. Surgery is also indicated to relieve the throbbing headache and for cosmetic reasons.

Acknowledgements.—We are grateful to Dr. T. Poltera for the histological reports and to Professor Sir Ian McAdam and other members of the Department of Surgery, Makerere University Medical School, who referred some of these cases to us. Our thanks are also extended to the Chief Medical Officer, Ministry of Health, Uganda, for permission to publish this paper.

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THE EFFECT OF VAGOTOMY ON THE INHIBITION OF GASTRIC SECRETION BY INTRADUODENAL FAT*

By A. S. WARD†

QUEEN ELIZABETH HOSPITAL, BIRMINGHAM, AND THE MIDDLESEX HOSPITAL, LONDON

SUMMARY

It has been suggested that the inhibition of gastric secretion by intraduodenal fat is a vagal phenomenon in man. Selective and highly selective vagotomy, by preserving this reflex, could offer advantages over truncal vagal section. This paper reports the effect of intraduodenal fat on pentagastrin-stimulated gastric secretion in duodenal ulcer patients before and after truncal vagotomy.

Marked inhibition of gastric secretion occurred in all the patients. In the postoperative group gastric secretion was almost totally abolished following fat infusion despite the absence of an abdominal vagal supply. The results suggest that inhibition of gastric secretion by intraduodenal fat is mediated by a non-vagal mechanism in man; from this point of view, therefore, there is little advantage in attempting to preserve the nerve-supply to the duodenum at vagotomy.

THE presence of fat in the duodenum is known to inhibit gastric secretion in animals (Lim, Ivy, and McCarthy, 1925; Sircus, 1958; Konturek and Grossman, 1965) and in man (Ewald and Boas, 1886; Shay, Gershon-Cohen, and Fels, 1939; Windsor, Cockel, and Lee, 1969). This response appears to be humoral (Feng, Hou, and Lim, 1929; Lim, 1933; Halvorsen, Middleton, Bibler, Harkins, and Nyhus, 1966; Debas, Bedi, Gillespie, and Gillespie, 1969), though Johnston and Duthie (1969) have suggested involvement of a vagal reflex in man. Selective or highly selective vagotomy, by preserving this reflex, could offer advantages over total vagal division (Griffith, 1969; Johnston and Wilkinson, 1970). In view of the lack of agreement on this point the present study was undertaken to reassess the effect of intraduodenal fat on gastric secretion in man before and after total vagotomy.

MATERIAL AND METHODS

Six patients with duodenal ulcer were investigated before operation and a further 6 patients after truncal vagotomy and pyloroplasty. One additional patient was successfully tested both before and after operation. It has not so far been possible to test other patients in this way because of the technical difficulties of the test, the natural reluctance of patients to attend for both pre- and postoperative investigation, and the difficulty in always securing a complete vagotomy in patients with a satisfactory preoperative test. Eleven men and 2 women were investigated; the mean age of the preoperative group was 48 years and of the postoperative patients 54 years. In the latter group completeness of vagal section was confirmed by a Hollander test as a preliminary to the main part of the study. All post-vagotomy tests were carried out after a minimum interval of 6 months.

The method of assessing duodenal inhibition was similar to that of previous reports (Ward, Wilkins, Cockel, and Windsor, 1969; Windsor and others, 1969). After an overnight fast a fine polyvinyl tube was introduced via the nose into the stomach and subsequently manipulated into the distal duodenum under fluoroscopic control. A Salem sump tube was then placed in the gastric antrum. Sampling was by continuous suction and 10-minute collections were made throughout. Basal secretion was collected for approximately half an hour and then an intravenous infusion of pentagastrin (6 μg. per kg. per hour) was commenced and continued until the end of the test. After a plateau response, i.e., three successive collections of similar volume had been obtained, 20 ml. of Prosparol (a commercial emulsion of ground-nut oil) at 37° C. were infused into the distal duodenum over a 5-minute period. Gastric collection was continued for a further hour. The Prosparol was labelled with 1 per cent polyethylene glycol (M.W. 4000) in all cases so that any reflux from the duodenum to the stomach could be measured. Reflux was less than 5 per cent in all the patients studied. Failure to provoke significant reflux may be attributed to the relatively slow infusion rate and to the distal siting of the perfusion zone. Nausea may also invalidate such investigations (Grossman, Woolley, Dutton, and Ivy, 1945) and careful observations were made to exclude this possibility.

Table I.—THE EFFECT OF INTRADUODENAL FAT ON GASTRIC ACID OUTPUT IN DUODENAL ULCER PATIENTS BEFORE VAGOTOMY

PATIENT No.	ACID OUTPUT DURING PLATEAU (mEq. per 10 min.)	ACID OUTPUT DURING INHIBITION (mEq. per 10 min.)	INHIBITION (mEq. per 10 min.)
1	11·5	0·0	11·5
2	7·6	2·9	4·7
3	11·4	2·6	8·8
4	7·7	3·1	4·6
5	7·2	2·6	4·6
6	8·1	0·6	7·5
W.A.*	15·4	3·1	12·3
Mean	9·8	2·1	7·7
Standard error	1·1	0·5	1·2

* *See Fig.* 4.

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* Based on a communication to the Surgical Research Society in January 1972.

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Control studies were carried out in 5 duodenal ulcer patients. In 3 cases a pentagastrin infusion alone was continued for 3 hours to detect possible diminution of the gastric secretory response with time. None was noted. In 2 patients 20 ml. of physiological (0·9 per cent) saline were instilled into the duodenum, again without effect on the plateau response.

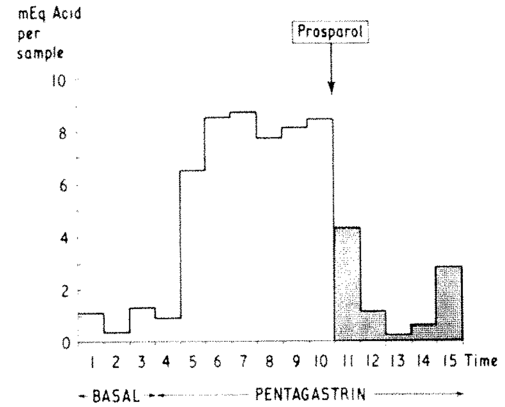

FIG. 1.—The effect of intraduodenal fat on gastric acid output in a duodenal ulcer patient before vagotomy. The open columns denote acid output prior to duodenal infusion and the shaded columns the post-instillation samples. The stimulus was pentagastrin infused at a rate of 6 μg. per kg. per hour.

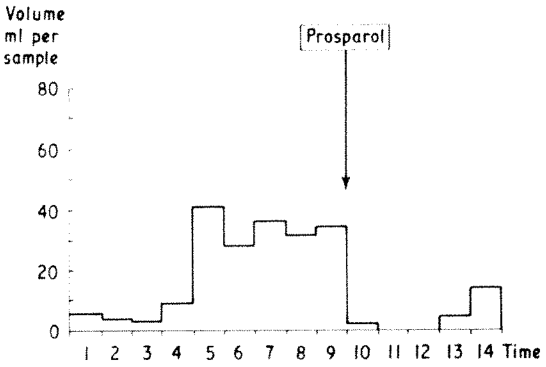

FIG. 3.—The effect of intraduodenal fat on the volume of gastric secretion in a vagotomized patient.

The following estimates were made on the gastric aspirate: (1) the volume of each sample per 10-minute collection period; (2) the *p*H and hydrogen ion concentration by titration to *p*H 7 with 0·1 *N* NaOH; (3) the polyethylene glycol concentration in the post-instillation samples by a turbidimetric method (Malawer and Powell, 1967).

RESULTS

The results are shown in *Tables I* and *II*. Acid output prior to duodenal infusion has been represented by the mean of the three 10-minute collections constituting the plateau. Acid output during inhibition is shown by the mean of the three lowest consecutive collections after the fat infusion. Mean acid output in the preoperative group (*Table I*) decreased from 9·8 ± 1·1 mEq. per 10 minutes during the plateau to 2·1 ± 0·5 mEq. per 10 minutes after the fat infusion, a highly significant response ($t = 6{\cdot}2$, $P < 0{\cdot}001$). Inhibition occurred within minutes of commencing the infusion in all the patients and lasted for approximately 40 minutes. A typical response is shown in *Fig.* 1.

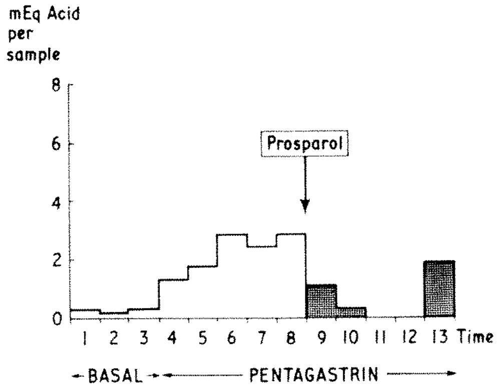

FIG. 2.—The effect of intraduodenal fat on gastric acid output in a duodenal ulcer patient after vagotomy.

Table II.—THE EFFECT OF INTRADUODENAL FAT ON GASTRIC ACID OUTPUT IN DUODENAL ULCER PATIENTS AFTER VAGOTOMY

PATIENT No.	ACID OUTPUT DURING PLATEAU (mEq. per 10 min.)	ACID OUTPUT DURING INHIBITION (mEq. per 10 min.)	INHIBITION (mEq. per 10 min.)
7	1·9	0·0	1·9
8	2·5	0·7	1·8
9	2·2	0·0	2·2
10	2·6	0·0	2·6
11	1·8	0·3	1·5
12	2·0	0·2	1·8
W.A.*	2·3	0·0	2·3
Mean	2·2	0·2	2·0
Standard error	0·1	0·1	0·1

* *See Fig.* 4.

In the vagotomized patients (*Table II*) marked inhibition was again apparent, the mean acid output falling from 2·2 ± 0·1 mEq. per 10 minutes during the plateau to 0·2 ± 0·1 mEq. per 10 minutes after intraduodenal fat. This reduction in acid output was highly significant ($t < 13{\cdot}3$, $P < 0{\cdot}001$). The latent period was slightly longer than before vagotomy in 2 patients, but in the remainder the onset of inhibition was immediate and the duration of the response again approximately 40 minutes. *Fig.* 2 shows a typical sequence of events in one of the vagotomized patients. Changes in acid output in this group are small in absolute terms and reduction in the volume of the gastric aspirate provides a clearer indication of the extent of the response (*Fig.* 3).

One patient was investigated both before and after vagotomy (*Fig.* 4). Intraduodenal fat produced marked inhibition of gastric secretion before operation; 6 months later after a complete truncal vagotomy a similar effect was again observed.

The acid concentration remained constant in both pre- and postoperative patients following fat infusion (*Fig.* 5). Inhibition of acid output was therefore due solely to reduction in volume of the gastric juice.

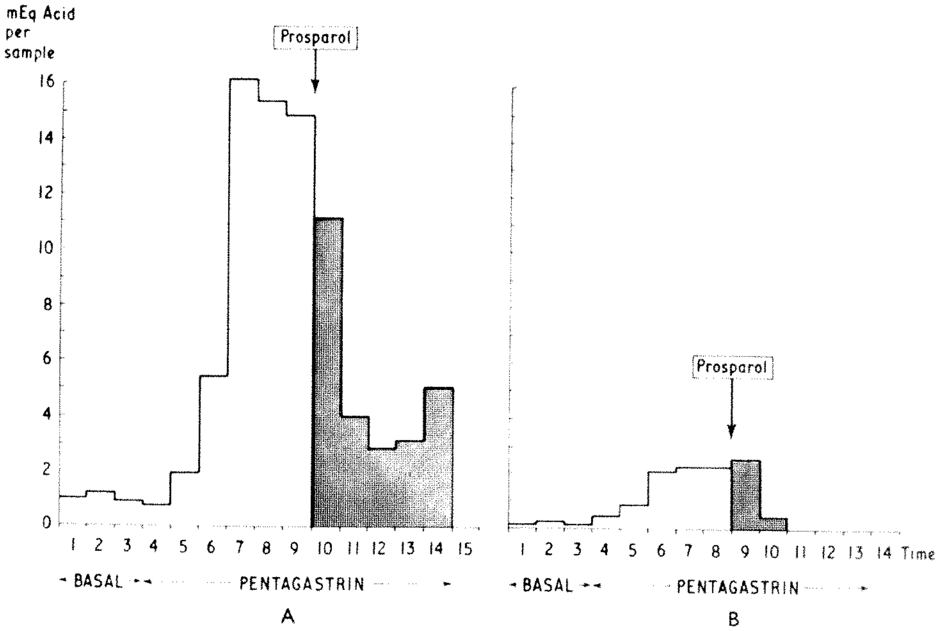

FIG. 4.—The effect of intraduodenal fat on gastric acid output in a duodenal ulcer patient before and after vagotomy. A, The preoperative response. B, The response 6 months after total abdominal vagotomy.

DISCUSSION

The results of this study show that fat in the duodenum inhibits gastric secretion in man both before and after vagotomy. Direct comparison of the magnitude of inhibition in the two circumstances is inappropriate but a highly significant response is apparent in both groups ($P<0\cdot001$). The latent period and duration of inhibition are also similar, suggesting that the underlying mechanism is the same. The almost total abolition of gastric secretion observed in vagotomized patients would appear to leave little room for involvement of a vagal component in this mechanism. Such a component cannot, however, be entirely excluded in patients with intact vagi because the absolute changes in acid output after fat infusion are so much greater in this group than in vagotomized subjects.

Inhibition of gastric secretion was due solely to a volume effect, the acid concentration remaining unchanged after duodenal fat infusion. A similar situation has been noted previously during inhibition by osmotic agents (Ward and others, 1969).

The claim that the inhibitory response to fat is independent of a vagal nerve-supply rests on satisfactory proof of the completeness of the vagal section. The early response to insulin is unreliable (Mason and Giles, 1969; Gillespie, Elder, Gillespie, Kay, and Campbell, 1970) and gastric investigations were therefore deferred until at least 6 months after vagotomy. Insulin tests were then judged positive or negative according to Hollander's original criteria (Hollander, 1948); in fact all the tests in this study were negative according to the additional criteria suggested by subsequent authors (Waddell, 1957; Bachrach, 1962; Stempien, 1962; Ross and Kay, 1964; Bank, Marks, and Louw, 1967). Furthermore, maximal acid output in the vagotomized patients did not exceed 15 mEq per hour, which is within the range of secretory activity expected after complete vagotomy (Bank and others, 1967; Mason and Giles, 1968). The 85 per cent reduction in maximal acid output noted in 1 patient after vagotomy (*Fig.* 4) is similarly in accord with a complete vagal section (Bank and others, 1967; Multicentre Study, 1967).

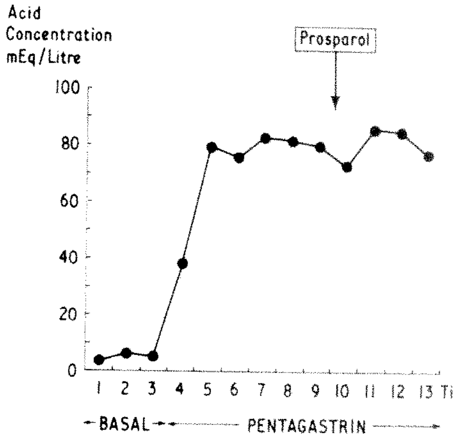

FIG. 5.—The effect of intraduodenal fat on the acid concentration of gastric juice in a vagotomized patient.

Inhibition of gastric secretion by intestinal fat has been shown to occur in the absence of a vagal nerve-supply in many animal studies (Feng and others, 1929; Sircus, 1958; Halvorsen and others, 1966; Debas and others, 1969). Isaza, Sugawara, Curt, and Woodward (1971), however, noted a reduction in the inhibitory response to fat after mesenteric denervation. This reduction was evident in dogs with an intact gastric nerve-supply but not in those with Heidenhain pouches so that it is difficult to draw definite conclusions from this report.

In a recent study in man Johnston and Duthie (1969) noted an increase in gastric secretion after intraduodenal fat in vagotomized patients. Their results were obtained in the immediate postoperative period when a degree of gastro-intestinal stasis and distension exists and the capacity to deal with an intraluminal fluid load is diminished. Relatively large volumes of fat were circulated through the duodenum and these volumes together with the resultant flow of bile and pancreatic juice may have produced appreciable distension of the duodenum and proximal small bowel with subsequent release of gastrin (Sircus, 1953; Nagano, Johnson, Cobo, Oberhelman, and Dragstedt, 1960). The use of submaximal gastric stimulation in their study may then have permitted an increase in gastric secretion due to endogenous gastrin released from such a source.

The magnitude of the response observed in the preoperative patients was similar to that of earlier reports (Sircus, 1958; Windsor and others, 1969) though others have failed to demonstrate such a marked effect (Konturek and Grossman, 1965; Johnston and Duthie, 1969). The explanation for this difference is uncertain. The degree of saturation of the constituent fatty acids is said to influence the extent of the response in man (Roberts, 1931), but since the iodine value of Prosparol is similar to that of the fats used in other studies this factor is unlikely to be of much importance. Variation in the chain length of the constituent fatty acids may be of greater significance.

Although the response to intraduodenal fat does not appear to depend upon an extrinsic vagal supply a local enteric reflex could still be involved. Animal studies, however, have shown that inhibition persists when the stomach and duodenum are completely disconnected (Lonnqvist, 1906; Lim and others, 1925; Konturek and Grossman, 1965), so that this explanation is unlikely to be correct.

There is considerable experimental evidence in favour of a humoral basis for inhibition by fat (Kosaka and Lim, 1930; Lim, 1933; Sircus, 1958; Konturek and Grossman, 1965). The precise nature of the humoral agent (or agents) remains, however, unknown; neither secretin nor cholecystokinin-pancreozymin appear to be implicated in the response in man and the existence of a specific chalone ('enterogastrone') seems likely. The subject is comprehensively reviewed by Johnson and Grossman (1971).

Although the precise details of the inhibitory mechanism remain uncertain the present results indicate that the response to fat persists after total abdominal vagotomy in man. One of the advantages which selective and highly selective vagotomy are said to offer compared with truncal division is that the nerve-supply to the duodenum is preserved and gastric inhibitory reflexes are thereby allowed to continue undisturbed (Griffith, 1969; Johnston and Wilkinson, 1970). The results of this study, however, suggest that inhibition of gastric secretion by intraduodenal fat is not a vagally dependent phenomenon in man and from this point of view, therefore, there is little advantage in preserving the nerve-supply to the duodenum at vagotomy. Whether the response to other inhibitory agents such as intraduodenal acid and osmotic solutions also persists after vagal denervation remains for further study.

Acknowledgements.—The technical assistance of Miss Sheila Nutter is gratefully acknowledged. Professor Le Quesne, Mr. Michael Hobsley, and Dr. Roy Cockel kindly advised in the preparation of the manuscript. This study was initiated through the financial support of the Endowment Research Committee of the United Birmingham Hospitals.

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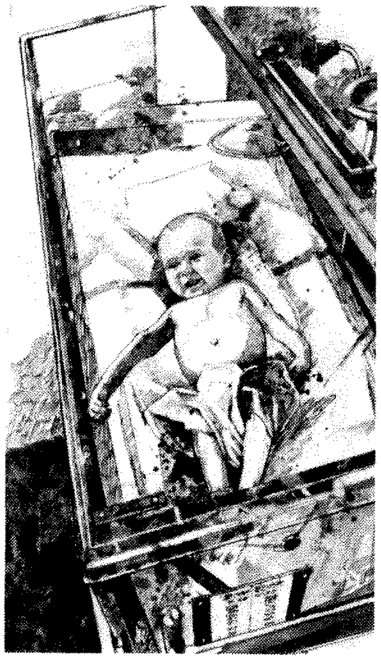

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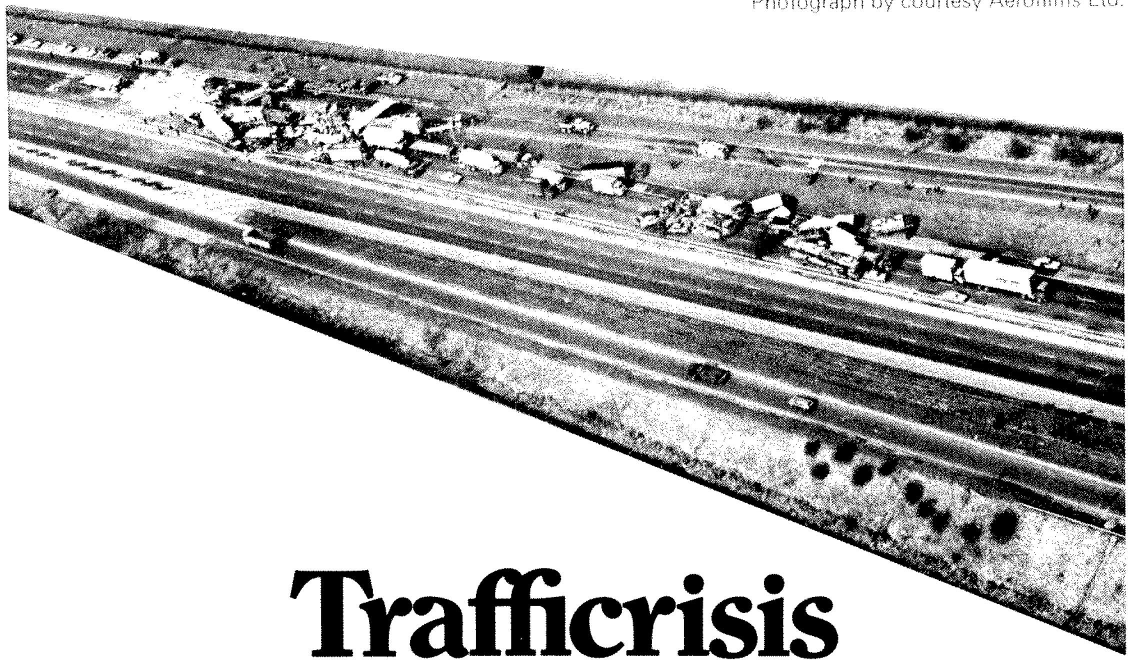

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ANORECTAL SUPPURATION: THE RESULTS OF TREATMENT AND THE FACTORS INFLUENCING THE RECURRENCE RATE

By R. BUCHAN* and R. H. GRACE†

DEPARTMENT OF SURGERY, WELSH NATIONAL SCHOOL OF MEDICINE, CARDIFF

SUMMARY

One hundred and eighty-three patients admitted to hospitals in the Cardiff teaching group (1961–5) with a diagnosis of anorectal abscess were studied; 147 of these patients were traced in 1969. It is shown that when the diagnosis was that of an ischiorectal abscess and that when a 'deroofing' procedure was used, the in-patient stay and the time lost from work were increased.

It is also shown that recurrence was related to a previous history of multiple abscesses, but not to the duration of the presenting history or the type of the presenting abscess or the initial drainage procedure employed. However, the detection and laying open of a 'fistula' at a second examination under anaesthesia within 2 weeks reduced the incidence of recurrence.

It is suggested that incision and drainage, followed by a second examination under anaesthesia within 2 weeks, should be the treatment of choice, and that there is now no place for saucerization or 'deroofing' procedures.

In England and Wales between 5000 and 6000 patients are admitted to hospital annually because of anorectal suppuration (Hospital In-patient Enquiry, 1964, 1965). We have reviewed the clinical features and treatment of patients with anorectal abscesses treated in Cardiff between 1961 and 1965 in an attempt to identify the factors influencing the outcome.

MATERIALS AND METHODS

The records of all the patients admitted between 1961 and 1965 to hospitals in the Cardiff teaching group with a diagnosis of anorectal suppuration (I.C.D. codes 574 and 575) were studied; these patients were treated in two hospitals by surgeons of varying experience. A few patients with very minor anorectal suppuration may have been treated in casualty departments, but the records of these patients were not available.

There were 183 patients admitted with a diagnosis of anorectal abscess, and information was obtained from their notes. In 1969 all the patients were sent a simple questionnaire regarding recurrent symptoms; 126 patients replied, and sufficient information was given by general practitioners for a further 21 patients, making a total of 147 patients for whom follow-up information was available. Thirty-six patients were lost to follow-up: 2 had died, 28 had left the area and could not be traced, and 6 did not reply and their family doctors were unable to give any information about them.

TERMINOLOGY

Recurrence.—Recurrence was defined as the appearance of a further abscess or of a fistula after the presenting abscess had healed.

'Fistula'.—A 'fistula' was defined as the finding of a connexion between the presenting abscess and the anal canal by the surgeon at the original drainage procedure.

Fistula.—The standard fistula-in-ano of anorectal surgery was described as a fistula (without inverted commas).

RESULTS

1. Original Group of 183 Patients.—

a. Incidence.—The incidence during this 5-year period was fairly steady at 33 cases per annum, with a slightly higher incidence in 1964. The incidence was highest in the third and fourth decades (*Table I*) and was low in children. In this series anorectal sepsis was about three times more common in males (*Table I*).

Table I.—AGE AND SEX INCIDENCE OF PATIENTS WITH ANORECTAL SUPPURATION

AGE (yr.)	TOTAL NO. OF PATIENTS	MALE	FEMALE
0–19	20	15	5
20–39	78	59	19
40–59	59	44	15
60 +	26	24	2

b. Associated Disease.—There was a low incidence of associated bowel disease: 2 patients had Crohn's disease, 3 had ulcerative colitis, and 2 had rectal cancer. Two patients had active tuberculosis. There were 3 diabetics. Two children had spina bifida, reflecting the high incidence of this defect in South Wales.

c. Previous History.—Thirty patients had a history of a single previous anorectal abscess, while 21 had had multiple previous abscesses (*Table II*); a previous history of a single fistula-in-ano was present in 7 patients and of multiple fistulae in 2 patients (*Table II*).

d. Duration of Symptoms.—Almost 50 per cent of the patients had symptoms for longer than 5 days, while only 21 patients (11·5 per cent) had a history of less than 48 hours (*Table III*). Patients with ischiorectal abscesses did not have a significantly longer history than those with perianal abscesses ($P > 0{\cdot}2$).

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e. Type of Abscess.—Perianal abscesses (102 patients) and ischiorectal abscesses (77 patients) accounted for 98 per cent of all the cases (*Table IV*).

f. Treatment.—

i. *Operation*: As shown in *Table IV*, saucerization was performed five times more often than incision and drainage; only 5 patients were treated by incision and primary suture. Four patients did not require operation because the abscess discharged spontaneously, and in 1 patient there was no record of the type of operation performed.

Table II.—Relationship of Previous History of Anorectal Suppuration to Recurrence

	Total No. of Patients	Recurrent Abscess	Recurrent Fistula	Recurrent Abscess and Fistula
Previous history of anorectal abscess				
None	132	15	17	7
Single abscess	30	6	1	1
Multiple abscesses	21	6	4	4
Previous history of fistula in ano				
None	174	27	21	7
Single fistula	7	0	1	0
Multiple fistulae	2	0	0	0

Table III.—Duration of Symptoms of Anorectal Suppuration

Duration of History (d.)	Perianal Abscess	Ischiorectal Abscess	Total
2	14	7	21
3–5	38	26	64
5 +	46	44	90
No information	4	—	4
Total	102	77	179

Table IV.—Type of Presenting Abscess and the Primary Treatment

Type of Abscess	Total No. of Patients	Incision and Drainage	Saucerization	Incision and Primary Suture	No Treatment
Perianal	102	20	75	3	4
Ischiorectal	77	8	68	1	
Submucous	1	1			
Pelvirectal	0				
Not known	3		1	1	
	183	29	144	5	4

ii. *Examination for 'fistula'*: Surgeons identified a connexion with the anal canal in 39 of 115 patients at the first operation, and in a further 13 of 18 patients who were examined again under anaesthesia within 2 weeks (*Table V*). No attempt was made to look for a 'fistula' in 46 patients.

iii. *Antibiotics*: A number of patients had been given antibiotics prior to admission, and 34 were given antibiotics in hospital.

g. Bacteriology.—Bacteriological swabs were sent for culture in only 120 of the total of 183 patients (*Table VI*). Coliform organisms (25·6 per cent) were most commonly cultured, followed by coagulase-positive staphylococci (16·9 per cent); in 14 patients more than one organism was grown. No growth was obtained in 22 cases.

Table V.—Incidence of Fistula-in-Ano at Presentation and its Effect on Recurrence

Fistula	Total No. of Patients	Recurrent Abscess	Recurrent Fistula
Fistula found at drainage operation	39	9	5
Fistula found within 10 days	13	0	1
No fistula found	81	13	9
No examination for fistula	46	5	7
Total	179	27	22

h. Duration of In-patient Treatment.—Seventy-one patients were in hospital for less than 1 week, while a further 59 patients were in-patients for less than 2 weeks; however, 16 patients were still in hospital 4 weeks after admission. Prolonged admission was related to the presenting abscess being ischiorectal ($P < 0{\cdot}001$), treatment by saucerization ($P < 0{\cdot}05$), and a 'fistula' being found at operation. While a 'fistula' was found in only 10 per cent of the patients who stayed in hospital for less than a week, 55 per cent of those who were in-patients for more than 3 weeks had a 'fistula' laid open.

2. Four-to-nine-year Follow-up Group of the 147 Patients who were traced.—Adequate information regarding the 4–9-year results was available in 80 per cent of the entire treatment group. There was no difference between the original 183 patients and the 147 who were successfully traced when they were compared for age of the patients ($P > 0{\cdot}5$), duration of symptoms ($P > 0{\cdot}3$), type of abscess ($P > 0{\cdot}3$), and type of operation ($P > 0{\cdot}3$), including examination for possible fistulae.

a. Recurrence.—Recurrence was defined as the appearance of a further abscess or a fistula after the presenting abscess had healed.

i. *Overall incidence* (*Table VII*): Thirty-seven patients (25·2 per cent) required further in-patient treatment. Fifteen patients had a recurrent abscess while 10 developed a fistula. Twelve patients had both a recurrent abscess and a fistula.

Table VI.—BACTERIOLOGY OF THE PRESENTING ABSCESS

Bacteriological Result	*No. of Patients*	*Percentage*
Staphylococcus aureus (coagulase positive)	30	16·9
Escherichia coli	47	25·6
Others	35	29·1
Sterile	22	12·0
Not cultured	63	34·4

Table VII.—OVERALL INCIDENCE OF RECURRENT ANORECTAL SUPPURATION IN 147 PATIENTS

Recurrence	*No. of Patients*	*Percentage*
Abscess	15	10·2
Fistula	10	6·8
Abscess and fistula	12	8·1

Table VIII.—TIME OF DETECTION OF RECURRENT ABSCESS OR FISTULA

TIME OF RECURRENCE (mth.)	ABSCESS	FISTULA
2	5	5
2–6	4	6
6–12	3	2
12–24	5	5
24 +	10	5

ii. *Onset* (*Table VIII*): Ten patients (5 with abscesses, 5 with fistulae) developed further symptoms within 2 months: one-third of the abscesses and half of the fistulae had recurred within 6 months of the primary treatment. However, about one-third of the patients developed their first recurrence longer than 2 years after the original operation.

iii. *Previous history*: There was a significant increase of recurrent abscess in patients with a previous history of multiple abscesses ($P < 0{\cdot}05$), but not following a single abscess ($P > 0{\cdot}2$) or fistula ($P > 0{\cdot}2$).

iv. *Relation to original abscess*: Although there was an apparently higher incidence of recurrent abscess when the original abscess had been ischiorectal this did not reach significant levels ($P > 0{\cdot}2$), and there was no difference in the occurrence of subsequent fistulae (*Table IX*). Of 27 recurrent abscesses, 24 were at the site of the original abscess, while most of the 22 fistulae also appeared at the site of the original abscess. Recurrence was not related to the duration of symptoms of the presenting abscess.

v. *Relation to operation*: Different drainage procedures did not influence the recurrence rate ($P > 0{\cdot}2$) (*Table X*).

The findings of a 'fistula' at the primary treatment did not reduce the subsequent recurrence rate when this was compared with no 'fistula' being found ($P > 0{\cdot}2$) (*Table V*). When a 'fistula' was identified at a further examination within 2 weeks of the original operation the recurrence rate was reduced ($P < 0{\cdot}02$), but the number of patients in this group was small.

b. Time off Work.—Although 66 patients (mainly housewives and retired persons) did not complete this part of the questionnaire, there were 81 patients who gave details. Forty-three patients were off work for longer than 4 weeks, 36 of these being for longer than 6 weeks.

Table IX.—TYPE OF ABSCESS AND INFLUENCE ON RECURRENCE

TYPE OF ABSCESS	TOTAL NO. OF PATIENTS	RECURRENCE			
		Abscess		*Fistula*	
		No.	Per cent	No.	Per cent
Perianal	80	12	15	12	15
Ischiorectal	64	14	21·9	9	14·1
Other	3	1		1	

Table X.—INFLUENCE OF THE TYPE OF OPERATION ON THE RECURRENCE RATES

OPERATION	TOTAL NO. OF PATIENTS	RECURRENCE			
		Abscess		*Fistula*	
		No.	Per cent	No.	Per cent
Incision and drainage	25	4	16	4	16
Saucerization	113	21	18·6	16	15·1
Other	5	1		1	

c. Group with Anal Discharge.—Thirteen patients replied stating that they had suffered anal discharge since their primary operation. Two patients refused further examination and 2 lived too far away to be seen; of the remaining 9 patients, 3 had definite fistulae and 6 had pruritus without clinical evidence of a fistula.

DISCUSSION

These results have confirmed the findings of other authors (Goligher, 1961; Wilson, 1964) that anorectal suppuration occurs commonly in males in the third and fourth decades, that perianal abscess is the commonest type, and that pelvirectal and submucous abscesses are very rare. There is also confirmation that when a large number of anorectal abscesses are followed there is a relatively low incidence of associated bowel disease (Rawls, Martin, Spencer, and Hoffman, 1963; Edwards and Truelove, 1965; de Dombal, Watts, Watkinson, and Goligher, 1966), but it is still of value to obtain biopsy material of the abscess cavity as suppuration may be an early manifestation of inflammatory bowel disease (Morson and Lockhart-Mummery, 1959).

In this country anorectal abscesses are usually treated by a 'deroofing' or saucerization procedure, which may be combined with a search for an internal opening: the wounds created are large and healing may take some weeks. An alternative method has been used by Ellis (1960), who described incision, exploration, and curettage of the abscess cavity followed by suture, under antibiotic cover. Patients usually returned to work with the wound healed in about a week (Wilson, 1964).

In North America treatment is influenced by the cryptoglandular hypothesis of the aetiology of anorectal suppuration. This has been supported in this country by Parks (1961). It is believed that infection tracks along the lumen of one anal gland to its termination between the internal and external sphincters. It is suggested that an intersphincteric abscess develops first and that this may extend downwards to present as a perianal abscess, or laterally to present as an ischiorectal abscess (Nesselrod, 1949; Eisenhammer, 1956a, b, 1961). The intersphincteric abscess and the associated anal gland are therefore believed to be the important area for surgical attack, which may explain why a 'fistula' is nearly always found in American reports. However, the rationale of this approach has been placed under considerable doubt following the report by Goligher, Ellis, and Pissidis (1967) that an intersphincteric abscess could be identified in only 8 of 28 cases of anorectal abscess. They concluded that anal continence would be risked unnecessarily if this intra-anal approach was used routinely. This is of particular importance when it is remembered that most anorectal abscesses are initially treated by relatively junior surgeons.

When any treatment of anorectal abscess is considered the incidence of recurrent abscess or fistula is very important. In the present series there was a high recurrence rate (25 per cent), but this is comparable to that of Wilson (1964), who quoted a 22 per cent recurrence rate. Most other reported series have had an inadequate follow-up (Naunton Morgan, 1929; Granet, 1948; Mcelwain, Alexander, and Maclean, 1966; Hill, 1967).

Several factors which might influence recurrence rates have been examined. We have no evidence that the duration of symptoms of the presenting abscess is related to recurrence, or that recurrence is influenced by the original drainage procedure.

Wilson (1964) reported a 33 per cent recurrence rate after ischiorectal abscess, which was more than twice that after perianal abscess; although our figures show a similar trend the difference is less striking (30 per cent after ischiorectal abscess, 23·9 per cent after perianal abscess) and it is not significant ($P > 0{\cdot}2$). We had expected that the demonstration of a connexion with the anal canal ('fistula') at the original operation would have reduced the recurrence rate, but this was not so ($P > 0{\cdot}2$). In the acute phase tissues are friable and oedematous, and it is easy to create false tracks; it is possible that some of the fistulae found in our cases (and perhaps in other reports) were iatrogenic. It may be more relevant that the recurrence rate was reduced when a 'fistula' was found after the acute phase had settled ($P < 0{\cdot}02$).

The time of the recurrence is of interest. Recurrent disease appearing within 2 months of treatment must arise because the initial therapy was inadequate, but while most abscesses and fistulae recurred within 2 years about 30 per cent of patients developed a recurrence more than 2 years after the primary treatment, and 3 fistulae were detected by examination after replying to our questionnaire 4 or more years later.

If the standard treatment of anorectal abscess produces no better results in terms of recurrence than the primary suture technique, then healing time becomes an important factor. Describing the results of the primary suture technique, Wilson (1964) stated: 'If it can be established that the long-term results from treatment by primary suture are no worse than those which follow "unroofing" then it is not irrelevant to include economic factors.' In our series about 50 per cent of the patients replying to our questionnaire were off work for longer than 4 weeks, an interval similar to the healing time quoted by Goligher and others (1967) for saucerization operations; in comparison, most patients treated by incision, curettage, and suture had returned to work within a week (Wilson, 1964). If Wilson's results were to be repeated elsewhere incision and primary suture might produce valuable medical and economic advantages for the patient (and for the National Health Service).

It is suggested that there is now no place for the traditional 'deroofing' or saucerization procedures in the treatment of anorectal abscess. Until the value of primary suture has been further explored it is thought that incision and drainage (possibly with immediate exploration for a fistula if the surgeon is experienced in anorectal disease) followed by a second examination under anaesthesia within 2 weeks produces the best results in terms of economy while not prejudicing the recurrence rate.

Acknowledgements.—We are grateful to the surgeons at the Cardiff Royal Infirmary and the Llandough Hospital for allowing us to study their patients, and to Professor A. P. M. Forrest and Mr. H. E. Lockhart-Mummery for their criticism of the manuscript.

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ACUTE MESENTERIC VASCULAR OCCLUSION OCCURRING ON TOP OF CHRONIC LOCALIZED OCCLUSION

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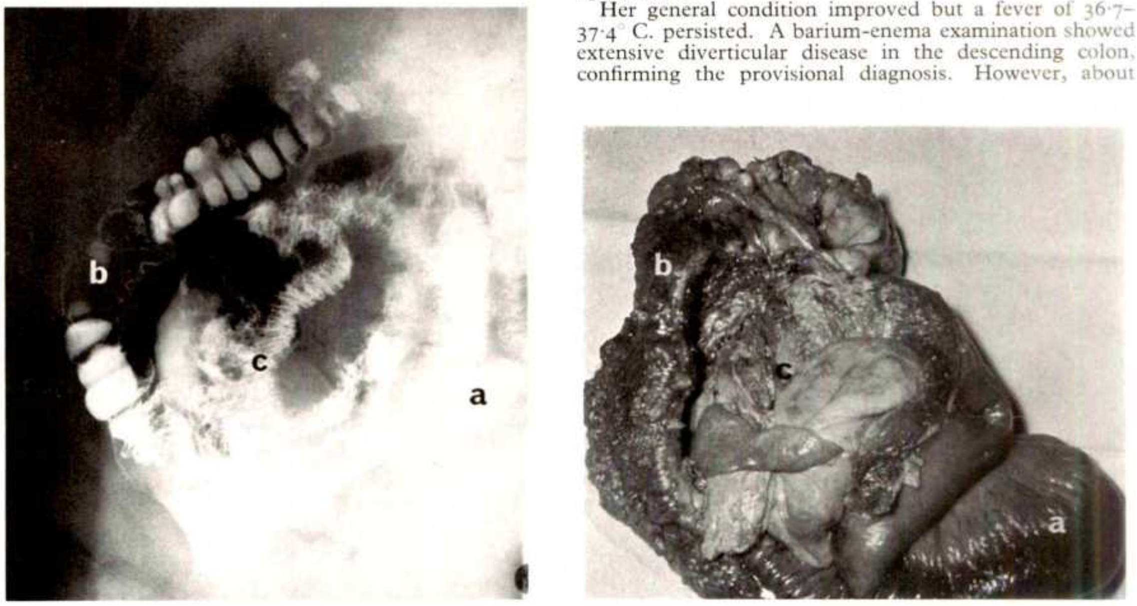
SUMMARY

Acute mesenteric arterial occlusion occurring on top of chronic occlusion and causing necrosis of a short length of bowel is rare.

Three such cases are described. All were operated upon but only 1 has survived.

The literature on the subject is discussed.

ACUTE ischaemia of the bowel is a well-recognized clinical entity, even though early diagnosis is usually difficult. Chronic ischaemia, though well documented in the literature, is difficult to diagnose and a much less clear-cut condition. Acute ischaemia occurring in chronic ischaemia of a localized area of bowel is a less well-documented entity. The purpose of this paper is to describe and discuss 3 such cases, in 2 of which acute vascular occlusion occurred and caused necrosis.



A B

FIG. 1.—*Case* 1. A, Barium-meal and follow-through film showing: a, terminal ileum; b, ascending colon; c, barium filling a large cyst cavity. B, Operation specimen: a, terminal ileum; b, ascending colon; c, cystic mass.

CASE REPORTS

Case 1.—Mrs. E. Y., aged 61 years, had no previous history suggestive of cardiovascular disease, but over the past 10 years she had had four or five short attacks of colicky abdominal pain and vomiting, each one being worse than the last. Apart from these she had been well.

She was admitted as an emergency with a 16-hour history of central abdominal pain, vomiting, and abdominal distension similar to but much more severe than the five previous attacks.

Examination showed an obese woman with a temperature of 36·7° C. and central abdominal tenderness. Her blood-pressure was 150/90 and she was not shocked. A provisional diagnosis of diverticular disease was made. Twenty-four hours after admission her symptoms had spontaneously disappeared.

Investigations showed the following: haemoglobin, 8 g. per 100 ml.; white-blood count, 9400; urea and electrolytes, normal; occult blood was negative on four occasions; an electrocardiogram was normal; plasma proteins: albumin, 2·5 mg. per cent, globulin, 3·8 mg. per cent; erythrocyte-sedimentation rate, 24 mm. in 1 hour. Sigmoidoscopy was carried out and showed no abnormality up to 20 cm.

Her general condition improved but a fever of 36·7–37·4° C. persisted. A barium-enema examination showed extensive diverticular disease in the descending colon, confirming the provisional diagnosis. However, about 10 days after admission severe abdominal pain and vomiting returned and a mass was felt in the right iliac fossa. Barium follow-through studies showed a grossly dilated segment of terminal ileum, which was thought most probably to be an ischaemic lesion (*Fig.* 1 A).

At laparotomy a huge cystic mass was found occupying almost the whole of the right side of the abdominal cavity. The cyst, its wall formed from bowel mesentery and omentum, contained several loops of pale necrotic bowel, free faeces, and barium (*Fig.* 1 B). The cyst was excised and bowel continuity was restored by end-to-end anastomosis of the ileum to the transverse colon.

Postoperative recovery was complicated by a short period of respiratory difficulty and a wound infection, but the patient was discharged home a month later, when she was very well.

She was readmitted about 6 weeks later with shortness of breath and left chest pain, and a radiograph of the chest showed an opacity in the right upper zone. The day after admission she collapsed and a diagnosis of pulmonary embolism was made. In spite of anticoagulants and antibiotics, her condition steadily deteriorated and she died 10 days after admission. Post-mortem examination was refused.

The operation specimen consisted of 62 cm. of terminal ileum, together with caecum and 20 cm. of ascending colon. In addition to an area of necrotic bowel with a perforation, the proximal ileum showed loss of villi and Paneth's cells, an increase in goblet cells (*Fig.* 2), and more proximally marked thickening, induration, and congestion. There were areas of fat necrosis and fibrosis and plasma-cell infiltration in the mesentery (*Fig.* 3). The artery

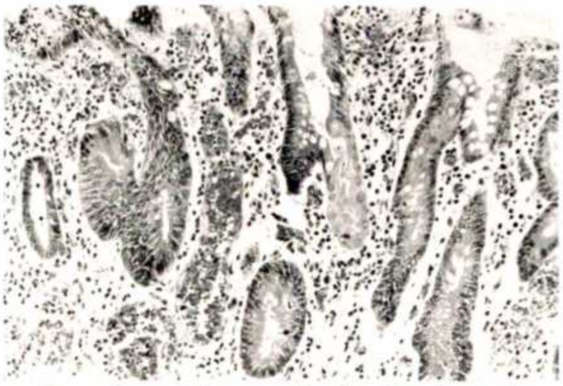


FIG. 2.—*Case* 1. Ileal mucosa of the affected bowel showing loss of villi and Paneth's cells and a marked increase in goblet cells. H. and E. (× 80.)

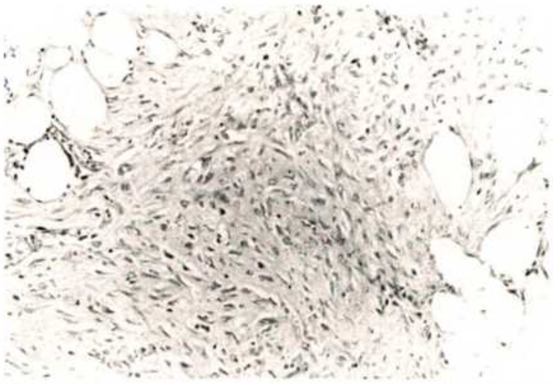


FIG. 3.—*Case* 1. Mesentery showing an area of fibrosis and plasma-cell infiltraton. H. and E. (× 80).

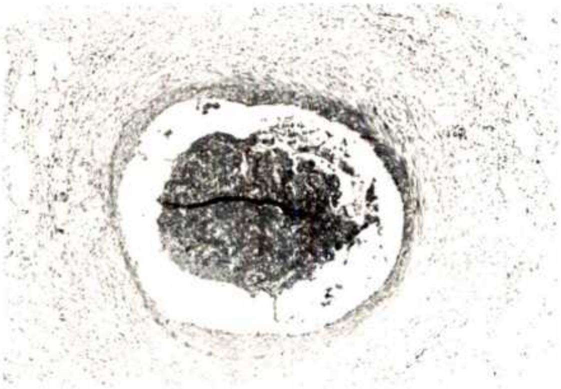


FIG. 4.—*Case* 1. Artery supplying the segment of affected bowel showing a fresh thrombus proximal to the original thrombus. H. and E. (× 80.)

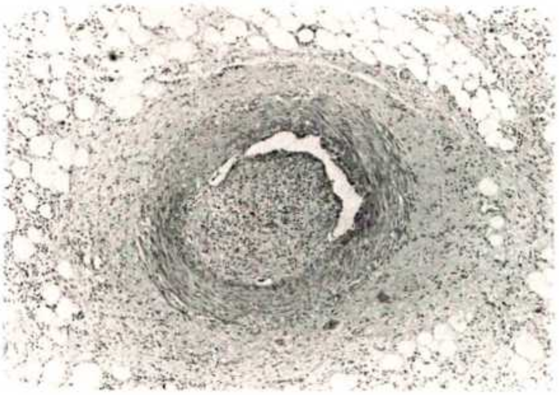


FIG. 5.—*Case* 1. Artery supplying the segment of affected bowel showing an organized partially recanalized thrombus. H. and E. (× 80.)

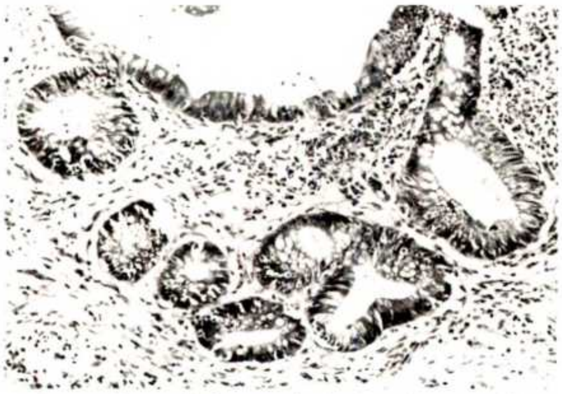


FIG. 6.—*Case* 2. Ileal mucosa showing loss of mucosal villi, a decrease in Paneth's cells, mucosal ulceration, and an infiltrate of chronic inflammatory cells. H. and E. (× 80.)

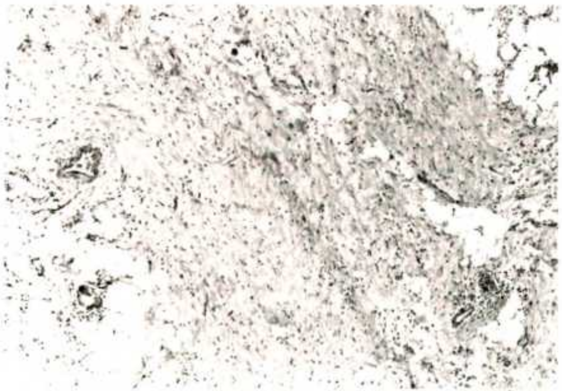


FIG. 7.—*Case* 2. Mesentery showing fat necrosis and marked fibrosis. H. and E. (× 32.)

supplying the bowel showed a fresh occlusive thrombus and also, nearer the bowel, an organized and recanalized thrombus (*Figs.* 4, 5). The appearance was thought to be the result of partial ischaemia of some duration, complicated by a sudden fresh occlusion.

Case 2.—Mr. H. D., aged 65 years, was admitted as an emergency with a 5-day history of colicky abdominal pain, diarrhoea, and vomiting. There was also some weight-loss. Previously he had had a slight stroke and was on hypotensive drugs. There was no past history of abdominal pain.

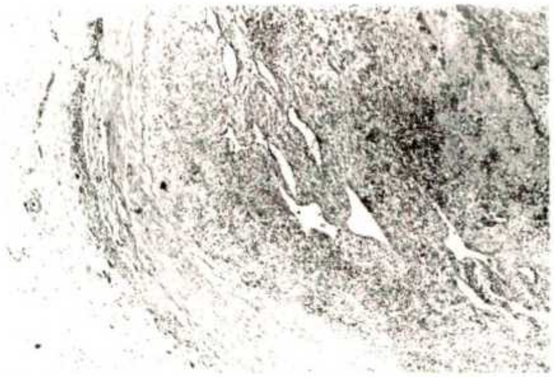


FIG. 8.—*Case* 2. Artery supplying the affected bowel showing a recanalizing thrombus. H. and E. (× 32.)

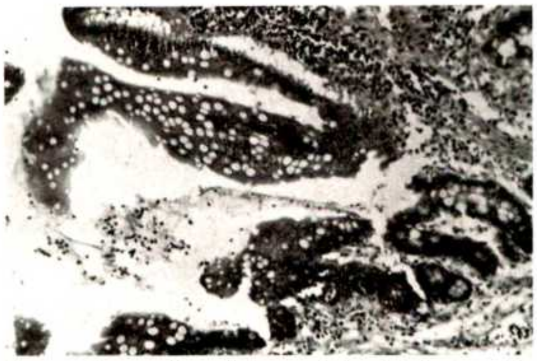


FIG. 10.—*Case* 3. Mucosal ulcers and chronic infarction with acute inflammatory-cell infiltration. H. and E. (× 80.)

The patient was obese and dehydrated, and had a temperature of 38·6° C. He had marked lower abdominal tenderness but no muscle rigidity.

A provisional diagnosis of diverticular disease was made and he was treated with intravenous fluids and antibiotics.

Shortly after admission he became stuporose and jaundiced, but recovered slowly and a barium-enema examination showed no abnormality. A barium follow-through study shortly afterwards demonstrated an abnormal loop of terminal ileum which was dilated and had loss of mucosal pattern. A possible diagnosis of lymphosarcoma was suggested.

The patient's condition again deteriorated and he became uraemic.

At laparotomy about 4 weeks after admission, several loops of ileum were found matted together and adherent to the anterior abdominal wall and liver. The mass of bowel was resected and continuity was restored by end-to-side anastomosis of the ileum to the transverse colon.

The patient's condition deteriorated and he died 11 days after operation.

The operation specimen of 70 cm. of bowel showed atrophy of the bowel with extensive mucosal ulceration, and fat necrosis and fibrosis in the mesentery (*Figs.* 6, 7). There was an organized and recanalized thrombus in the artery supplying the bowel (*Fig.* 8) and a recent thrombus.

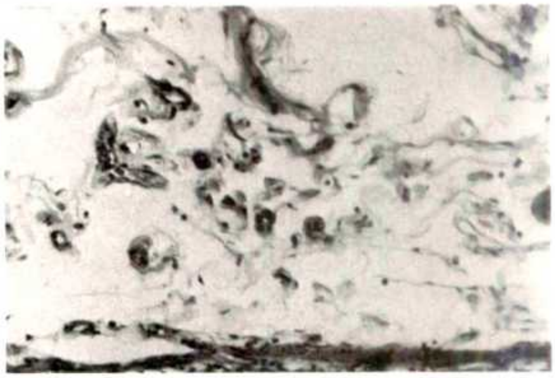


FIG. 9.—*Case* 3. Oedema of the mesentery of the bowel with a few inflammatory cells and arterioles showing a narrowed lumen. H. and E. (× 80.)

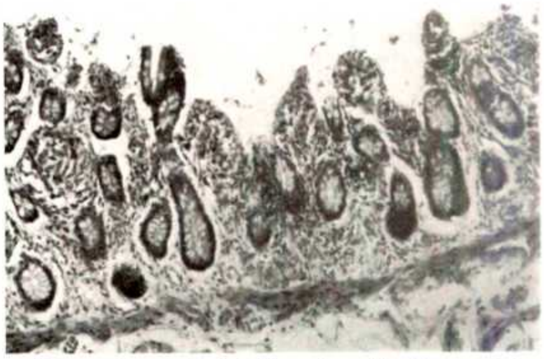


FIG. 11.—*Case* 3. Acute inflammatory-cell infiltration of the mucosa and submucosa with an area of mucosal ulceration. H. and E. (× 80.)

Post-mortem examination showed a recent right pulmonary embolus, severe atherosclerotic changes in the aorta, an infarct of the left kidney, and thrombosis of the left femoral vein. In the superior mesenteric artery a fresh thrombus was found and the entire small and large bowel showed areas of intense congestion.

Case 3.—Mrs. I. D., aged 72 years, was a long-term in-patient at a geriatric hospital, with a diagnosis of senile dementia. There was a very vague history of intermittent abdominal pain.

In July, 1970, after a short history of abdominal pain and vomiting, a strangulated femoral hernia was diagnosed. No bowel resection was necessary and the hernia was repaired. The rest of the bowel was not examined.

She made an uneventful recovery but about a month later she again developed abdominal pain and vomiting. Examination revealed marked upper abdominal tenderness but no mass. A straight abdominal radiograph showed no abnormality. The blood-count, electrolytes, and the serum amylase were all within normal limits. A diagnosis of acute intestinal obstruction was made and laparotomy was carried out at once. A length of terminal ileum which had obviously been involved in the femoral hernia was found to be thickened and deformed, and was resected. In addition, a 7-cm. length of proximal ileum was found to be thickened, red, oedematous, and densely adherent to the sigmoid colon. At one point the bowel was almost perforated. There was fibrosis and oedema of the mesentery (*Fig.* 9). This length of bowel was also resected.

Examination of this specimen showed areas of bowel in which there were atrophic changes in the mucosa and acute inflammatory infiltrate involving all the coats and extending into the peritoneum (*Figs.* 10, 11). The infiltrate in the submucous and serous coats included a number of haemosiderin-containing histiocytes. A number of diverticula were seen and there were areas of fat necrosis in the mesentery. Some arteries in the bowel wall showed thickening of the wall, irregularity and fragmentation of elastic tissue, and evidence of recanalized thrombi. The histology suggested that the lesion was due to chronic partial ischaemia.

The patient made a slow recovery and remains well.

DISCUSSION

Acute ischaemia of short lengths of bowel is seen in volvulus, strangulated hernia, and intussusception. Resection may be required or a fibrous stricture may develop later (Marston, 1964; Cunningham and Regan, 1965). It is, however, difficult to understand how localized ischaemia of bowel can otherwise occur because of the rich blood-supply and extensive anastomoses (Mavor, Lyall, Chrystal, and Proctor, 1962a; Mavor, Lyall, Chrystal, and Tsapogas, 1962b; Reiner, Platt, Rodriguez, and Jimenez, 1960; Reiner, Rodriguez, Jiminez, and Platt, 1962; Marston, 1972). Mavor and others (1962b) stated that a peripheral vascular occlusion will cause a limited or no infarction of the bowel, and Vargas (1967) concluded that such peripheral occlusions are always asymptomatic. Dunphy and Whitfield (1940) pointed out that a gradual occlusion of the superior mesenteric artery may also be asymptomatic. There are a few reports of localized bowel infarction (McClenahan and Fisher, 1948; Arosemena and Edwards, 1967) but none of acute infarction occurring in chronic localized disease.

The cases described here are unusual. In each a limited area of bowel was involved and chronic ischaemia and perforation was survived for years in the first patient. In each case the typical history in chronic bowel ischaemia of postprandial pain was absent—perhaps owing to the limited length of bowel involved—yet all the patients presented as an acute abdominal emergency with abdominal pain and vomiting. The first patient improved, then deteriorated, and developed an abdominal mass. Barium follow-through studies showed an abnormal terminal ileum, suggesting the diagnosis of chronic bowel ischaemia. The initial episode of abdominal pain probably followed the fresh occlusion—necrosis and perforation of the bowel occurring before laparotomy 12 days later.

At laparotomy extensive fibrosis and disorganization of the bowel, with a long-standing occlusion in the main artery and a fresh thrombus, were the findings in the first 2 patients. In the third patient no fresh thrombus was found but the resected bowel was red and swollen. A striking feature in each case was marked areas of fibrosis in the mesentery, of varying size and severity, which may have been the result of leakage of intestinal contents. The fibrosis was obvious at laparotomy and may be of diagnostic value.

Mucosal atrophy and infiltration of the mucosa and submucosa by iron-rich histiocytes were constant pathological findings. Boley, Schwartz, and Williams (1971) have described a characteristic pattern of mucosal destruction and fibrosis, but not the mesenteric changes found in the present cases. The vascular thrombosis may be secondary to Fredrickson type 3 hyperlipoprotinaemia, though Marston (1972) pointed out that biochemical investigation is usually normal even in well-established lesions.

Chronic ischaemia of a localized length of bowel complicated or not by a fresh thrombus is rare. It is of interest that 1 patient has survived resection and is alive and well 2 years later. It is accepted that ancillary investigation is of little value in supporting the clinical diagnosis of ischaemia, but barium follow-through examination showed abnormal small bowel in the first 2 patients and a confident preoperative diagnosis of chronic ischaemia was made in the first case.

Acknowledgements.—The authors wish to thank Mr. R. A. Piachaud, F.R.C.S., under whose care *Case* 2 was admitted, for permission to report his case.

The authors are grateful to Dr. B. J. Smith and Dr. Subbuswamy who carried out the pathological examination and helped in the preparation of this paper, Dr. Sheila Hale who carried out the radiological examinations, and Miss J. E. Tomlison for her help in organizing and typing the manuscript.

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EVALUATION OF ORAL THYMOXAMINE IN PATIENTS WITH PERIPHERAL VASCULAR OCCLUSION OF THE LOWER LIMBS

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SUMMARY

To determine the effectiveness of oral thymoxamine (Opilon) as a cutaneous vasodilator in patients with peripheral vascular occlusion of the lower limb, double-blind trials of a placebo, of tolazoline in a dose of 50 mg., and of thymoxamine in single doses of 20, 40, 60, 80, and 100 mg. have been undertaken using skin temperature and skin blood-flow as measures of response. Thymoxamine produced no significant increases in skin temperature and blood-flow at any dose level, whereas in the same patients tolazoline produced highly significant increases.

THERE is doubt regarding the value of vasodilator drugs in patients with atherosclerotic arterial occlusion affecting the lower limbs. It has been shown that alcohol (Gillespie, 1967) and tolazoline (Priscol) (Thomas, Campbell, and Heard, 1968) have no effect on the skin blood-flow in the feet of patients with ischaemia severe enough to cause continuous rest pain. Thomas and others (1968) have shown that there is a good response to tolazoline if the nutrition of the feet is normal, whereas in patients with intermediate grades of nutritional disturbance (i.e., persistent colour change at rest, ulceration, or intermittent pain but no continuous rest pain) there is a smaller but significant response to tolazoline. It is in the latter group of patients that vasodilator drugs may (or may not) be of value.

Furthermore, most of the available vasodilator drugs have certain side-effects, some of which are attributable to the non-specific action of the drug; e.g., tolazoline has in addition to an α-adrenergic blocking action a direct effect on smooth muscle and also a histamine-like vasodilator effect.

Recently, the drug thymoxamine (Opilon) has attracted interest. Its pharmacology has been investigated by Birmingham and Szolcsanyi (1965). It has an α-adrenergic blocking effect but no β-adrenergic blocking action, and it may prove to be the most specific α-adrenergic blocking agent (Brownlee, 1966). It has theoretical advantages as a vasodilator of skin vessels. It has been shown to increase blood-flow in the foot distal to an arterial occlusion when given intravenously (Myers, Hobbs, and Irvine, 1968; Kane, 1970).

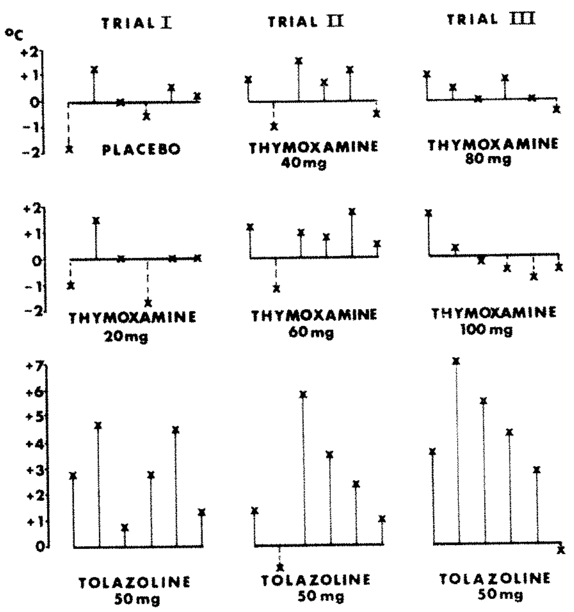

FIG. 1.—Skin temperature changes in response to different dosages of thymoxamine and tolazoline or a placebo in individual patients.

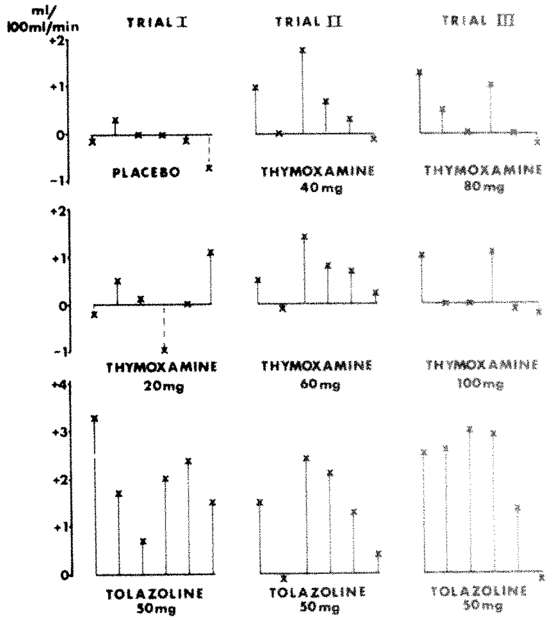

FIG. 2.—Blood-flow changes in response to different dosages of thymoxamine and tolazoline or a placebo in individual patients.

The present investigation has been undertaken to determine the effectiveness of thymoxamine as a cutaneous vasodilator when administered orally in patients with peripheral vascular occlusion of the lower limb. It has been designed to permit comparison of a range of single doses of thymoxamine with a placebo and with tolazoline.

MATERIAL AND METHODS

Eighteen patients who had chronic atherosclerotic arterial occlusion in a lower limb were studied. All the patients presented with claudication. Diabetic and sympathectomized patients were excluded from this series. Fifteen of the patients had normal foot nutrition at rest (grade I), while the remaining 3 patients had mild persistent colour changes at rest (grade II).

Table I.—MEAN RESTING TEMPERATURE AND BLOOD-FLOW BEFORE THE ADMINISTRATION OF A DRUG OR PLACEBO (MEAN OF 6 PATIENTS)

	TEMPERATURE (° C.)	BLOOD-FLOW (ml. per 100 ml. per min.)
Trial I		
Tolazoline, 50 mg.	26·62	1·28
Thymoxamine, 20 mg.	26·85	1·33
Placebo	26·08	1·08
Mean of trial I	26·48	1·23
Trial II		
Tolazoline, 50 mg.	26·00	1·47
Thymoxamine, 40 mg.	26·71	1·30
Thymoxamine, 60 mg.	27·67	1·36
Mean of trial II	26·79	1·38
Trial III		
Tolazoline, 50 mg.	26·12	1·33
Thymoxamine, 80 mg.	26·50	1·25
Thymoxamine, 100 mg.	26·67	1·27
Mean of trial III	26·43	1·28

Table II.—SKIN TEMPERATURE AND BLOOD-FLOW IN THE PATIENTS IN TRIAL I BEFORE AND AFTER THE ADMINISTRATION OF A DRUG OR PLACEBO

PATIENT	PLACEBO		THYMOXAMINE, 20 mg.		TOLAZOLINE, 50 mg.	
	Temperature (° C.)	Resting Flow (ml. per 100 ml. per min.)	Temperature (° C.)	Resting Flow (ml. per 100 ml. per min.)	Temperature (° C.)	Resting Flow (ml. per 100 ml. per min.)
1. Pre	26·75	1·00	27·00	1·10	29·25	1·50
Post	25·00	0·90	26·00	0·90	32·00	4·80
2. Pre	26·90	0·80	25·50	0·80	26·50	0·90
Post	28·25	1·10	27·00	1·30	31·25	2·60
3. Pre	24·00	1·00	24·00	1·10	24·10	1·00
Post	24·00	1·00	24·10	1·20	24·75	1·70
4. Pre	29·75	1·80	29·25	1·80	27·25	1·80
Post	29·25	1·80	27·40	0·80	30·00	3·80
5. Pre	24·25	0·90	26·75	1·80	25·50	1·00
Post	24·75	1·00	26·75	1·80	30·00	3·40
6. Pre	24·75	1·00	28·00	1·40	27·25	1·50
Post	25·10	1·70	28·00	2·50	28·60	3·00

Each patient was observed at three sessions during which he received orally one of the following: tolazoline, a placebo, or different doses of thymoxamine. The orders of the three treatments were randomized so as to form balanced blocks for each group of 6 patients. Any response was observed by measurement of the skin temperature and skin blood-flow. So that proprietary preparations of the active drugs could be employed, placebos resembling both tolazoline and thymoxamine were used at random.

Three trials, studying 6 patients in each, have been carried out.

In *trial I* the patients (all grade I) received the placebo; 20 mg. thymoxamine; 50 mg. tolazoline.

In *trial II* the patients (3 grade I and 3 grade II) received 40 mg. thymoxamine; 60 mg. thymoxamine; 50 mg. tolazoline.

In *trial III* the patients (all grade I) received 80 mg. thymoxamine; 100 mg. thymoxamine; 50 mg. tolazoline.

In each trial the drugs or placebo were administered so that each medication appeared in all possible orders, but the patients were allocated to the various regimens at random.

Skin temperature was measured by an electric thermometer using a thermocouple attached to the dorsum of the foot just proximal to the first web. Room temperature and rectal temperature were also observed.

Skin blood-flow was measured by venous occlusion plethysmography using the mercury-in-rubber strain gauge and the method of calibration of Whitney (1953). The gauge was applied around the forefoot, and since the flow through tendon and fascia in this area is small, this technique is considered to measure the blood-flow through the skin and subcutaneous tissues (Cooper, Edholm, and Mottram, 1955).

The collecting cuff producing venous occlusion was applied just above the ankle and was inflated automatically for 6 seconds and released for 6 seconds, giving five inflow slopes per minute. The collecting cuff pressure was determined individually using the lowest pressure giving the maximal resting flow.

PROCEDURE

The patient, having fasted for 2 hours and with an empty bladder, was brought to a quiet laboratory with an air temperature maintained at 22° C. (± 1° C.).

1. The standing blood-pressure and pulse were recorded.

2. The patient was placed in a supine position, with his head on a single pillow, the foot under study slightly elevated, and his trunk covered with a single blanket.

3. The thermocouple was arranged. The strain gauge was fitted, its position was marked, and it was calibrated.

4. The optimum collecting cuff pressure was determined.

Table III.—SKIN TEMPERATURE AND BLOOD-FLOW IN THE PATIENTS IN TRIAL II BEFORE AND AFTER THE ADMINISTRATION OF A DRUG

PATIENT	THYMOXAMINE, 40 mg.		THYMOXAMINE, 60 mg.		TOLAZOLINE, 50 mg.	
	Temperature (°C.)	Resting Flow (ml. per 100 ml. per min.)	Temperature (°C.)	Resting Flow (ml. per 100 ml. per min.)	Temperature (°C.)	Resting Flow (ml. per 100 ml. per min.)
7. Pre	28·25	1·20	28·00	1·10	27·25	1·50
Post	29·00	2·20	29·25	1·60	28·60	3·00
8. Pre	25·20	0·80	25·25	0·80	25·10	0·9
Post	24·20	0·80	24·00	0·70	24·20	0·8
9. Pre	24·25	2·00	30·50	3·00	26·10	3·00
Post	25·75	3·80	31·50	4·40	31·75	5·40
10. Pre	29·40	1·20	29·00	1·20	27·40	1·50
Post	30·25	1·90	29·75	2·00	31·00	3·60
11. Pre	27·90	1·60	27·25	1·10	25·20	1·20
Post	29·20	1·90	29·00	1·80	27·50	2·50
12. Pre	25·00	1·00	26·00	1·00	25·10	0·70
Post	24·60	0·90	26·50	1·20	26·00	1·10

Table IV.—SKIN TEMPERATURE AND BLOOD-FLOW IN THE PATIENTS IN TRIAL III BEFORE AND AFTER THE ADMINISTRATION OF A DRUG

PATIENT	THYMOXAMINE, 80 mg.		THYMOXAMINE, 100 mg.		TOLAZOLINE, 50 mg.	
	Temperature (°C.)	Resting Flow (ml. per 100 ml. per min.)	Temperature (°C.)	Resting Flow (ml. per 100 ml. per min.)	Temperature (°C.)	Resting Flow (ml. per 100 ml. per min.)
13. Pre	29·00	1·90	27·75	1·50	26·60	2·00
Post	30·10	3·20	29·40	2·50	30·00	4·50
14. Pre	25·00	0·80	25·60	0·90	24·10	1·00
Post	25·50	1·30	25·75	0·90	31·00	3·60
15. Pre	23·75	0·90	25·25	0·90	25·60	0·90
Post	23·75	0·90	24·90	0·90	30·90	3·90
16. Pre	27·90	1·40	29·40	1·90	28·80	1·40
Post	28·75	2·40	30·00	3·00	33·00	4·20
17. Pre	28·20	1·40	25·90	1·40	27·00	1·50
Post	28·20	1·40	25·30	1·30	29·75	2·80
18. Pre	25·00	1·10	25·00	1·00	25·00	1·20
Post	24·50	0·90	24·40	0·80	24·80	1·00

5. The resting blood-flow and skin temperature were recorded until a steady skin temperature had been attained (usually 45–60 minutes).

6. A single dose of a drug or placebo was administered.

7. The resting skin blood-flow, skin temperature, pulse-rate, and blood-pressure were recorded at 15-minute intervals for a further 90 minutes.

8. Any subjective symptoms and other side-effects were noted.

RESULTS

Table I shows the mean initial skin temperature and blood-flow before the administration of a drug or placebo in each of the three trials. There were no differences of any statistical significance between any of these initial measurements.

Tables II, III, and *IV* show the skin temperature and blood-flow in each patient before the administration of a drug or placebo and 90 minutes afterwards. The individual responses to the different forms of treatment are illustrated in *Fig.* 1 (skin-temperature changes) and *Fig.* 2 (blood-flow changes). It can be seen that in each of the trials and in 16 out of 18 patients tolazoline produced increases while there was little change following the placebo or the various doses of thymoxamine.

The mean changes in temperature and blood-flow in response to the different drugs and dosages are given in *Table V*, where the statistical significance of the results is indicated. All the changes following tolazoline were statistically significant, while neither the placebo nor any dose of thymoxamine produced a significant change.

Table VI shows the accumulated observations of the three trials. The effect of tolazoline is clear-cut while thymoxamine produced no increase in skin temperature or blood-flow greater than might have been achieved by chance with the use of a placebo.

There was no alteration of blood-pressure or pulse-rate after the taking of the drugs.

DISCUSSION

The results show that as a cutaneous vasodilator in the foot in the presence of atherosclerotic arterial occlusion, oral thymoxamine (Opilon) in the single doses used did not produce a significant increase in the temperature of the foot or in the rate of blood-flow although in the same patients oral tolazoline (Priscol) 50 mg. did produce statistically significant effects.

Table V.—MEAN CHANGES IN SKIN TEMPERATURE AND BLOOD-FLOW IN RESPONSE TO DIFFERENT DRUGS AND DOSAGES

	TEMPERATURE (°C.)		BLOOD-FLOW (ml. per 100 ml per min.)	
	Mean	*t*	Mean	*t*
Trial I				
Tolazoline, 50 mg.	+2·82	4·7***	+1·93	6·2***
Thymoxamine, 20 mg	−0·20	−0·3	+0·08	0·3
Placebo	−0·07	−0·1	+0·17	0·5
Trial II				
Tolazoline, 50 mg.	+2·18	3·6**	+1·27	4·1***
Thymoxamine, 40 mg.	+0·47	0·8	+0·62	2·0
Thymoxamine, 60 mg	+0·68	1·1	+0·58	1·9
Trial III				
Tolazoline, 50 mg.	+3·80	6·4***	+2·00	6·4***
Thymoxamine, 80 mg.	+0·30	0·5	+0·43	1·4
Thymoxamine, 100 mg.	0·00	0·0	+0·30	1·0
Pooled standard deviation	±0·60		±0·31	

In each trial there are 6 patients giving 5 degrees of freedom.

Significant values. $P = 0·05$ ($t = 2·57$); ** $P = 0·02$ ($t = 3·36$); *** $P = 0·01$ ($t = 4·03$).

Table VI.—ACCUMULATED OBSERVATIONS OF THE THREE TRIALS

	NO. OF READINGS	CHANGES IN TEMPERATURE (°C.)			CHANGES IN BLOOD-FLOW (ml. per 100 ml. per min.)		
		Mean	S.E.	*t*	Mean	S.E.	*t*
Placebo	6	−0·07	0·60	−0·1	+0·17	0·31	0·5
Tolazoline	18	+2·93	0·35	8·4	+1·73	0·18	9·6
Thymoxamine	30	+0·25	0·27	0·9	+0·40	0·14	2·9

Furthermore, there is no evidence of a dose-response curve with increasing doses of thymoxamine. An inactive placebo was not used in trials II and III, but in every trial the contrast therapy used for all the patients was a 50-mg. dose of tolazoline. In trial I the advantage of tolazoline, 50 mg., over thymoxamine, 20 mg., was 3·0° C. in increased temperature and 1·8 ml. per 100 ml. per minute in blood-flow; in trial III the advantage of tolazoline, 50 mg., over thymoxamine, 100 mg., was 3·8° C. and 1·7 ml. per 100 ml. per minute. A fivefold increase in thymoxamine had not narrowed the comparison with tolazoline. In trial II half the patients were rather more severely affected by atherosclerotic disease than in the other two trials and the potency of tolazoline in producing a vasodilatation, although still statistically significant at a level of $P = 0·02$, was reduced so that the advantage of tolazoline, 50 mg., over thymoxamine, 60 mg., was only 1·7° C. and 0·7 ml. per 100 ml. per minute. This is in accord with our previous findings (Thomas and others, 1968) that there is a decrease in response to tolazoline with increasing severity of disease. As a consequence the contrast between the drugs was not so large in trial II as it was in trials I and III; it is also apparent that in trial II no effect was produced by increasing the dose of thymoxamine from 40 to 60 mg.

The oral dose of thymoxamine needed to obtain an optimum response is uncertain. Myers, Hobbs, and Irvine (1966) reported increased skin-flow in patients with peripheral vascular disease after intravenous thymoxamine using a dose of 0·1 mg. per kg. Subsequent studies of blood levels have suggested that an equivalent oral dose would be 40 mg. (Hobbs, 1967). This is the dose recommended by the manufacturers. We employed single oral doses of 20, 40, 60, 80, and 100 mg. without a significant effect.

Working with tolazoline, Thomas and others (1968) found a single oral dose to have different results from those observed by Gillespie (1966) using intravenous drugs. Thus, while Gillespie encountered a reduction of the peripheral blood-flow (the borrowing–lending phenomenon) in 60 per cent of the limbs with arterial occlusion, we found that oral vasodilators produced a reduction in only 1 of 24 limbs (4 per cent). It would appear unwise to assume from studies with intravenous drugs a similar action when the drug is given orally.

Doses of 20 and 40 mg. of thymoxamine produced no side-effects but with the larger doses (60 mg. and above) there were side-effects in 2 of the 12 patients; headache and nausea in 1 patient and profuse sweating in the other. This is a similar incidence to the side-effects that we have encountered with 50 mg. of tolazoline orally.

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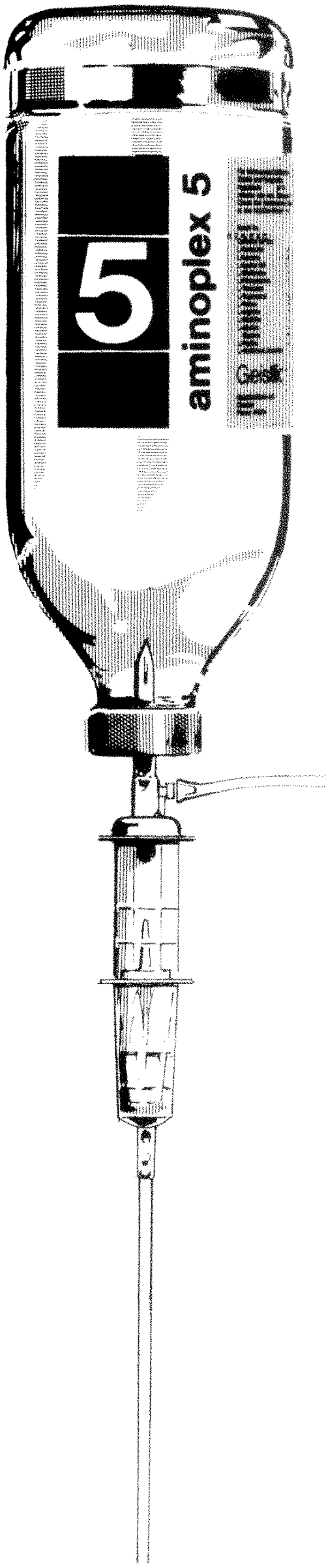

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OESOPHAGEAL PERFORATION

A REPORT OF 13 CASES

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SUMMARY

A series of 13 cases of oesophageal perforation seen between 1961 and 1972 is reported. The various causes of perforation are discussed, with emphasis on the need for rapid diagnosis.

Conservative treatment is considered to lead to a high mortality-rate. One of the 10 patients who were treated surgically in this series died. It is recommended that patients with a carcinoma be treated in a single operation, and in achalasia of the cardia the use of a rigid oesophagoscope should be avoided.

ALTHOUGH many diagnostic and therapeutic methods require the passage through the oesophagus of various instruments (bougie, gastric tube, oesophagoscope, gastroscope), perforation of the oesophagus is fortunately a rare complication. The literature contains only a few series of perforation of the oesophagus comprising 10 or more patients, including cases of spontaneous perforation and perforation due to swallowed objects (Seybold, Johnson, and Leary, 1950).

Between 1961 and 1972, 13 patients with an oesophageal perforation were treated in the University Hospital Dijkzigt at Rotterdam. In 9 cases the perforation was the result of a diagnostic or therapeutic procedure (iatrogenic trauma), in 3 cases it was caused by a foreign body, and 1 case was a spontaneous perforation (*Table I*).

Table I.—CAUSE OF OESOPHAGEAL PERFORATION IN 13 PATIENTS IN THE PRESENT SERIES

Cause	*No. of Cases*
Iatrogenic trauma	
Oesophagoscopy	5
Dilatation	2
Biopsy	2
Accidental	
Foreign body	3
Spontaneous	1

In the treatment of these cases the main emphasis was consistently put on early diagnosis on the basis of the history, clinical findings, and radiographic appearance of the thorax and oesophagus. Usually a thoracotomy was performed with closure of the perforation, high doses of antibiotics being administered preoperatively. This treatment represents a combination of the recommendations in the literature, i.e., on the one hand, surgical treatment with prompt performance of a thoracotomy and closure of the perforation and, on the other hand, conservative treatment with parenteral feeding and high doses of antibiotics. Many authors now support rapid surgical treatment (Weisel and Raine, 1952; McBurney, Kriklin, and Hood, 1953; Overstreet and Ochsner, 1955; Blalock, 1957; Nealon, Cuddy, and Gibbon, 1961; Lauschke, Han, and Perper, 1970; Bertelsen, 1971; Dubost, 1971; Mühe, Bünte, Bürger, and Kuhnlein, 1972), but a few continue to advise conservative treatment (e.g., Mengoli and Klaassen, 1965).

Oesophageal perforations can be divided into four groups according to cause: iatrogenic trauma, accidental, spontaneous, and microperforation (Terracol, 1951).

Iatrogenic oesophageal perforations can occur during oesophagoscopy (5 patients in the present series), instrumental dilatation of the oesophagus (2 patients), and the taking of a biopsy specimen (2 patients) (Bertelsen, 1971), but cases have also been reported resulting from instrumental manipulations during difficult intubations for intratracheal anaesthesia (Dubost, 1971).

Accidental perforations are caused by foreign bodies, such as pieces of wood, fish bones, chicken bones, etc. (3 patients).

Spontaneous perforations occur when the oesophagus ruptures, in most cases as the result of violent vomiting; this type of perforation is called the Boerhaave syndrome (1 patient).

*Micro*perforations which do not give rise to clinical signs or symptoms are caused by the swallowing of fine-pointed objects (e.g., safety pins swallowed by children), or occur during oesophagoscopy, biopsy, or electromyography of the oesophagus. Neither this type of perforation nor that caused by oesophageal abscesses or other complications following thoracic or abdominal surgery is included in the present series and therefore they are not discussed.

SYMPTOMS AND DIAGNOSIS

In the early stages the patient's complaints are not particularly characteristic in either proximal or distal perforation of the oesophagus (Wichern, 1970). The main complaints associated with distal perforations are epigastric discomfort, persistent retrosternal pain, pain between the shoulder-blades, difficulty in breathing, and elevated temperature. With a proximal perforation the patient immediately experiences severe pain on swallowing, movement of the head, and respiration, often accompanied by excessive salivation, and there is usually a rise in the temperature within 8 hours. Special attention must be given to the latter group of complaints after oesophagoscopy.

In cases of perforation due to a foreign body, stenotic complaints predominate. Foreign bodies are usually trapped above natural constrictions in the oesophagus, i.e., just under the pharynx, centrally at the level of the aortic arch, and above the hiatus (Seybold and others, 1950). Dysphagia and pain on swallowing accompanied by an elevation of the body temperature within 24 hours constitute useful diagnostic indications.

In spontaneous post-emetic oesophageal perforations (Boerhaave syndrome) the occurrence of sudden violent vomiting with the simultaneous development of severe retrosternal and epigastric pain is highly suggestive of oesophageal rupture. A predisposing disease is almost always present, for instance oesophagitis (Muller and Nauta, 1952), gastric or duodenal ulcer, or a carcinoma of the cardia. At operation the mucosal tear usually proves to be much longer than outward inspection of the oesophageal lesion suggests (Lauschke and others, 1970, Keighley, Girdwood, Tonescu, and Wooler, 1972).

Clinical examination almost always reveals a slight subcutaneous emphysema in the neck, regardless of the type of perforation involved, the reason being that unlike other hollow organs the oesophagus is not provided with a serous membrane. Because the oesophagus 'hangs' within the loose network of connective tissue of the mediastinum an inflammatory process arising from a perforation can spread unhindered to the hiatus, the neck, and interpleurally in a lateral direction.

If the diagnosis is not made promptly (within 24 hours) mediastinitis, pleural emphysema, or even a subdiaphragmatic abscess can develop rapidly. If this stage is reached a lethal course cannot be prevented in more than 80 per cent of the cases (Seybold and others, 1950; Derbes and Mitchell, 1956). For the differential diagnosis, gastric perforation, acute peptic ulcer, cardiac infarction, strangulated hernia of the oesophageal hiatus, pancreatitis, and other acute processes of the upper abdomen should be taken into consideration (Keighley and others, 1972).

The occurrence of a pneumomediastinum on a routine chest radiograph suggests an oesophageal perforation. Air escaping from the oesophagus spreads rather easily through the loose connective tissue of the mediastinum, which widens within a few hours as an early symptom of mediastinitis. In some cases an exudate in the pleural cavity shows on the side of the oesophagus where the perforation is located. In addition, subcutaneous emphysema is often seen in the region of the neck and at the base of the skull owing to the upward dispersion of the escaping air at each inspiration and expiration. In some cases there is also an appreciable accumulation of air in the pleural cavity a few hours after the perforation has occurred and this is seen on the chest radiograph as a distinct fluid level.

The final diagnosis and localization of the perforation are based on an investigation of the oesophagus with Gastrografin, the contrast medium accumulating outside the oesophagus and in the pleural cavity on the perforated side. This method sometimes fails to reveal small perforations (Callaghan, 1972), but when the diagnosis is probable on clinical grounds the Gastrografin may be detected in the urine a few hours after the radiological examination. This medium is not resorbed in the digestive tract but when there is extravasation it is immediately resorbed by the tissues surrounding the digestive tract and excreted by the kidneys (Mühe and others, 1972).

MATERIAL

The present series includes 6 men and 7 women, ranging in age from 38 to 72 years. Of the 13 patients, 3 suffered from a malignant neoplasm (squamous-cell carcinoma of the oesophagus, gastric adenocarcinoma, and adenocarcinoma of the cardia), 4 from achalasia, 2 from an oesophageal stricture due to ingestion of acid or lye, and in 4 cases the perforation was caused by a foreign body.

In the 3 patients with carcinoma the perforation occurred during oesophagoscopy in 1 case, during the taking of a biopsy specimen in the second case, and in the third patient during violent vomiting. In all 4 patients with achalasia the perforation was caused by endoscopy. In the 2 patients with a stricture the perforation resulted from dilatation with a mercury bougie. Of the 4 patients admitted with a foreign-body perforation, the perforation was caused directly by the foreign body in 3 cases, while in the fourth perforation occurred during the taking of a biopsy sample after careful removal of a hard lump of food (*Table II*). Thus, in this series the oesophagus was twice perforated by taking a biopsy, the other patient having a squamous-cell carcinoma of the distal part of the oesophagus.

Table II.—ORIGINAL DISEASE AND CAUSE OF PERFORATION

ORIGINAL DISEASE	NO. OF CASES		CAUSE OF PERFORATION	NO. OF CASES
Carcinoma		3	Spontaneous	1
Gastric	2		Oesophagoscopy	1
Oesophageal	1		Biopsy	1
Achalasia		4	Oesophagoscopy	4
Foreign body		4	Foreign body	3
			Biopsy	1
Oesophageal stenosis		2	Dilatation	2
Lye	1			
Acid	1			
Total		13		

Perforations resulting from the use of a rigid oesophagoscope mainly occur in two areas: in the cervical part of the oesophagus and just above the diaphragm. The cervical perforation occurs where the posterior wall is pressed against the cervical vertebrae by the oesophagoscope. The introduction of the oesophagoscope is particularly difficult in patients with spondylolisthesis or cervical arthrosis. Distal perforations are not rare in achalasia, occurring in the region where the oesophagus makes an S-shaped curve over the diaphragm.

The frequency of oesophageal perforation, as a complication of the use of a rigid oesophagoscope (with or without biopsy), is rather low, according to the literature being between 0·4 and 1 per cent (Quintana, Bartley, and Wheat, 1970). In the University Hospital Dijkzigt 1050 oesophagoscopies were performed with this instrument between 1 Jan., 1961, and 1 Jan., 1972, with 7 perforations, or 0·67 per cent (*Table III*). It is therefore evident that the use of this instrument is not entirely without risk. It does, however, have the advantage of easy removal of small foreign bodies. The flexible fibroscope is much less likely to cause a perforation and is therefore being increasingly used for diagnostic purposes.

Our series includes 2 cases of a perforation in the proximal oesophagus, 1 occurring during oesophagoscopy of a patient with achalasia and severe kyphosis and the other being caused by a foreign body.

The middle part of the oesophagus was perforated twice; once by a foreign body and once by bougienage performed by the patient herself.

Table III.—Frequency of Oesophageal Perforation in Oesophagoscopy at the University Hospital Dijkzigt between 1961 and 1970

Year	*No. of Oesophagoscopies*	*No of Perforations*
1961	5	
1962	30	
1963	68	1
1964	82	
1965	84	1
1966	111	
1967	109	1
1968	114	
1969	133	1
1970	150	2
1971	164	1
	1050	7 (0·67 per cent)

Table IV.—Position and Cause of the Perforation

Part of Oesophagus	No. of Cases	Cause of Perforation	No. of Cases
Proximal	2	Oesophagoscopy (severe kyphosis)	1
		Foreign body	1
Middle	2	Foreign body	1
		Dilatation	1
Distal	9	Oesophagoscopy	4
		Biopsy	2
		Foreign body	1
		Dilatation	1
		Spontaneous	1

Table V.—Results of Treatment

Cause	No. of Cases	Surgical Treatment		Conservative Treatment	
		Survived	Died	Survived	Died
Oesophagoscopy	5	3	—	—	2
Biopsy	2	2	—	—	—
Dilatation	2	2	—	—	—
Foreign body	3	2	—	1	—
Spontaneous	1	—	1	—	—
	13	9	1	1	2

The distal portion of the oesophagus was perforated in 9 cases; in 4 cases during oesophagoscopy (3 achalasia cases, 1 carcinoma of the cardia), in 2 during a biopsy (the patient with squamous-cell carcinoma of the oesophagus and in the other case after removal of a foreign body), in 1 by a foreign body, in 1 by instrumental dilatation (the patient with a stricture after lye burns), and once spontaneously during violent vomiting (the patient with gastric carcinoma) (*Table IV*).

TREATMENT

When the diagnosis of oesophageal perforation was confirmed surgical treatment was carried out as soon as possible in the form of closure of the perforation and drainage of the pleural cavity. Antibiotics were administered both before and after surgery (usually penicillin and streptomycin in high doses).

Conservative treatment consisting of antibiotics and parenteral feeding was used in 3 cases (*Table V*). One of these was a patient with a deep mucosal tear and a small perforation of the muscular wall caused by a sharp foreign body who showed no signs of mediastinitis and recovered rapidly. In the second case, a patient with achalasia who after oesophagoscopy had a perforation located only 18 cm. from the teeth, preference was incorrectly given to conservative treatment. This patient died 2 months later despite intensive treatment with antibiotics, parenteral feeding, tracheotomy, and a jejunostomy. The third patient was treated conservatively because the diagnosis could not be confirmed by oesophagoscopy. This woman had achalasia with a complete stenosis. Since a nasal catheter could not be introduced via the oesophagoscope a gastrostomy was made for feeding. Postoperatively she developed a high fever, which was attributed to an infection of the urinary tract. Later a subdiaphragmal abscess was diagnosed, but because of the patient's poor general condition conservative treatment was instituted. The patient died and at autopsy an old perforation was found in the distal oesophagus.

The other 10 patients were treated surgically. Only 1 of these cases had a fatal course (the patient with an inoperable gastric carcinoma and a post-emetic rupture of the oesophagus).

Of the 3 cases of a perforation caused by a foreign body, 1 was only diagnosed after 3 days had elapsed. This patient was a woman suffering from lupus erythematosus and was on cortisone treatment. Primary closure of the perforation was performed, and later abscess drainage was required. The second patient had received conservative treatment elsewhere despite early diagnosis. After being referred to the University Hospital Dijkzigt he was treated initially with drainage and flushing of the abscess cavity in the thorax and later by thoracotomy with abscess drainage and exploration of the mediastinum. In the third patient, who had had a biopsy of the site from which the foreign body had been removed, the perforation was closed surgically within 24 hours.

In the 3 carcinoma patients the perforation was treated surgically. In the first patient, who had a small oesophageal polyp, the perforation had occurred during the taking of a biopsy specimen. Primary closure of the perforation was done. Three years later a definite diagnosis of squamous-cell carcinoma was made and a colon interposition was performed. The patient died a year later from metastases. The second patient, who suffered from gastric carcinoma, developed a perforation spontaneously as a result of violent vomiting. In this case the carcinoma had been diagnosed some time before, but for personal reasons the patient had consistently refused surgical treatment. Treatment consisted in the first instance of primary closure, and a primary oesophagogastrectomy was not considered (McBurney and others, 1953). Later, under much worse conditions pleural drainage and a jejunostomy were carried out and finally a total gastrectomy was performed. The patient died 50 days after the perforation had occurred. As Keighley and others (1972) have pointed out, the consequences of a spontaneous rupture are always more serious than those of an instrumental perforation. This is probably due to the autolysis of the contents of the stomach, which are forced into the mediastinum under high pressure. In the third patient, who had a carcinoma of the cardia, the perforation occurred during oesophagoscopy. Six hours later, via a left-sided thoraco-abdominal incision, the perforated part of the oesophagus and the cardia were resected with an oesophagogastrostomy. The patient made an uneventful recovery.

Two of the 4 patients with achalasia and a perforation due to oesophagoscopy were treated surgically. Within 6–10 hours the perforation was closed via a thoracotomy and a Heller's operation was performed. Both patients recovered uneventfully. The other 2 patients with achalasia were treated conservatively with a fatal result and have already been discussed.

In the 2 patients with stenosis of the oesophagus and a perforation due to dilatation, thoracotomy and primary closure of the perforation gave good results. One of these patients had a stenosis due to lye burns incurred in his youth. During dilatation of the stenosis with a mercury bougie the oesophagus was perforated just above the stricture. The second patient had a stenosis due to acid burns suffered in childhood, and was accustomed to dilate the oesophagus with a Pilling bougie, which ultimately caused the perforation. Two months after primary closure a colon interposition was performed, and at present the patient has no complaints.

CONCLUSIONS

1. Surgical treatment, consisting of closure of the oesophageal perforation and drainage of the pleural cavity in combination with high doses of antibiotics is the treatment of choice (*Table V*).

2. When perforation occurs in patients with carcinoma of the oesophagus or stomach, primary oesophagogastrectomy should be considered instead of simple closure of the perforation.

3. In patients with achalasia, diagnostic oesophagoscopy with a rigid oesophagoscope is dangerous. Because of the risk involved, oesophagoscopy, possibly with a flexible instrument, should only be considered when a malignant process is suspected.

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NON-PULMONARY SURGICAL TUBERCULOSIS*

By R. G. FABER†

HIGH WYCOMBE GROUP OF HOSPITALS

Summary

Fifty-one cases of non-pulmonary surgical tuberculosis are reviewed, 29 of the cases being immigrants. Of the 44 'new' cases, tuberculosis was not among the preoperative differential diagnoses in 15. Lymph-nodes were the site of the disease in more than half the cases. In only 29 cases was an operative specimen sent for bacteriological culture, and the necessity for culturing operative specimens and the reasons for the failure of isolation of tubercle bacilli in 50 per cent of the cultures are discussed. The impression that tuberculosis is not sufficiently considered by doctors in the preoperative differential diagnosis of several surgical presentations, especially in English patients, is confirmed.

Fifty-one cases of tuberculosis who were in-patients in the surgical departments of the High Wycombe group of hospitals during the years 1966–70 are reviewed. Apart from 1966 the number of 'new' cases of tuberculosis each year has been constant in contrast to the Tuberculosis Notifications (Public Health Laboratory Service, 1971) for the same years (*Table I*). Cases of tuberculosis, including 11 gynaecological cases, who were not under the care of the surgical departments are not included. The review was prompted by the emergence of a surprising number of clinically unsuspected cases of tuberculosis in 1970, and confirmed that tuberculosis was frequently not among the differential diagnoses of several surgical presentations. In some cases this led to a delay in diagnosis since the appropriate diagnostic procedures were not employed.

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* This paper is based on the prize-winning entry for the Oxford Regional Board Surgical Prize, 1970, and a paper presented to the Chiltern Medical Society on 23 Sept., 1970.

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PATIENTS

The number of 'new' cases of tuberculosis presenting each year in this series is shown in *Table I*. Apart from 1966, when possibly the records were incomplete, the incidence of the disease was constant. There were no deaths in the series. Twenty-nine of the patients (58 per cent) were immigrants to the United Kingdom, the majority (22 patients) being from Pakistan. There were 22 males and 7 females among the 29 immigrants, and 9 males and 13 females among the 22 English-born cases. The ages of the patients (*Table II*) ranged from 12 to 85 years with an average of 46 years for the English cases and 28 years for the immigrants. The 12-year-old patient was the only child in the series and was born in England. There were 3 patients over the age of 70 and these were all females born in England.

Table I.—Number of Cases of Tuberculosis per Year between 1966 and 1970 in the Present Series compared with the Tuberculosis Notifications for the Same Years

	Year				
	1966	1967	1968	1969	1970
Notifications					
Total	14,616	13,223	12,984	21,162	11,907
Deaths	3,242	2,050	2,196	1,835	1,563
Present series					
Total	3	9	14	13	12
Immigrants	1	5	7	10	6
Deaths	0	0	0	0	0

Table II.—Age Distribution in the Present Series

	English	*Immigrant*
Average age	46	28
Youngest	12	17
Oldest	85	52

Seven of the 51 cases were classified as 'old' cases, as they gave a history of having had tuberculosis in the past and therefore aroused the suspicion of tuberculosis being the cause of the present admission. Only 2 of these 7 patients were immigrants. Four cases had undergone surgery for tuberculosis in the pre-antibiotic era, but the other 3 cases had received inadequate chemotherapy at the time of their previous diagnosis. There were 3 further cases in the series who received inadequate chemotherapy initially and this resulted in a protracted course to their illness. Of the 44 'new' cases (i.e., with no previous history of tuberculosis), tuberculosis was considered in the differential diagnosis in 29 (66 per cent), while in 15 patients (34 per cent) the diagnosis came as a surprise when the histology of the operative specimen was reported. Of the 15 unsuspected cases, 8 (53 per cent) were English born, while only 8 out of the 29 clinically suspected group (27 per cent) were English born.

SITE OF TUBERCULOSIS DISEASE

Table III compares the site of tuberculosis in the 51 patients with the number of cases classified as 'old' cases, 'new' cases in which tuberculosis was among the preoperative differential diagnoses, and 'new' cases in which the histological diagnosis came as a surprise. The most common site of tuberculosis was the lymph-nodes; in 23 cases the cervical region was the site of the disease, 1 case having involvement of the inguinal and axillary nodes as well. One case each of solitary axillary and inguinal tuberculous lymphadenitis occurred, and there were 2 cases of intestinal tuberculosis, in which the diagnosis was confirmed by histology and culture of the mesenteric lymph-nodes.

Of the 11 cases of genito-urinary tuberculosis, there were 6 cases with urinary-tract involvement and 5 cases of genital-tract disease. Two of the latter 5 patients had been subjected to nephrectomy in the pre-antibiotic era for renal tuberculosis but excretion urography and cystoscopy at the time of the present review showed a normal remaining kidney and bladder. Similarly, intravenous pyelography and cystoscopy were normal in the 3 cases with no previous history of urinary-tract tuberculosis. Two patients with renal tuberculosis were subjected to nephrectomy during the time of the review. In the first case nephrectomy was carried out because of a ureteral stricture and pyonephrosis despite adequate chemotherapy. The other case had a ureteral stricture and a non-functioning kidney. There was no growth of tubercle bacilli on early morning urine culture and therefore this case was not treated preoperatively with anti-tuberculous chemotherapy, because the diagnosis had not been made although it had been suspected clinically. Another case required re-implantation of the ureter into the bladder because of a fibrous stricture at the lower end.

Table III.—Site of Tuberculous Disease in Patients in the Present Series

	Lymph-nodes	Genito-urinary System	Intra-abdominal	Bone and Joint	Multiple Subcutaneous Cold Abscesses	Larynx	Breast
'Old' cases	2	3	0	1	0	0	1
'New' cases clinically suspected of having tuberculosis	16	8	3	1	1	0	0
'New' cases not clinically suspected of having tuberculosis	9	0	6	1	0	1	0
Total	27*	11	9*	3	1	1	1

* Includes 2 cases with intestinal tuberculosis as well as mesenteric tuberculous lymphadenitis

Of the 9 cases of intra-abdominal tuberculosis, there were 3 cases of intestinal disease, 2 having localized tuberculous appendicitis, of which 1 had enlarged tuberculous mesenteric lymph-nodes. One case presented with small-bowel obstruction due to an active tuberculous stricture of the ileum approximately 1 m. from the ileocaecal valve. This patient also had enlarged tuberculous mesenteric lymph-nodes. The other 6 cases had tuberculous peritonitis, 5 patients presenting with generalized peritonitis and being submitted to emergency laparotomy, while the sixth patient was also noted to have a pleural effusion and the diagnosis was made from the pleural biopsy. Despite a clinical suspicion of tuberculosis in only 3 of the 6 patients, in none was there any delay in operating and obtaining biopsy material from which an early diagnosis was made.

The sites of disease in the 3 cases of bone and joint tuberculosis were the spine, knee, and ankle respectively. The first case was diagnosed on the classic radiographic appearance of the collapse of two adjacent thoracic vertebral bodies with a surrounding paravertebral abscess, and was treated for 3 weeks before drainage of the abscess. The other 2 cases were diagnosed from the biopsy of discharging sinuses.

The case with multiple subcutaneous cold abscesses was suspected initially to be suffering from tuberculosis, but several abscesses had to be biopsied and aspirated before a positive culture of *Mycobacterium tuberculosis* was obtained. The patient with tuberculosis of the larynx was thought to have a carcinoma of the vocal cords before the histology of the biopsy was seen. The tuberculous breast abscess occurred in an 85-year-old woman who had had a tuberculous lymph-node many years before and had received no chemotherapy.

INVESTIGATIONS

Chest Radiography.—Thirty-five patients (69 per cent) had normal chest radiographs even though some of these cases had generalized disease (*Table IV*). In 11 cases the chest radiograph showed evidence of active pulmonary tuberculosis. However, 10 cases did not have a chest radiograph performed preoperatively, and on reviewing the postoperative films it was seen that in 3 of the cases the diagnosis could have been made from the chest radiograph alone. Five cases showed evidence of old healed tuberculosis and in all of these cases this aroused the suspicion that tuberculosis was the cause of the disease at the present time.

Table IV.—Findings of Chest Radiography in the Present Series

	Normal	Evidence of Old Tuberculosis	Evidence of Active Tuberculosis
Performed preoperatively	28	5	8
Not performed preoperatively	7	0	3
Total	35	5	11

Mantoux or Heaf Test.—This was performed preoperatively in only 8 cases and was positive in 7 and negative in only 1 patient who was severely ill with tuberculous peritonitis.

Erythrocyte-sedimentation Rate.—This was measured preoperatively in 21 cases, being normal in 4 and raised in 17.

Bacteriological Culture.—In only 29 cases (57 per cent) were either an operative specimen or early morning urine specimens (in the case of genito-urinary tuberculosis) sent for bacteriological culture (*Table V*).

Table V.—Bacteriology of the Operative Specimens from Patients in the Present Series

Result	*No of Cases*
Specimens not sent for culture	22
Isolation of *M. tuberculosis* on culture	15
No growth of *M. tuberculosis* on culture	14

Of those specimens which were sent for culture, *M. tuberculosis* was isolated in only 15 cases.

DISCUSSION

The number of cases presenting each year remained constant, apart from 1966 (*Table I*), and this contrasts with the falling incidence of National Notifications (Public Health Laboratory Service, 1971). The incidence of tuberculous disease in immigrants of 58 per cent in the present series is considerably more than the figure of 16·5 per cent of the notifications in England and Wales during a 3-month period in 1965, at which time immigrants formed 4 per cent of the population (British Thoracic and Tuberculosis Association, 1971). The large proportion of immigrants in the present series is simply a measure of the large immigrant population in the area served by the High Wycombe group of hospitals, and contrasts strongly with the 4 immigrant cases out of 71 patients (6 per cent) reported in the Edinburgh series for the years 1964–8 inclusive (Stack, 1971). Although the average age of the immigrant cases was appreciably lower than that of the native population the range of ages in both groups prevents this being used as a diagnostic criterion, and probably merely reflects the younger age of the immigrant population in general.

Six cases received inadequate chemotherapy; 3 before the period covered by the review, and 3 who were initially diagnosed during the period of this review. For chemotherapy to be considered adequate it must be continued for about 2 years to ensure freedom from relapse (Leading Article, 1970b). There are two reasons for inadequate chemotherapy. First, there is the natural reluctance of surgeons to condemn a patient to 2 years of treatment with drugs which sometimes have unpleasant side-effects, and it needs the enthusiasm of the physician specializing in tuberculosis to ensure that the drugs are taken. Gabriel (1971) made a plea for co-operation between surgeon and physician in this respect. Secondly, there is frequent 'patient-failure', especially among some immigrants whose mobility and language problems make follow-up very difficult. However, there is a medical responsibility to impress upon the patients the seriousness of the condition and the necessity for continued chemotherapy.

The inclusion of tuberculosis in the initial differential diagnosis of 66 per cent of the 'new' cases compares with the figure of 69 per cent in non-thoracic cases of tuberculosis reported by Stack (1971).

There were no deaths in the present series compared with 5 in Stack's review. Although the percentage of cases in which tuberculosis would have been included in the initial differential diagnosis must have been much higher 25 years ago when surgeons saw many more cases and were more aware of the incidence of the disease, it is hard to believe that any similar series then could have had no deaths. The relatively high incidence of English-born cases in the group of patients in which tuberculosis was not included in the differential diagnosis (53 per cent), compared with only 27 per cent of English-born patients occurring in the group in which tuberculosis was considered in the differential diagnosis, suggests that in the High Wycombe area especially doctors are not aware of the amount of tuberculosis in the native population.

More than half of all the cases had tuberculous lymphadenitis. There were 318 lymph-node biopsies in the High Wycombe group of hospitals during the years of the review, giving an incidence of tuberculous disease in 8 per cent. This incidence is far greater than that in Stack's (1971) series from Edinburgh (12 out of 71 cases), but the distribution of the disease in his series is similar with all the cases having cervical lymph-node involvement, which was true in all but 4 of the cases in this series.

The fact that in the present series only 2 out of the 5 cases with genital-tract disease, all having tuberculous epididymitis, had suffered from urinary-tract disease would seem to support the theory that genito-urinary tuberculosis is not a single entity (Konstam, 1966). However, Wells (1938) clearly showed over 30 years ago that the commonest route of infection of the genital tract is the urinary tract, and it is possible that the urinary-tract disease was either healed or dormant, which in the latter case would have been cured by an adequate course of chemotherapy.

The finding of 2 cases of tuberculous appendicitis with no associated general disease is surprising, and Bochus (1969) quoted only 4 cases in 7847 appendices removed from 1928 to 1948. However, with tuberculous disease elsewhere in the body, tuberculous appendicitis becomes more common, rising to 24 per cent in sanatoria. A review of intra-abdominal tuberculosis, including the 9 cases in this series, is in preparation.

The case with multiple cold abscesses was typical of the description of these cases given by Shaw and Bassu (1970) and in a Leading Article in the *British Medical Journal* (1971). The patient was a Pakistani immigrant who developed multiple subcutaneous abscesses of the scalp and both arms. The diagnosis was made clinically, but the histology was non-specific and confirmation was only obtained by a very weak growth of tubercle bacilli on a culture of the third abscess drained.

The high percentage of normal chest radiographs shows that it is necessary to be aware of the possibility of non-pulmonary tuberculosis in the absence of radiological pulmonary changes. However, it is regrettable that in 10 cases a chest radiograph was not performed preoperatively, and ironic that in 3 of these cases there was evidence of active pulmonary tuberculosis.

Only 8 of the 51 cases had a Mantoux or Heaf test performed. In patients with active tuberculosis the tuberculin test is only negative during the incubation period of 3–9 weeks while cell-mediated delayed hypersensitivity is being built up. In critically ill patients the test may become negative, and revert to positive on the recovery of the patient with treatment, as occurred in this series in 1 patient with tuberculous peritonitis (Howard, Klopfenstein, Steininger, and Woodruff, 1970; Leading Article, 1970c). As a method of clinical diagnosis the tuberculin test is only of value in an area where there is a low infection rate and B.C.G. vaccination is not used extensively, as it is in England (Crofton and Douglas, 1969a). However, if the patient is not critically ill a negative tuberculin test excludes tuberculosis as the cause of the disease, and it should therefore have been performed more frequently.

The erythrocyte sedimentation rate (E.S.R.) was carried out preoperatively in only 21 cases, being normal in 4 (20 per cent) and raised, sometimes only slightly, in 17 (80 per cent). It has been suggested by Kay (1970) that E.S.R. surveys can be of diagnostic value despite their lack of specificity. However, the 20 per cent normal figure in the present series supports the contention of Crofton and Douglas (1969c) that active lesions may be associated with a normal E.S.R. and that the investigation is of little diagnostic value.

It is regrettable that in only 29 cases (57 per cent) were operative specimens sent for bacteriological culture. When the diagnosis was not suspected preoperatively it was the rule that no specimens were cultured. When the diagnosis was suspected, specimens have occasionally been put into formalin by mistake when it had been the surgeon's intention to send some for culture, and he must accept responsibility for not informing the nursing staff clearly in advance (author's own experience). Furthermore, it must be said that some surgeons have not appreciated the necessity of sending a good specimen for bacteriological culture as well as for histology. One reason for having all specimens cultured is that it is impossible to be sure of the diagnosis of tuberculosis in every case on histological grounds alone and in 2 cases in this series, when the histology was non-specific, the diagnosis was made by the growth of tubercle bacilli on a culture. One cannot help considering whether in this 5-year period there may have been other cases in which the diagnosis was not made on histological grounds and an operative specimen was not sent for culture. Secondly, without culturing the tubercle bacilli it is impossible to be sure that the lesion has not been caused by one of the atypical mycobacteria. Finally, it is not possible to know the drug sensitivities of the tubercle bacilli if it has not been cultured. Springett (1972) stated that in Asian immigrants with tuberculosis in Birmingham between 1961 and 1963, 3 per cent per year excreted resistant bacilli on the first diagnosis, but between 1968 and 1970 13 per cent excreted resistant bacilli. There is controversy about the value of sensitivity tests in the individual patient—a Leading Article in the *British Medical Journal* (1970a) and Citron (1972) decrying their value, especially as performed outside central specialized laboratories—except in cases which relapse or which have had previous chemotherapy with a recurrence of the disease. However, Bruce (1970) and Marks (1970) strongly disagreed but stated that they believe that the best results are obtained at reference laboratories.

It is apparently disappointing that in only 15 of the 29 operative specimens sent for bacteriological culture in the present series was a growth of *M. tuberculosis* obtained. Medlar, Bernstein, and Steward (1952) and Medlar (1955) found that in 356 solid pulmonary lesions or filled-in cavities which were resected only 20 (5 per cent) grew tubercle bacilli. They concluded that although definite proof of the reasons for this was lacking there were several factors which adversely affected the isolation of the tubercle bacilli under laboratory conditions. First, in any patient who had been submitted to chemotherapy the drugs may have killed the bacilli in the operative specimen. Secondly, as a result of the host-immune response there may be a decreased pathogenicity of *M. tuberculosis*, and this is confirmed by tubercle bacilli being seen on microscopy but being non-pathogenic in guinea-pigs. In closed lesions tubercle bacilli can remain alive for many years without the ability to grow on a culture medium or in a guinea-pig, but the patient in whom this has occurred may relapse many years later. It is suggested that changes in the life process enabling these bacilli to survive hypoxia and the host-immune response render them incapable of reproducing on artificial media. Thirdly, specimens in which there are only a few tubercle bacilli require culturing for 3 months and the routine laboratory period of time of 6 weeks is insufficient. Fourthly, some viable tubercle bacilli are not capable of reproducing on artificial media. Better results may be obtained with the use of fluid media reinforced with glycerol which enhances the growth of sick *M. tuberculosis*. *Mycobacterium bovis* grows better in the absence of glycerol but with the media having added pyruvate (Crofton and Douglas, 1969a), and it is possible that some of the cases of cervical tuberculosis in the present series may have been caused by this organism. Davies (1971) noted that, curiously, caseous material from tuberculous lymph-nodes frequently shows no acid-fast bacilli on a smear or culture, but only suggested that the surgical practice of putting specimens into formalin may be a cause. The figure of 50 per cent of the operative specimens growing a culture of *M. tuberculosis* in the present series compares with the recent results from the Bacteriology Department at St. George's Hospital (Hilson, 1972).

Acknowledgements.—I am grateful to the late Mr. K. H. Taylor for suggesting carrying out this review, and to him and the other surgeons in the High Wycombe group of hospitals for permission to present their cases. I wish to thank Dr. A. O. Robson, Dr. D. A. Leigh, and Professor G. R. F. Hilson for their advice and help, and Dr. C. R. Tribe without whose excellent pathology records this review would have been impossible.

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SIGNIFICANCE OF RECTAL BLEEDING IN DIVERTICULAR DISEASE IN PATIENTS AT ST. MARK'S HOSPITAL

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SUMMARY

The site of the rectal bleeding in diverticular disease was sought by examination of the surgical specimen and found in 28 of 49 cases examined. It was related to the diverticular disease in 9 cases and to other pathological conditions in 19 (39 per cent), 16 of which were polyps. Fourteen of the polyps were demonstrated by preoperative barium-enema examination.

Adequate clinical and radiological examination demonstrated these other colonic conditions preoperatively in most of the patients.

RECTAL bleeding in the presence of known diverticular disease is a difficult clinical problem. The significance of the rectal bleeding is unclear as it is now recognized that non-inflamed diverticula may bleed and that other pathological conditions may be present in the bowel, the diverticular disease being a red herring. The present investigation was undertaken to determine the incidence and nature of these other pathological conditions in patients with diverticular disease in whom there was a preoperative history of rectal bleeding and to see whether any clinical features or investigations will distinguish these patients from those in whom the rectal bleeding is related to the diverticular disease.

Bleeding is usually of two distinct types: minimal and massive. The second variety has been the subject of many communications and will not be considered further.

METHODS

All the cases of sigmoid diverticular disease which had undergone resection at St. Mark's Hospital from 1964 to 1969 were reviewed. The cases in which there was a preoperative history of minimal rectal bleeding were selected. The operative specimens had been specifically examined for a site of the bleeding. The results of these examinations were studied and correlated with the nature of the rectal bleeding and the preoperative diagnosis. Specimens containing malignant neoplasms were excluded as they all had been suspected preoperatively.

RESULTS

Forty-nine specimens (one-third of the specimens of diverticular disease resected over this period) were reviewed. The indication for the resection was to determine whether cancer was present in 27 cases, persistent abdominal pain in 15, and a specific complication of the disease (fistula, abscess, perforation, or previous proximal colostomy) in the remaining 7 patients.

Site of the Bleeding.—In 28 specimens (57 per cent) a site for the bleeding was found. In 9 patients there were ulcerated diverticula, some containing granulations, and no other pathological condition. In the other 19 specimens (an incidence of 39 per cent) the bleeding was from an associated pathological condition (*Table I*). The metaplastic polyp was 1 cm. in diameter, which is unusually large in our experience. The 2 cases of ulcerative colitis were mild and not suspected preoperatively but were confirmed histologically.

Table I.—NATURE OF OTHER PATHOLOGICAL CONDITIONS FOUND IN SIGMOID COLON SPECIMENS

Pathology	*No. of Cases*
Polyps	
Adenomas	13
Hamartomatous	1
Peutz-Jegher's	1
Metaplastic	1
Ulcerative colitis	2
Endometriosis	1

Nature of the Rectal Bleeding.—There was no correlation in the incidence of other pathological conditions in the specimens of patients in whom the rectal bleeding was only seen once or twice and in those in whom it was a more frequent occurrence.

Preoperative Diagnosis.—All the patients had had a double-contrast barium-enema examination preoperatively. Of the 15 patients who showed a polypoid filling defect suggestive of a polyp as well as the diverticular disease, only 1 was found to be a false positive. In 2 patients a polyp, each 7 mm. in diameter, was missed. The 2 cases of ulcerative colitis showed no suggestion of colitis on a roentgenogram. Unfortunately neither patient had had a rectal biopsy.

DISCUSSION

In the patients in whom no source of the rectal bleeding could be found the possibility of bleeding from haemorrhoids exists. It is impossible to tell whether the haemorrhoids were the cause of the bleeding.

Many different opinions have been expressed regarding the significance of minimal rectal bleeding, particularly since the conclusive recognition that uncomplicated diverticula may bleed (Maynard and Voorkees, 1956; Mobley, Dockerty, and Waugh, 1957). Some workers have concluded that other pathological conditions are the cause of bleeding in most cases (Smith, 1951; Gilchrist and Economou, 1955; Scarborough, 1958). Yet Mobley and others

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(1957) found ulceration related to diverticula in over 56 per cent of their cases and felt that more careful examination of specimens would reveal an even higher incidence, and Greene (1957) examined 60 specimens and was unable to find other pathological conditions in any. Noer (1955) demonstrated the closeness of blood-vessels to diverticula, suggesting their vulnerability to trauma. Other workers have been undecided as to the site of the bleeding but stressed the importance of looking for a neoplasm (Lloyd-Davies, 1953; De Cosse and Amendola, 1957; Colcock, 1965). Rigg and Ewing (1966), in reviewing the literature, came to a similar conclusion. Our results agree with the latter findings—associated disease is the source of rectal bleeding in many of these patients but a similar proportion of patients have no demonstrable site despite meticulous examination of operative specimens. Ulcerated diverticula are found in only a small percentage of cases.

Thorough anorectal and barium-enema examinations have demonstrated the presence of polyps in most of the colons which were subsequently found to contain them. The high success rate in detecting these polyps preoperatively is to a large extent due to the excellence of the radiology. If a biopsy of rectal mucosa is included in all suspicious cases most of the other pathological conditions will be detected. The remainder of these cases present a clinical problem. However, since the introduction of the colonoscope it would seem that they would have been accurately diagnosed preoperatively by its use. A patient who has known diverticular disease and a history of rectal bleeding should in our opinion be investigated for the rectal bleeding as if the diverticular disease were not present.

Acknowledgements.—I would like to thank the staff of St. Mark's Hospital, London, for allowing me to study their records, and especially Dr. Basil Morson and Mr. Charles Mann for helpful criticism in the preparation of this paper.

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PRESSURE MEASUREMENTS IN THE CERVICAL PORTION OF THE THORACIC DUCT IN MAN

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SUMMARY

Pressures were measured in the cervical portion of the thoracic duct during a surgical procedure performed to drain lymph in 8 male patients. Cyclic variations depending on respiration were observed. Smaller oscillations in pressure were synchronous with the pulse-rate and result from rhythmic compression of the thoracic duct by the aorta in the thorax. In 2 patients the recordings showed superimposed pressure waves which were independent of breathing and the heart-rate and which are thought to be due to spontaneous contractile activity of the duct.

During the past 4 years we have cannulated the thoracic duct in the neck of 50 patients in terminal chronic renal insufficiency. Usually, lymph-flow in the catheter depends on respiration and is maximal at the end of expiration. However, in some patients gushes of lymph could be observed which were independent of breathing. This suggested a spontaneous contractile activity of the duct. Reports on this subject are scarce and the published results are discrepant. Pflug and Calnan (1968) did not observe peristalsis in the thoracic duct of dogs, and Pomerantz, Herdt, Rockoff, and Ketcham (1963) stated that there was no intrinsic motor activity in the duct of 115 patients undergoing lymphography. On the other hand, in a radiographic study conducted in dogs Browse, Lord, Rutt, and Taylor (1969) described rapid forward movements of the contrast medium which sometimes occur without any detectable changes of pressure gradiants. Nusbaum, Baum, Hedges, and Blakemore (1964) noted segmental contractions of the upper part of the thoracic duct in man, and Kinmonth and Taylor (1956) described spontaneous rhythmic contractions of the duct. These results prompted the present study.

MATERIAL AND METHODS

Eight male patients were studied during a surgical procedure performed to drain the thoracic duct lymph. Their ages ranged from 16 to 49 years. All were in chronic terminal renal insufficiency and were treated by regular haemodialysis. They had been dialysed 2 days prior to operation and were in good physical condition; in particular, there was no sign of cardiac failure and they were in a good nutritional state.

At 7.30 a.m. on the day of the operation 6 of the 8 patients received a premedication consisting of 0·25 mg. of atropine i.m. and 50 mg. of pethidine or 1 ml. of a mixture containing 2·5 mg. of droperidol and 0·0785 mg. of fentanyl per ml.* (*Table I*). Succinylcholine was injected to intubate the patients. After recovery from curarization the patients were allowed to breathe spontaneously in the anaesthetic circuit. Anaesthesia was maintained with a mixture of droperidol and fentanyl and with 2-bromo-2-chloro-1,1,1-trifluoroethane (halothane) and nitrous oxide in 5 cases. Nitrous oxide was not administered in 3 cases, 2 of which received supplements of fentanyl (*Table II*).

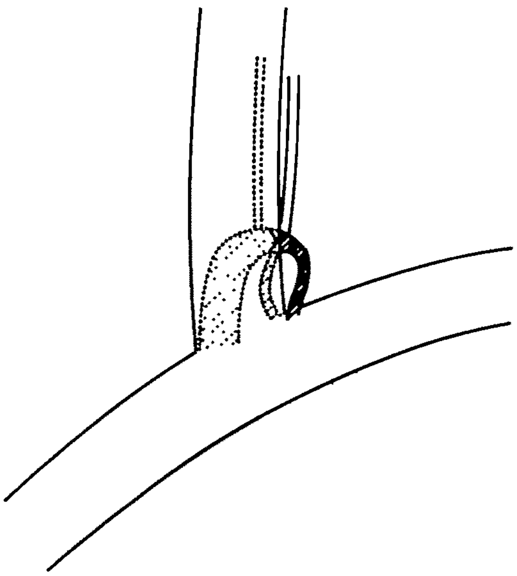

FIG. 1.—Diagram of the terminal portion of the thoracic duct in patient W. The common trunk divides into two branches before entering the main vein.

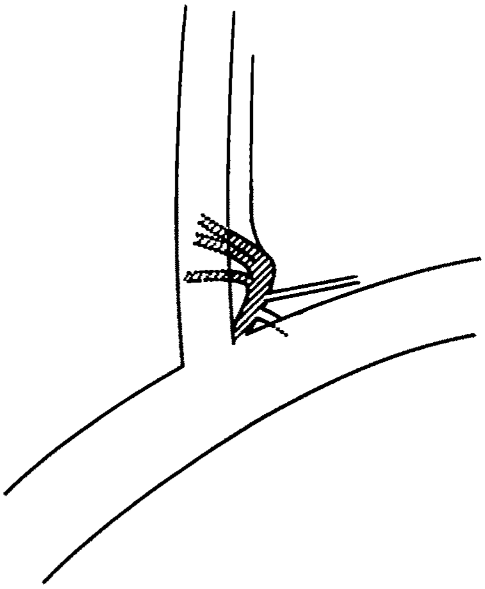

FIG. 2.—Diagram of the terminal portion of the thoracic duct Multiple lymphatic channels join in a common trunk before opening into the vein.

Table I.—DETAILS OF THE DRUGS USED FOR PREMEDICATION

PATIENT	ATROPINE	PETHIDINE	DROPERIDOL + FENTANYL*
T	+	o	+
S	o	o	o
C	+	+	o
B	o	o	o
V	+	+	o
Z	+	+	o
P†	+	+	o
W†	+	o	+

* Thalamonal.
† Patients showing spontaneous activity of the thoracic duct.

The patients were laid supine, the neck being slightly extended and the head rotated to the right. The thoracic duct was approached through a small incision made above the medial extremity of the clavicle. The lymphatic vessels and the veins were dissected sufficiently to allow easy puncture by a small needle. Manipulation of the lymphatic ducts was avoided as much as possible prior to pressure measurements. The location of the lymphovenous junction for each subject is given in *Table III*. Seven of the thoracic ducts ended in a single orifice in the venous system and one duct divided into two branches, both entering the subclavian vein (*Fig.* 1). Nevertheless, in all the cases there was a common channel which usually resulted from the junction of two or more lymphatic vessels (*Fig.* 2). This portion of the duct was punctured with a 25-gauge needle.* Pressures were recorded continuously for several minutes using an Elema or a Sanborn venous strain-gauge transducer. In 5 cases the venous pressure close to the lymphovenous junction was recorded simultaneously. After this procedure the thoracic duct was further dissected and cannulated in order to create a thoracic duct fistula.

RESULTS

Pressure curves in the thoracic duct showed cyclic oscillations with respiration. The highest values were registered during expiration and ranged from +2·6 mm. Hg to +22 mm. Hg, while the lowest occurred at the peak of inspiration and ranged from −5 mm. Hg to +17 mm. Hg (*Table IV*). Smaller oscillations up to 4 mm. Hg were synchronous with the heart-rate and are probably due to compression of the thoracic duct by the aorta in the thorax (*Fig.* 3). In 6 of our 8 patients no other pressure variations were observed. In 2 individuals superimposed pressure waves were seen which were independent of respiration and the pulse-rate. In the first patient they occurred every 5–7 seconds at the beginning of the recording (*Fig.* 4). A few seconds later their frequency had dropped to 4–5 per minute. In the second patient autonomic pressure waves were noted every 12–15 seconds. No contraction of the thoracic duct was observed in the neck throughout the procedure.

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* Thalamonal, Janssen Pharmaceutica.

* Minicath 25 infusion set, Deseret.

The thoracic duct pressure varies with the venous pressure, higher values being recorded when the venous pressure is elevated (*Table IV*). However, various patterns can be observed, as was shown in 5 patients where the venous pressure and the thoracic duct pressure were measured simultaneously. In 2 cases the thoracic duct was continuously higher than the venous pressure (*Fig.* 5). One subject had a higher pressure in the thoracic duct than in the adjacent vein during expiration, but at the peak of inspiration the gradient was inverted and the difference between the two pressures amounted to as much as 7 mm. Hg (*Table IV*). Nevertheless, no venous reflux was noted in the thoracic duct, demonstrating that the valves at the lymphovenous junction were in this case perfectly competent with very low pressures. Finally, in the 2 patients where autonomous activity of the thoracic duct was found the pressure curves showed, besides the peaks of spontaneous contractile activity, higher values in the thoracic duct than in the vein during inspiration but lower values during some of the expiration movements (*Fig.* 4).

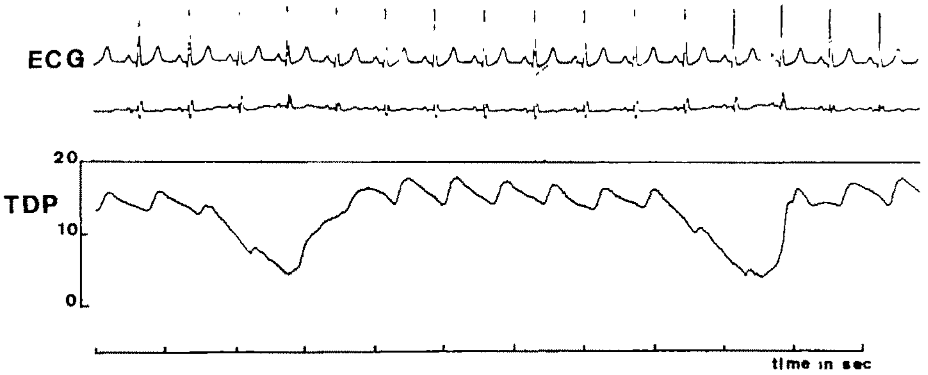

FIG. 3.—Electrocardiogram (ECG) and thoracic duct pressure (TDP) tracings showing cyclic oscillations due to breathing and smaller variations which are synchronous with the heart-rate. Pressure values are given in mm. Hg.

Table II.—DETAILS OF THE DRUGS USED FOR ANAESTHESIA

PATIENT	SUCCINYLCHOLINE	METHOHEXITAL	DROPERIDOL + FENTANYL*	2-BROMO-2-CHROMO-1,1,1-TRIFLUOROETHANE	NITROUS OXIDE	FENTANYL
T	+	+	+	+	0	0
S	+	+	+	+	+	0
C	+	+	+	+	+	0
B	+	+	+	+	+	0
V	+	+	+	+	0	+
Z	+	+	+	+	+	0
P†	+	+	+	+	+	0
W†	+	+	+	+	0	+

* † *See Table I.*

Table III.—LOCATION OF THE LYMPHOVENOUS JUNCTION

Patient	*Location of the Lymphovenous Junction*
T	Subclavian vein
S	Angulus venosus
C	Subclavian vein
B	Angulus venosus
V	Angulus venosus
Z	Angulus venosus
P†	Internal jugular vein
W†	Subclavian vein (2 orifices)

† *See Table I.*

Table IV.—MINIMUM AND MAXIMUM VENOUS AND THORACIC DUCT PRESSURES

PATIENT	VENOUS PRESSURE (mm. Hg)	THORACIC DUCT PRESSURE (mm. Hg)
T‡	+2, +19·2	+ 3 5, +19·2
S	+7, ±12	+17, +21
C	+18	+14 5, +22
B	−2, + 2	0, + 3
V	+2, +16	− 5, +17
Z	—	0, + 2 6
P†	−4 4, + 7·8	+ 2, +12·4
W†	+2 5, + 8	− 0·4, +11

† *See Table I.*
‡ Venous pressure and thoracic duct pressure were measured successively.

DISCUSSION

Several authors have cannulated the thoracic duct in the neck and determined maximum end-pressures. Shafiroff and Kau (1959) reported values ranging from 10 to 28 cm. saline, while Werner (1965) obtained figures which ranged from 6 to 28 cm. Dumont and Mulholland (1962) and Dumont, Clauss, Reed, and Tice (1963) measured pressures of 15–70 cm. saline in cirrhotic patients, 17–80 cm. in patients in cardiac failure, and 6–15 cm. in normal individuals. These figures do not necessarily represent the true values in the intact thoracic duct. Indeed, because of the cannulation the thoracic duct is disconnected from the venous system. The possible influences of venous pressure and the lymphovenous junction are therefore suppressed. Dumont and Mulholland (1962) found side-pressures of 4–6 cm. saline in the unopened duct. The higher values that we noted in some patients are probably due to an increased extracellular fluid volume 2 days after dialysis, as is suggested by the concomitant elevated venous pressure.

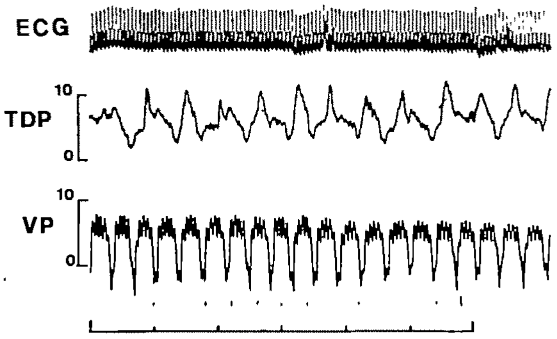

FIG. 4.—Electrocardiogram, thoracic duct pressure, and venous pressure (VP) tracings showing autonomous pressure waves in the thoracic duct which are independent of respiration and the heart-rate. Pressure values are given in mm. Hg. Time is divided in to units of 10 seconds.

Oscillations due to respiration and aortic percussion have been described in the pressure curves of dog thoracic ducts (Pflug and Calnan, 1968; Browse and others, 1969). No pressure variation due to intrinsic contraction of the duct was noted in the anaesthetized animals. On the contrary, we observed spontaneous contractile activity in 2 patients, thus confirming previous studies in man (Kinmonth and Taylor, 1956; Nusbaum and others, 1964; Edwards, Gough, Kinmonth, and Pierce, 1965). The question remains why only 2 of our 8 subjects showed autonomous activity of their thoracic duct. Anaesthesia could be incriminated; however, it can be seen from *Tables I* and *II* that there was no significant difference in the drugs which were administered to both groups of patients. Tilney and Murray (1967) measured end thoracic duct pressures in 2 waking patients and found no intrinsic activity in 1. From the present data pressure in the thoracic duct and eventual stretching of its muscular fibres do not seem to be determinant factors (*Table IV*). Increase in flow and variations in lymph biochemical content could be responsible factors; these are commonly seen after a meal. Our patients had all fasted for 12 hours before cannulation, but some surgeons administer milk or cream prior to operation in order to visualize the lymphatic vessels better. This could explain the fact that some authors (Sharpey-Schafer and Kinmonth, 1957; Edwards and others, 1965) observed constant waves of contractions. This possibility has not been explored in the present study.

From our data it is impossible to draw any conclusion on the exact nature of the autonomic activity of the thoracic duct: whether it is peristalsis or segmental contractions (Nusbaum and others, 1964; Edwards and others, 1965). It is not surprising that we did not observe any contraction in the neck. Kausel, Reeve, Stein, Alley, and Stranahan (1957) have shown that the amount of muscular fibres in the thoracic duct wall is reduced in the proximal part. The absence of any visible motor activity in the neck does not exclude the possibility of peristaltic waves in the thoracic portion of the duct.

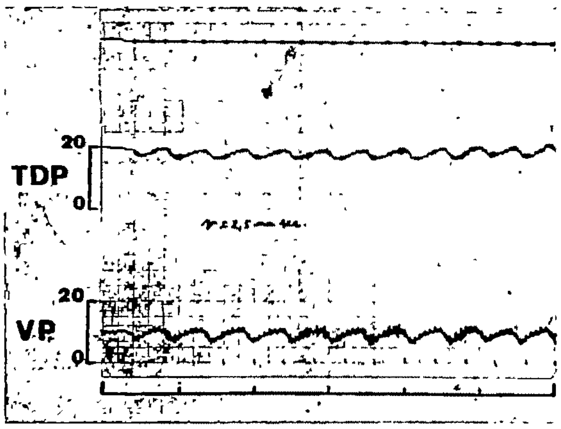

FIG 5.—Thoracic duct pressure and venous pressure tracings showing parallel variations. Units are as in *Fig*. 3.

Finally, blood reflux in the thoracic duct was seen in all except 2 cases. Pflug and Calnan (1968) stated that the valves at the lymphovenous junction close when the vein is distended by an increase in pressure. However, 1 patient in the present series had a negative duct pressure at the peak of inspiration while venous pressure remained positive. There was no blood reflux in this case. Consequently, it must be admitted that the valves were perfectly competent and that their closure occurred during the phase of lowest venous pressure. Further information is needed to elucidate the exact mechanism of the valves of the lymphovenous junction.

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RENOVASCULAR HYPERTENSION: THE PLACE OF RENAL AUTOTRANSPLANTATION

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SUMMARY

Six cases of hypertension due to renal artery stenosis were treated by renal autotransplantation, with cure in 4 cases and significant improvement in the other 2 cases. The procedure allows reconstruction of complex arterial lesions before revascularization, and should be preferred to nephrectomy whenever technically possible.

THE place of surgery in the management of hypertension of renovascular origin is now well established (Smith, Muller, and Beckwith, 1968; Foster, Oates, Rhamy, Klatte, Burko, and Michelakis, 1969; Buda, McAllister, and Sommers, 1970), but the standard surgical procedures of by-pass grafting or thrombo-endarterectomy have been performed almost entirely for lesions involving the main renal artery itself. Where the disease process has affected more distal renal vessels the usual alternative has been nephrectomy. The condition is frequently bilateral (Foster and others, 1969), and even when this is not the case primarily, the other kidney has usually been affected secondarily by hypertensive vascular disease. Thus, every effort should be made to avoid nephrectomy and to preserve functioning renal tissue. When disease of major vessels occurs beyond the bifurcation of the main renal artery, or where there are multiple arteries supplying the affected kidney, we believe that correction of the lesion can be achieved most satisfactorily by removal of the kidney, correction of the defect, and revascularization by anastomosis to the pelvic vessels of the same side. Five such cases have been treated by renal autotransplantation over a 3-year period, and the procedure has proved so satisfactory that it has been applied to a sixth patient suffering from a less complicated stenosis of the renal artery.

CASE REPORTS

Details of the 6 patients are summarized in *Table I.*

Table I.—SUMMARY OF THE DETAILS OF THE 6 CASES WITH RENOVASCULAR HYPERTENSION IN THE PRESENT SERIES

CASE	INITIAL BLOOD-PRESSURE	INTRAVENOUS PYELOGRAM	DIVIDED FUNCTION STUDIES	RENAL VEIN RENIN RATIO*	LESION	DATE OF OPERATION	RECENT BLOOD-PRESSURE	THERAPY
1	260/170	+	+	Not performed	Fibromuscular hyperplasia	13 March, 1969	130/80	Nil
2	230/155	+	Not performed	1·7	Fibromuscular hyperplasia	23 April, 1970	130/80	Nil
3	165/110	+	Not performed	1·75	Congenital stenosis; secondary thrombosis	14 June, 1970	120/70	Nil
4	230/150	Non-function of right kidney	Not performed	1·7	Atheroma	3 Feb., 1971	145/75	Prindolol, 30 mg. per day
5	210/120	+	Not performed	1·7	Atheroma	26 Jan., 1972	140/70	Methyldopa, 500 mg. per day
6	220/130	+	+	1·1	Fibromuscular hyperplasia	19 Aug., 1971	150/90	Nil

* The ratio of plasma renin measured in blood-samples taken simultaneously from both renal veins. A ratio of 1 : 5 was considered positive (Pawsey, Vandongen, and Gordon, 1971).

Case 1.—This patient has been reported in detail previously (Clunie, Murphy, Lukin, Nicoll, and Marsden, 1971).

C. N., a 25-year-old woman, presented in late 1968 with severe hypertension which was poorly controlled by medical therapy, and investigations revealed a functional stenosis of the right renal artery owing to fibromuscular hyperplasia. Both kidneys were explored through a right paramedian incision on 13 March, 1969. The stenosis of the right renal artery extended to the point of bifurcation near the hilum, and the lower pole of the kidney was supplied by a small accessory vessel. Direct reconstruction of the main artery was not considered possible because of the extent of the disease, and it was felt that the vessels beyond the bifurcation were too small to allow for adequate by-pass. Autotransplantation was therefore performed. The two renal arteries were divided, the larger at the point of bifurcation where it was macroscopically free from disease, and the renal vein was divided flush with the inferior vena cava. End-to-end anastomoses were carried out between the renal arteries and the cut ends of the mobilized right internal iliac artery, which had been divided just distal to its first division. The renal vein was anastomosed end to side to the common iliac vein. The ureter was gently freed in its middle third without disturbing its blood-supply, and was allowed to take up a redundant course without reimplantation. There was immediate control of the patient's hypertension, and the patient has remained normotensive without further therapy in the 4 years since operation.

Case 2.—K. D., a 25-year-old woman, was seen in early 1970 with severe hypertension, which was poorly controlled by medical therapy. Investigations revealed a functional stenosis at the bifurcation of the right renal artery as a result of fibromuscular hyperplasia. Autotransplantation was carried out on 5 Feb., 1970, the renal artery anastomosis in this case being carried out well into the hilum beyond the bifurcation of the artery because of the extent of the disease. The blood-pressure remained slightly elevated for 1 year following operation, but 3 years later it is within normal limits without therapy.

Case 3.—K. D., a 14-year-old boy, was found to have hypertension at a routine medical examination in 1970. The presence of a functional congenital stenosis at the origin of the left renal artery with a marked ureteric collateral supply was demonstrated (*Fig.* 1). On 10 June, 1970, direct reimplantation of the artery into the aorta was carried out, with an immediate reduction of the blood-pressure to normal. However, on 13 June there was a recrudescence of the hypertension, and an aortogram showed occlusion of the renal artery with marked collateral flow. At a re-exploration thrombus was found adherent to and extending beyond the bifurcation. Since there was some dilatation of the duplex right collecting system, it was felt important to preserve function in the left kidney of this young patient. Autotransplantation was therefore performed, the kidney in this instance being inverted since the vascular anastomosis lay most conveniently in this position. The blood-pressure was immediately controlled and has remained within normal limits in the 3 years since operation. An intravenous pyelogram taken 2 years after operation demonstrated satisfactory function without dilatation of the collecting system of the transplanted left kidney in spite of the unusual position (*Fig.* 2).

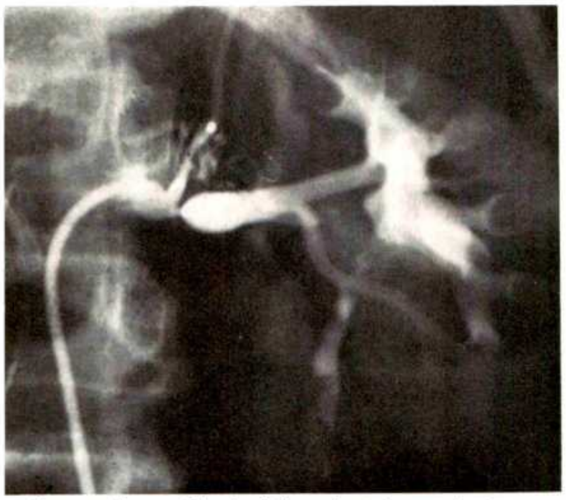

FIG. 1.—*Case* 3. Selective left renal arteriogram showing a congenital stenosis with post-stenotic dilatation.

Case 4.—H. H., a 59-year-old man, had been treated for mild hypertension for some years before his emergency admission with malignant hypertension in December, 1970. An intravenous pyelogram at that time showed no function of the right kidney and an aortogram revealed marked atheroma of the aorta with no apparent right renal artery. The serum creatinine was raised, and it was felt important to attempt to restore function to the right kidney, which was presumed to be viable and to be primarily responsible for the hypertension and its exacerbation. At exploration on 3 Feb., 1971, the right kidney was found to be atrophic, but there was a well-developed ureteric collateral circulation. The renal artery was completely occluded with recent thrombus up to and beyond its bifurcation. Autotransplantation was carried out with a satisfactory appearance of the kidney on revascularization. Hypertension has been easily controlled medically in the 2 years since operation, and the serum creatinine has returned to normal levels. An intravenous pyelogram and an isotope scan taken 1 year after operation showed satisfactory function in the transplanted kidney.

Case 5.—J. P., a 37-year-old woman, presented with poorly controlled hypertension due to an atheromatous plaque at the origin of the larger of two left renal arteries. Autotransplantation was carried out on 20 Jan., 1972, with good immediate control of hypertension. The blood-pressure gradually rose in the month after operation but is now easily controlled within normal limits by medical therapy.

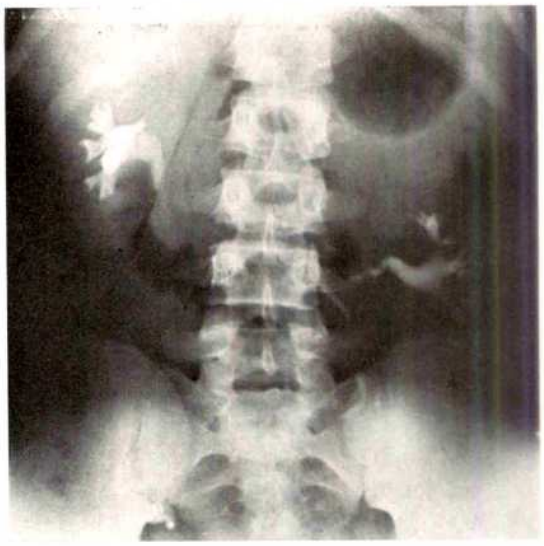

FIG. 2.—*Case* 3. Intravenous pyelogram taken 1 year post-operatively showing the redundant left ureter without proximal dilatation, and the duplex right collecting system.

Case 6.—G. H., a 50-year-old woman, presented with uncontrolled severe hypertension. Although the renal vein renin ratio was not significantly altered (*Table I*), divided renal function studies indicated a functional right renal artery stenosis. Arteriography demonstrated a fibromuscular hyperplasia of the right renal artery. This lesion would normally have been treated by by-pass grafting from the aorta, but autotransplantation was considered to be preferable in the light of experience with the previous cases. This procedure was performed on 19 Aug., 1971, with immediate and persisting control of the hypertension without further therapy in the 18 months since operation.

DISCUSSION

Autotransplantation of the kidney was first performed by Hardy (1963) for a complicated ureteral injury involving a single kidney, the shortened ureter being reimplanted into the bladder after vascular anastomosis in the pelvis. A similar case was reported by Marshall, Whitsell, McGovern, and Miscall (1966), and the technique has also been used in a patient with multiple ureteral tumours (Murphy, Staubitz, and Kenny, 1971). The procedure was first performed for the relief of renovascular hypertension by Woodruff, Doig, Donald, and Nolan in 1963, and later reported briefly in 1966 following descriptions of similar cases by

Marshall and others (1966) and Serrallach-Mila, Paravisini, Alberti, Mayol-Valls, Casellas, Torner-Soler, and Nolla-Panades (1966). Further single cases have been described since (Kuss, 1967; Kauffman, Alferez, and Vela Navarette, 1969; Whitsell, Goldsmith, and Nakamura, 1970; Clunie and others, 1971). Gil-Vernet, Caralps, Revert, Vidal, and Carretero (1969) reported 5 cases of renovascular hypertension treated in this fashion with excellent early results.

The operative technique used in the present 6 cases has been described previously (Clunie and others, 1971) and presents no difficulty for surgeons familiar with the operation of renal allotransplantation. In order to minimize ischaemic damage the kidneys were perfused with 200–300 ml. of solution C3 (Collins, Hartley, and Clunie, 1971) at 4° C. from a height of 1 m., the ureter being lightly clamped to prevent escape of this high potassium content solution into the general circulation. None of the operations in this series involved renal ischaemic intervals of greater than 40 minutes, and the degree of protection against ischaemic damage reported by such a cold flush in renal allotransplantation (Hartley, Collins, and Clunie, 1971) suggests that this simple procedure is preferable to the more complex continuous perfusion proposed by Belzer, Keaveny, Reed, and Pryor (1970) in reconstruction prior to renal autotransplantation. Reimplantation of the ureter into the bladder appears to be unnecessary in the correction of renal artery stenosis, and the ureter has simply been freed while retaining its normal blood-supply in all the reported cases. There has been no evidence of dilatation of the collecting system in the 6 cases reported here, although long-term follow-up is clearly necessary before such a complication can be excluded.

The procedure has proved so simple technically and so satisfactory in terms of immediate and late results in the control of hypertension that it may have a wider application. It allows reconstruction of extensive lesions involving the bifurcation of the renal artery, and there can be no doubt that it is preferable to nephrectomy whenever it is technically feasible. Revascularization with a by-pass vein autograft running from the aorta to the distal renal artery is at present the standard procedure for the relief of renovascular hypertension. In cases of atheroma where the aorta may well be extensively involved by the disease, surgery involving the aorta itself is clearly hazardous and we believe that autotransplantation offers significant advantages for this reason. With the increasing numbers of surgeons familiar with techniques of renal allotransplantation, we suggest that renal autotransplantation may in time come to be the procedure of choice in the surgical treatment of the majority of cases of renovascular hypertension.

Acknowledgements.—We wish to thank our colleagues for referral of patients and Dr. E. R. Jay of the Department of Radiology, Princess Alexandra Hospital, for the radiological investigations in these patients.

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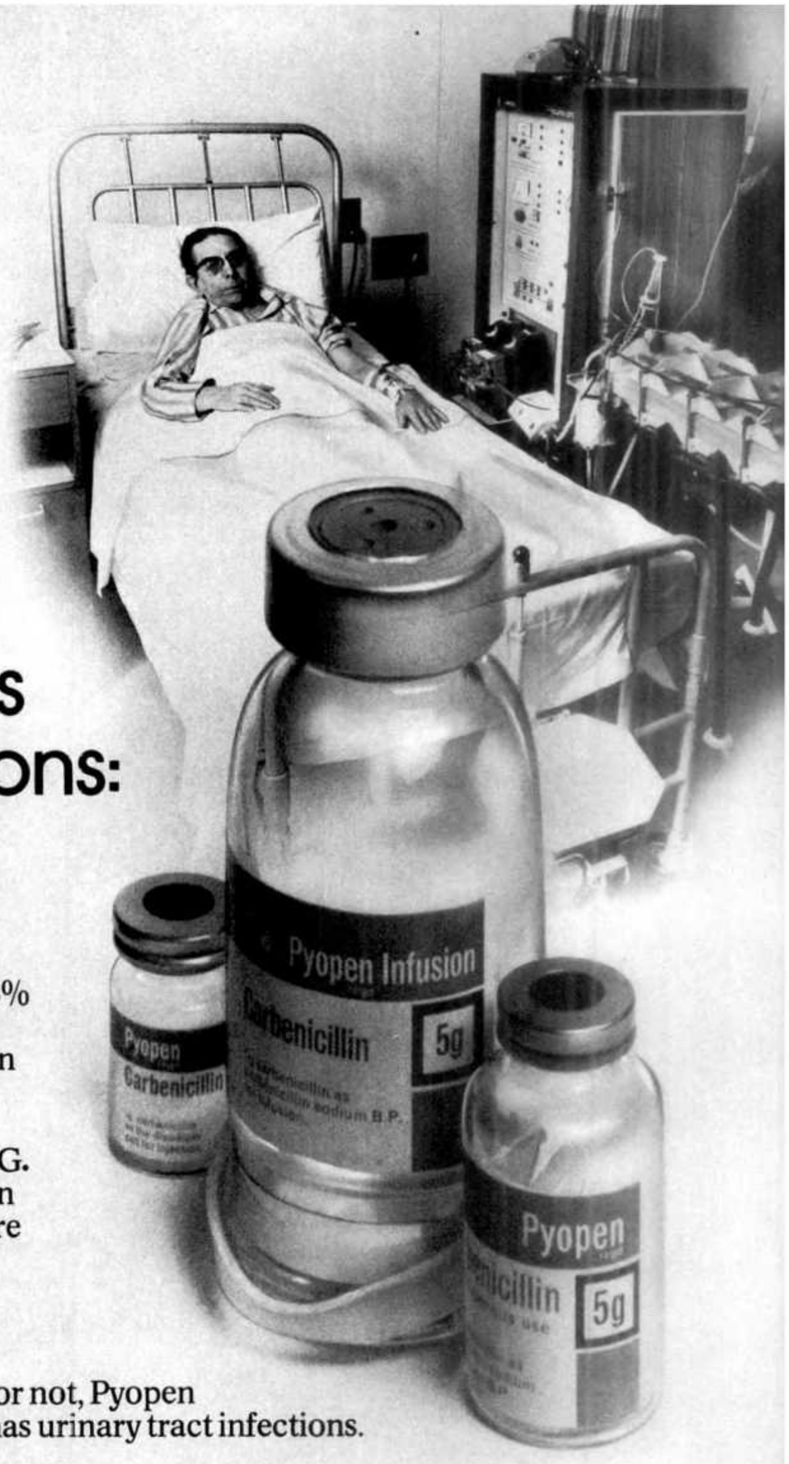

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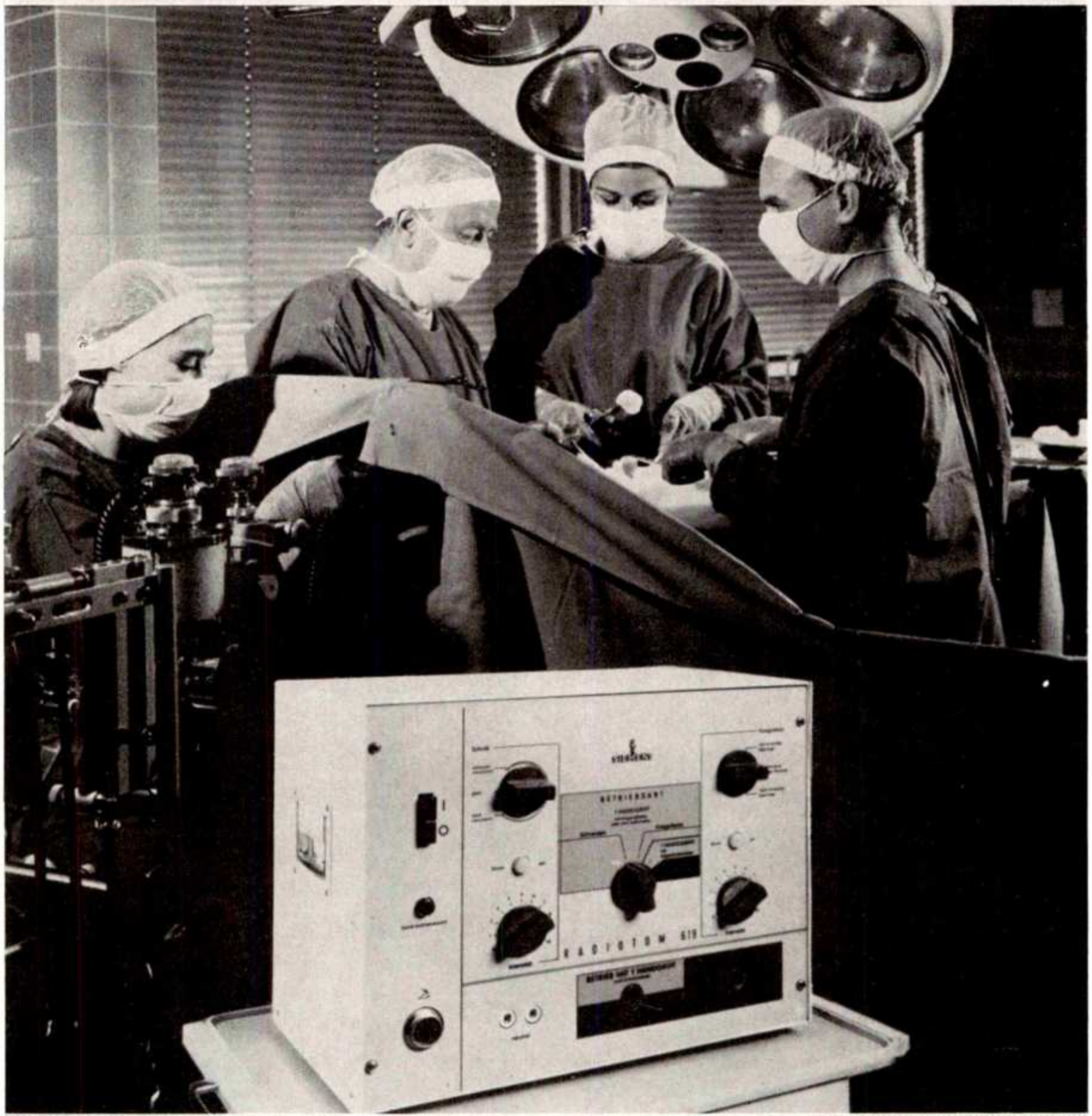

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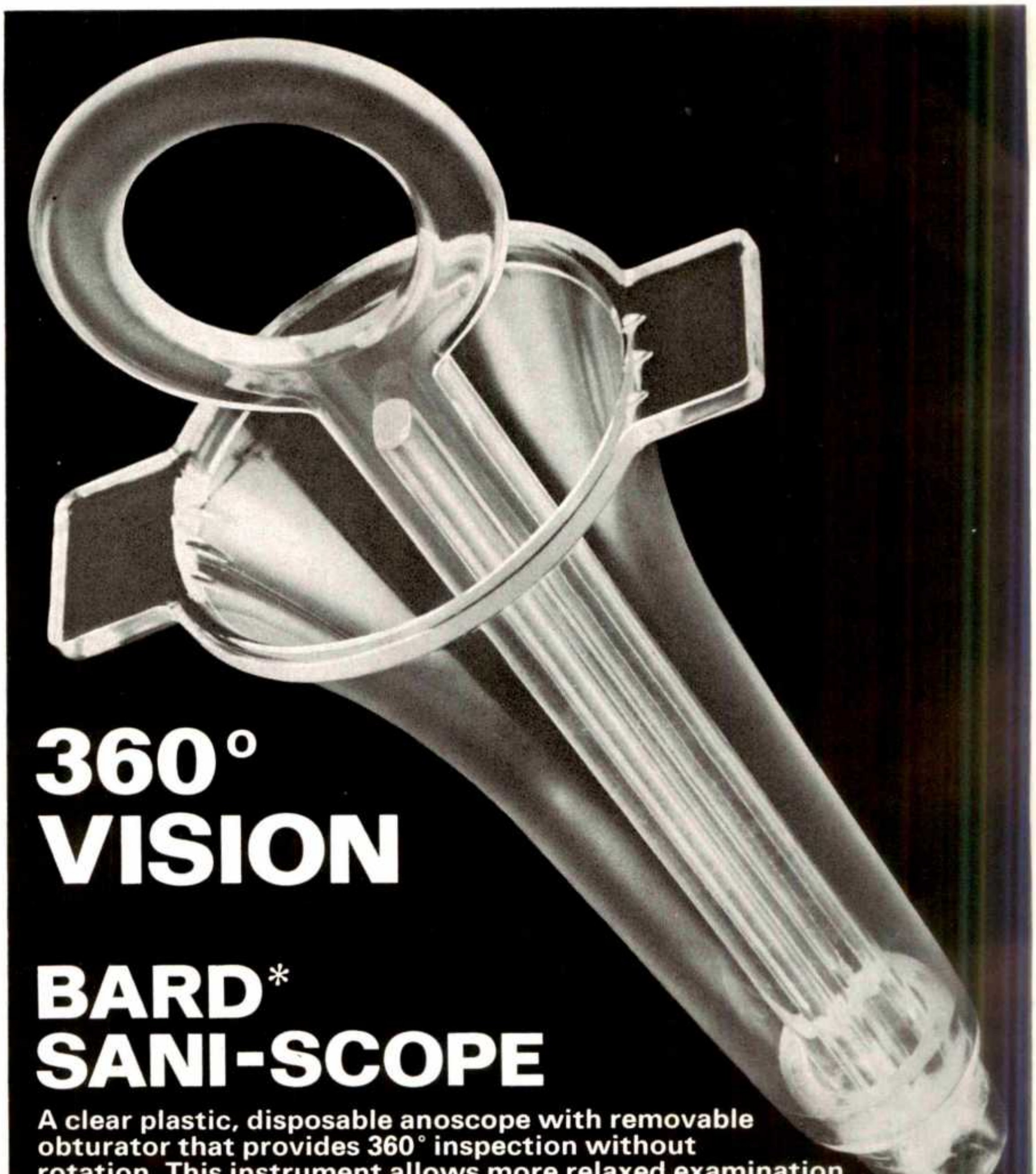

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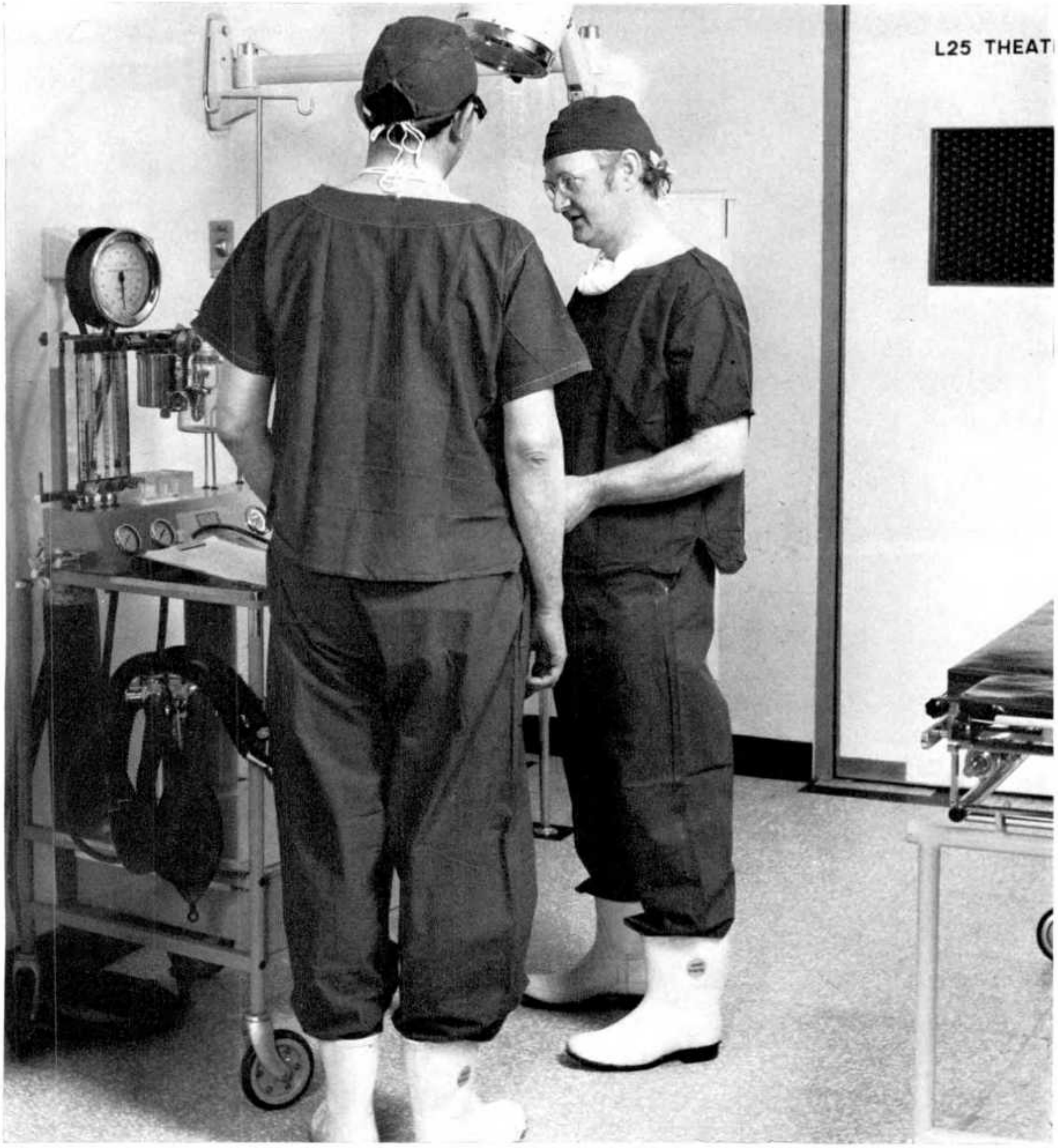

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THE SURGICAL MANAGEMENT OF PRIMARY HEPATOCELLULAR CARCINOMA IN UGANDA

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SUMMARY

Hepatocellular carcinoma is a common tumour in Uganda. Thirty-six of 120 patients with hepatoma admitted during a 2½-year period were submitted to surgery. Major hepatic resections were performed in 10 patients and a further 10 cases had placement of a hepatic artery catheter for regional infusion chemotherapy. In the surgically resected and regionally infused patients survival was improved compared with those receiving either systemic chemotherapy or no treatment. Hepatic resection offers a chance of cure for a small minority of patients with hepatoma, whilst regional chemotherapy via a directly placed arterial catheter at the time of exploratory laparotomy may benefit others and is being further evaluated by a controlled trial.

THE treatment of liver cancer by partial hepatic resection is not new (Keen, 1899). Only in recent years, however, has this approach been widely practised following advances in the understanding of hepatic anatomy and physiology (Hobsley, 1958; McDermott, Greenberger, Isselbacher, and Weber, 1963), together with improvements in anaesthesia and intensive care of patients. Treatment by partial hepatic resection appears to have met with limited success, whereas untreated hepatocellular carcinoma usually runs a rapidly fatal course (Foster, 1970).

In Uganda hepatocellular carcinoma is common; in a large part of the country it is the second most frequently encountered cancer in males (Davies, Knoweldon, and Wilson, 1965). The following report is based on patients with this tumour who were treated surgically at Mulago Hospital during a 2½-year period since the opening of the Uganda Cancer Institute in 1969.

MATERIAL AND METHODS

One hundred and twenty patients with primary hepatocellular carcinoma were admitted to the Uganda Cancer Institute between August, 1969, and March, 1972. On admission all the patients were evaluated from their history, physical examination, chest radiographs, radiographs of painful bones, complete blood-count, liver-function studies, blood-clotting studies, blood-urea, total proteins and protein electrophoresis, α-fetoprotein, and liver scan.

After evaluation, 36 patients who were thought to have potentially resectable lesions were submitted to laparotomy. Preoperative coeliac axis arteriography was carried out in the majority of this group. There were 24 males and 12 females with a mean age of 38 years (range 16–65 years). The diagnosis of hepatocellular carcinoma was confirmed histologically in all but 2 patients who have been excluded from further discussion. The subsequent management of the remaining 34 patient is shown in *Table I*. Partial hepatic resection was carried out in 10 patients. Ten patients with unresectable tumours had a catheter placed in the hepatic artery for subsequent infusion with anti-tumour drugs. The other patients were treated by either systemic chemotherapy or a placebo.

OPERATIVE TECHNIQUES

The techniques of major hepatic resection and hepatic artery catheterization are well documented (McDermott and Ottinger, 1966; Pack and Islami, 1970; Watkins, Khazei, and Nahra, 1970). Those used in the present series are briefly summarized.

Table I.—MANAGEMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA WHO WERE ADMITTED TO THE UGANDA CANCER INSTITUTE BETWEEN AUGUST, 1969, AND MARCH, 1972

	No. of Patients
Patients admitted with hepatocellular carcinoma	120
Patients submitted to surgery	36
Subsequent treatment of 34 surgical patients:—	
Partial hepatic resection	10
Hepatic artery catheter placement	10
Systemic chemotherapy	7
None	7

1. Partial Hepatic Resection.—Left hepatic lobectomy was carried out through an upper abdominal incision. The left lobe of the liver was mobilized and the left branches of the hepatic artery, portal vein, and hepatic duct were ligated in the porta hepatis. The left hepatic vein and sometimes the middle hepatic vein were ligated and the liver was resected through a line joining the inferior vena cava superiorly and the gall-bladder fossa inferiorly. For division of the liver substance cutting diathermy or finger dissection was used with additional ligature of vessels as necessary. The cut surfaces of the liver were approximated and, where possible, re-peritonealized by utilizing the falciform ligament.

For right hepatic lobectomy an extended lobectomy or a thoraco-abdominal approach was used. An upper abdominal incision was made initially to assess the extent of the tumour, and if deemed resectable the incision was extended into the chest through the eighth or seventh intercostal space and the diaphragm was incised radially to the inferior vena cava. After mobilization of the right lobe and division of the cystic duct, right hepatic duct, and right hepatic vessels, liver resection was carried out in the line of the gall-bladder fossa in a right lobectomy or just medial to the falciform ligament in an extended resection.

2. Hepatic Artery Catheterization.—A careful dissection was made to expose and identify the common hepatic artery and its right and left branches and the gastroduodenal artery. A fine Teflon catheter (external diameter 1·0 mm.) was placed in the hepatic artery towards the coelic axis via an arteriotomy in the gastroduodenal vessel. The extent of perfusion was checked by injecting fluorescein through the catheter and observing the distribution of the dye under ultra-violet light. Adjustments were made in the position of the catheter until an optimum distribution was obtained. On occasions when it was not possible to identify the gastroduodenal artery the catheter was inserted into the right gastro-epiploic vessel. In 1 case where the anatomical variation of a replaced left hepatic artery was encountered the splenic artery was utilized. Infusion was carried out by gravity or, more recently, by means of a Watkins Chrono-Fusor (U.S. Catheter & Instrument Corp.) which delivers 5 ml. of infusate in 24 hours.

RESULTS

Table II shows the duration of symptoms before diagnosis and survival in the 34 patients who underwent surgical exploration. The median duration of symptoms was similar in all the groups. The median survival of the patients whose tumour was resected was 7 months and that of the other groups between 1 and 1·5 months. However, of the 10 patients who underwent hepatic artery catheterization only 6 actually received chemotherapy and in these patients the median survival was 6 months.

Table II.—LENGTH OF HISTORY BEFORE DIAGNOSIS AND DURATION OF SURVIVAL AFTER SURGICAL EXPLORATION

TREATMENT	NO. OF PATIENTS	LENGTH OF HISTORY (mth.)		NO. OF PATIENTS STILL ALIVE	SURVIVAL AFTER EXPLORATION (mth.)	
		Median	Range		Median	Range
Resection	10	3·0	1–7	3	7·0	0–34
Hepatic artery catheterization		2·5	1–24			
a. All patients	10			1	1·5	0–22
b. Patients who received chemotherapy	6			1	6·0	1·5–22
Systemic chemotherapy	7	2·0	1–9	1	1·0	0·25–4
None	7	3·0	0·5–12	1	1·0	0–11

Table III.—DETAILS OF THE 10 PATIENTS WHO UNDERWENT HEPATIC RESECTION

AGE AND SEX	SITE OF LESION	PROCEDURE	COMPLICATIONS	RESULT
18 M.	Right lobe; superficial nodule in the left lobe	Right lobectomy; wedge resection of the nodule on the left side	Jaundice; pleural effusion	Alive 29 months after surgery
53 M.	Right lobe	Right extended lobectomy	—	Died on first postoperative day
59 M.	Right lobe	Right lobectomy	—	Operative death
31 M.	Right lobe	Right lobectomy; right extended lobectomy 4 months after first operation	Subphrenic abscess	Died 18 months after surgery
37 M.	Right lobe	Right lobectomy	Pleural effusion; subphrenic abscess	Died 4 months after surgery
40 F.	Left lobe	Left lobectomy	Jaundice; pleural effusion	Died 10 months after surgery
45 M.	Left lobe	Left lobectomy	Portal hypertension and haematemesis 2 years after lobectomy; gastric transection performed	Alive 34 months after surgery
28 M.	Left lobe; two nodules in the right lobe	Left lobectomy; wedge resection of one nodule in the right lobe	Jaundice; chest infection; wound infection	Died 6 months after surgery
22 F.	Right lobe	Right lobectomy	Hepatic failure	Died 2 weeks after surgery
33 M.	Caudate lobe	Caudate lobectomy	—	Alive 9 months after surgery

The main features of the 10 patients who underwent resection are summarized in *Table III*. The right lobe was resected in 6 patients and the left in 3. The tumour was confined to the caudate lobe in 1 patient. Two patients had apparently isolated tumour nodules in the remaining lobe, and these were removed by wedge resection. There were 2 operative deaths and a third patient died in the early postoperative period. Three patients are still alive—9, 29, and 34 months after surgery.

Ten patients who were found at laparotomy to have unresectable tumours had placement of a catheter into the hepatic artery (*Table IV*). There were 3 deaths in the early postoperative period. Two other patients did not receive chemotherapy by this route as the catheter was found to be unsatisfactory, although 1 subsequently received treatment by a percutaneously placed catheter. The percutaneous method was used to give further courses of chemotherapy in 3 patients after the operatively placed catheter blocked. Catheter position and patency were maintained for up to 1 month with a mean of 13 days.

Thus, 6 patients received intra-arterial chemotherapy in the form of dichloromethotrexate (DCM) at a dose of 10 mg. per m.^{2} for 7–10 days according to toxicity.

Table IV.—DETAILS OF THE 10 PATIENTS WHO UNDERWENT HEPATIC ARTERY CATHETERIZATIONS

AGE AND SEX	PLACEMENT OF CATHETER	NO. OF COURSES OF CHEMOTHERAPY	COMPLICATIONS	RESULT
40 M.	Via right gastro-epiploic artery	0	—	Died on third post-operative day
26 F.	Via gastroduodenal artery	2	Diarrhoea; catheter removed after 3 weeks; subsequent percutaneous catheterization and infusion	Died 22 months after surgery
24 M.	Via right gastro-epiploic artery	0	Diarrhoea; catheter removed after 5 days as distribution unsatisfactory	Died 5 weeks after surgery
50 M.	Via splenic artery	0	Ascites; oliguria	Died on third post-operative day
26 F.	Via gastroduodenal artery	0	Acute tubular necrosis	Died on first post-operative day
40 M.	Via gastroduodenal artery	3	Catheter removed after 9 days because of infection; subsequent percutaneous catheterization and infusion (× 2); left subphrenic abscess	Died 8½ months after surgery
27 M.	Via gastroduodenal artery	3	Catheter removed after 1 month; subsequent percutaneous catheterization and infusion (× 2)	Died 7 months after surgery
52 M.	Via gastroduodenal artery	1	Catheter removed after 2 weeks; developed pulmonary metastases	Died 6 weeks after surgery
28 M.	Via right gastro-epiploic artery	3	Catheter removed after 10 days as not in position; subsequent percutaneous catheterization and infusion (× 3)	Died 5 months after surgery
26 F.	Via gastroduodenal artery	1	Catheter removed after 8 days as not in position	Alive 6 weeks after surgery

Of the remaining 14 patients with unresectable tumours, 7 received systemic chemotherapy in the form of DCM,* CCNU,† or a combination of BCNU,‡ and 5FU,§ and 7 received no treatment. There were no responses in the sytemically treated group and no increase in survival compared with untreated patients (*Table II*).

DISCUSSION

In assessing the results of treatment in hepatocellular carcinoma the survival after surgical exploration may be compared with the natural history of the disease from diagnosis to death in untreated patients (*Table II*). In the present series patients whose tumour was resected survived considerably longer than those receiving no treatment (median, 7 months and 1 month respectively), as did those who received intra-arterial chemotherapy (median, 6 months). Since no patient who succumbed within 1 month of catheter placement received chemotherapy, early postoperative deaths are automatically excluded from this group. These figures suggest a favourable response to surgery and regional infusion chemotherapy. This is in contrast to systemic chemotherapy which has, so far, proved unsuccessful (Chan, 1967; Geddes and Folkson, 1970; Vogel, Adamson, Devita, Johns, and Kyalwazi, 1972). In Chan's (1967) series of 108 cases of hepatoma the patients who were treated surgically had a mean survival of 22·5 months compared with 0·5 month for those who were untreated. Admittedly these figures, as in the present series, are biased in that patients who underwent resection had more limited disease than the untreated patients or those receiving other forms of treatment. However, results expressed in this way fail to emphasize patients who are still alive. *Fig.* 1 is a life-table analysis for the 34 patients who underwent surgical exploration in the present series and clearly shows the superior results of surgical resection.

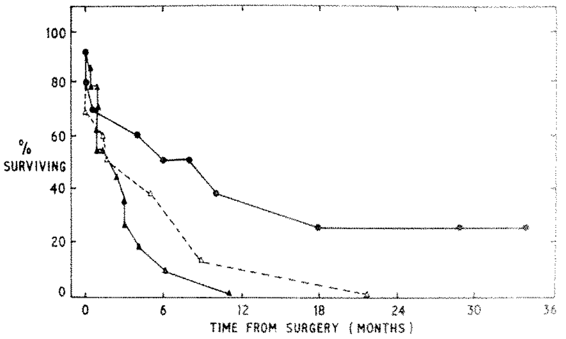

FIG. 1.—Survival curves following surgical exploration. Type of treatment: ●——●, resection, △ - - - -△, catheterization; ▲——▲, systemic chemotherapy or none.

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* NSC 29630; glutamic acid, *N*-(3,5-dichloro-4(2,4-diamino-6-pteridinyl)-methyl methylamino) benzoyl.

† NSC 79037; 1-(2-chloroethyl)-3-cyclohexyl-1-nitroso-urea.

‡ NSC 409962; 1,3-bis-(2-chloroethyl)-1-nitroso-urea.

§ NSC 19893; 5-fluorouracil.

Foster (1970) reviewed the surgical treatment of primary liver cancer in 227 patients from 35 different sources and calculated a mean 5-year survival of 14 per cent in patients who underwent hepatic resection. There is thus evidence to encourage an aggressive surgical approach to this tumour.

Major hepatic resection carries a considerable mortality. In Foster's (1970) review of hepatoma series reported within the past 10 years there was an overall mortality of 24 per cent. The operative mortality in the present series was 30 per cent. In an attempt to reduce the surgical mortality the pre- and postoperative management of our patients now follows a careful protocol. All the patients selected for surgical exploration are potential candidates for a major resection and are prepared as such. Intravenous fluids and measurement of the urine output are commenced the day before operation. A minimum of 10 units of blood must be available. A central venous pressure line is established and the central venous pressure is closely monitored during and after surgery. A urine output exceeding 50 ml. per hour for the first 48 hours is aimed at. Metabolic disturbances which follow major hepatic resections (McDermott and others, 1963; McDermott and Ottinger, 1966) should be anticipated. Thus, albumin levels which tend to fall progressively during the first 7–10 days and may result in significant shifts in body fluids can be maintained by giving albumin intravenously in the following arbitrary amounts: 75 and 50 g. in the first and second 24 hours after surgery, and 25 g. daily for the subsequent 4–7 days. Hypoglycaemia is another potential, if more theoretical, problem and can be prevented by incorporating 10 per cent glucose solution into the postoperative fluid régime. Intensive physiotherapy and early mobilization are directed at reducing the risks of respiratory and other complications.

Subphrenic abscess is a particular hazard of right hepatic lobectomy and 2 patients in the present series developed abscesses, 1 patient requiring drainage on three occasions. The importance of establishing and maintaining adequate drainage of the subdiaphragmatic space after resection is illustrated by a case reported by Lloyd-Davies and Angell (1958) in which the subdiaphragmatic drain was not finally removed until 7 months after surgery.

The high mortality of hepatic resection and the demanding postoperative care make it essential to select patients carefully for surgery. In Uganda, where medical resources are limited and overburdened, this is even more pertinent. Ideally only patients with localized disease which is potentially curable by resection should be submitted to surgery. A staging system (*Table V*) has recently been devised (Vogel and Linsell, 1972) and its prognostic value is currently being evaluated in a prospective study. On this system only Stage IA – lesions (or IA +, if in the left lobe) are considered resectable. The corollary to more strictly defined criteria for selection is fewer patients undergoing surgery. In the present series the 36 patients submitted to laparotomy represent only 28 per cent of the patients presenting with hepatoma. However, though fewer patients may be explored it is hoped that more of these will have operable tumours.

Although systemic chemotherapy has not met with success, regional perfusion has been more encouraging (Chan, 1967; Provan, Stokes, and Edwards, 1968; Geddes and Folkson, 1970; Vogel and others, 1972). The life-table analysis of the present series (*Fig.* 1) also suggests a favourable response. In addition to any improvement in survival, regional chemotherapy often produced relief of symptoms. The operative procedure of catheter placement is a relatively minor procedure although enlargement of the liver by tumour may distort the anatomy and make dissection of the coeliac axis difficult. The postoperative mortality in patients having catheter placement was similar to that for resection, but the results of more recently performed catheterizations suggest that a much lower mortality can be anticipated for this procedure. Hepatic artery catheters have been placed only in patients found at surgery to have a localized but unresectable tumour. Selection was initially on an arbitrary basis but a controlled trial is now in progress in which patients are randomized on the basis of the stage of the disease at the time of surgery into receiving either catheter chemotherapy or no chemotherapy. If the controlled results substantiate the trends of the present series it will then be possible to offer alternative treatment to those patients who, in spite of careful selection, are found at surgery to be inoperable. Percutaneous catheter placement via the femoral artery is a useful alternative to operative placement, but is less accurate and reliable (Watkins and others, 1970).

Table V.—FUNCTIONAL/ANATOMICAL STAGING. OF HEPATOCELLULAR CARCINOMA

FUNCTIONAL (Assessed on General Condition and Liver-function Studies)	ANATOMICAL (Extent of Tumour)
I = Good	A = One lobe
II = Moderate	B = More than one lobe
III = Poor	C = Metastatic

In addition the presence or absence of cirrhosis is denoted by the symbols + and –. The stage is modified if necessary at surgical exploration.

It has been estimated that only 1 per cent of all patients with hepatocellular carcinoma may be cured by surgery (Vogel and Linsell, 1972). In the present series 10 patients (8·5 per cent) had resectable disease of whom 3 are still alive, although only 1 appears to be tumour free. The majority of patients have advanced disease by the time the diagnosis has been made; surgery has nothing to offer these patients. The discovery of biochemical abnormalities in liver cancer, such as α-fetoprotein, proline hydroxylase, and fibrinogen (McIntire, Vogel, Princler, and Patel, 1972; Alpidovsky, Vogel, Sadikali, and Primack, 1973; Keiser, Vogel, and Sadikali, 1973), may make it possible to detect the tumour earlier, at a time when more patients have resectable disease. Similarly, biochemical markers may help to detect relapse and enable re-exploration or the initiation of further therapy at an opportune moment.

CONCLUSIONS

Although it must be accepted that the treatment of hepatocellular carcinoma is far from satisfactory, surgery continues to play a small but significant rôle in the management. Since this tumour is common in

Uganda controlled clinical trials with large numbers of patients are now possible. There is hope that in this way further progress will be made in rationalizing the treatment of this challenging tumour.

Acknowledgements.—The study of hepatoma is a team effort and we gratefully acknowledge the contribution of many others to this project: in particular, Dr. Margaret Dodson (Anaesthetics), Dr. C. L. Vogel and Dr. J. L. Ziegler (Uganda Cancer Institute), Dr. D. Truscott and Dr. P. Briers (Radiology), and Dr. B. Cady (Lahey Clinic Foundation, Boston, U.S.A.). Our thanks are also due to the sisters and nursing staff of the Intensive Care Unit, Mulago Hospital, and of the Uganda Cancer Institute.

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THE MANAGEMENT OF CARCINOMA OF THE BREAST BY RADICAL SUPERVOLTAGE RADIATION

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SUMMARY

A high-dose radiation technique for the management of inoperable carcinoma of breast is described, and the results of the treatment of 385 consecutive cases are outlined. The morbidity is considerable. Supervoltage radiotherapy can usually arrest the primary disease and cure a substantial number of cases. The quality of life enjoyed by the survivors is good.

'THE best treatment for a patient with early cancer of the breast is not known' (Editorial, 1969). Four years later most surgeons would still agree with this statement, though the next decade may do something to sharpen our ideas. In any unselected series of patients with operable breast cancer the same salvage rate is achieved by a variety of surgical techniques, ranging from restricted removal to ultraradical resection.

The present paper describes the treatment of 385 personally observed breast cancers which were deemed to be too advanced for surgical cure or were unsuitable for surgery on general grounds.

HISTORY

Breast cancer has been treated by ionizing radiation since the pioneer days of radiotherapy. Early published accounts were few and unreliable; moreover, the classic Halsted dissection so dominated the clinical scene that radiotherapists saw only the hopeless stages of the disease. It is thus not surprising that the early impressions of radiotherapy were discouraging. In addition, methods of dose estimation were primitive, so if an occasional good tumour response was obtained it was impossible to say what order of dose had achieved it.

It was left to Geoffrey Keynes to show that if enough radium were used, the response in selected cases was excellent. Keynes carried out meticulous radium implants 'to the breast itself, beneath the pectoral muscles, in the axilla, on the costocoracoid membrane, above the clavicle and in the upper three or four intercostal spaces' (Keynes, 1930, 1932, 1937), though he doubted the value of these last needles. The radiation dose received by the operator is not recorded, but it must have been high, bearing in mind that up to 100 mg. of radium were used in needles of 1–3 mg. strength per needle.

The art of Keynes's technique was that the whole volume of tissue likely to be involved in the disease was implanted. A typical Keynes-style implant is shown in *Fig.* 1. A degree of radiation soft-tissue damage had to be accepted, but Keynes showed that many breast cancers responded well if the dose were right. This justified the later use of high-energy X-ray beams which have the enormous advantage of not irradiating the surgeon or the theatre and ward staff.

Until about 20 years ago so-called orthovoltage X-ray therapy with beams generated at about 250 kV. was the standard radiotherapy treatment. The main dose fell on the patient's skin which, even at moderate levels, reacted to the point of moist desquamation. This often occurred at a dose level below that known to be cancericidal and was the practical limiting factor in treatment, that is, irradiation had perforce to be stopped at a dose known to be ineffective for most breast cancers.

Supervoltage X-ray therapy uses beams generated at more than a million volts. These beams have the great advantage of sparing the skin and because of the laws of physics that govern them, the maximum radiation dose occurs at 0·5–2·0 cm. below the skin. Skin desquamation is therefore no longer the forced end-point of treatment and a higher and therefore more effective dose can be given to the depths of the breast substance and to the apex of the axilla. The brunt of the dose falls in the soft tissues and the problems caused by this are deferred.

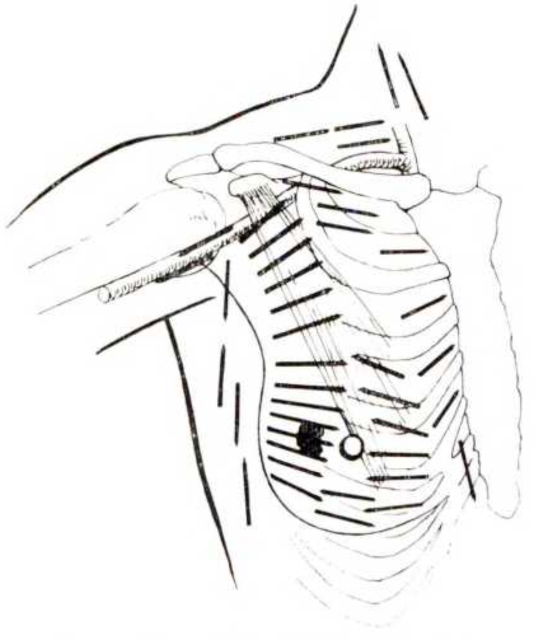

FIG. 1.—A Keynes-style radium implant to a breast.

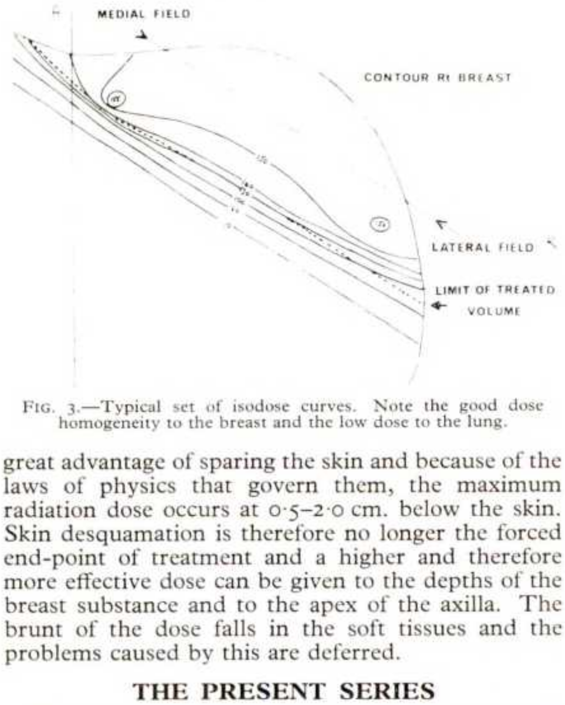

FIG. 3.—Typical set of isodose curves. Note the good dose homogeneity to the breast and the low dose to the lung.

THE PRESENT SERIES

Whenever high-dose radiation is used agreement on a management plan with the group of referring surgeons must be sought in advance. Routine mastectomy, whether 'toilet' or otherwise, becomes a hazardous procedure because of the risk of delayed wound healing and tissue sloughing. It has been the author's good fortune to work with colleagues who accepted this view.

Between 1955 and 1966, 429 consecutive cases of carcinoma of the breast were referred with a view to radical radiotherapy as the definitive treatment. Of these, 44 had metastases beyond the lymph-drainage area when first seen and were therefore rejected, leaving a group of 385 cases on which the present report is based. The TNM Classification of Malignant Tumours (1968) was used retrospectively; there were 86 T.2 cases, 275 T.3 cases, and 24 T.4 cases. If this is translated into conventional staging, then there were no Stage I cases, 56 stage II cases (27 T.2 N.1a and 29 T.2 N1b), with all the rest Stage III and beyond. In ordinary clinical terms most cases were large primary growths with substantial skin involvement and ulceration and evidence of fixation to underlying muscle. Supraclavicular nodes were occasionally palpable. Every case was histologically proved. In no case was later mastectomy performed.

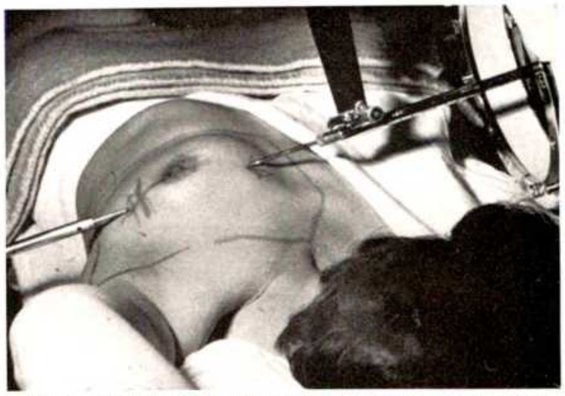

FIG. 2.—Medial breast field with a patient in the treatment position.

TECHNIQUE

The X-ray beam deriving from a 4 million volt Metropolitan Vickers linear accelerator was used in all the cases. The breast and its lymph-drainage areas were included within three X-ray fields. Two of the three fields were truly opposing and covered the breast, the internal mammary chain on the affected side, and the axillary contents. A third small field covered the supraclavicular fossa and that part of the axillary apex not adequately covered by the opposing field pair.

Radiation homogeneity is essential if underdosage or high-dose effects are to be avoided, so the opposing fields must be accurately opposing. This was achieved by tilting the patient and maintaining the angle of tilt constant for all three fields. The lateral beam was brought in 15° above the horizontal and the medial 15° below the horizontal. A high degree of accuracy was vital, and front and back pointers helped to secure it (*Fig.* 2). A typical set of isodose curves is shown in *Fig.* 3; it will be noted that dose homogeneity to the whole breast volume is good and that the dose to the lung parenchyma is low.

A tumour dose to the whole breast of 6500–7000 rad was given by daily fractions (5 per week) in an overall time of 35–42 days. During the same time an applied dose of 6500 rad was given to the third field, shielding the trachea and shoulder-joint.

Towards the end of the treatment course, retrosternal soreness was usual and was sometimes severe. Some degree of oesophagitis was invariable and gave moderate dysphagia that could take several weeks to settle down. Skin reactions were usually trivial but the skin was sometimes moist in the hollow of the axilla and beneath a pendulous breast. These complications resolved rapidly.

RESULTS

Typical cases submitted can be seen in *Figs.* 4 and 5. The results of the treatment technique described are shown in *Table I*. The 'disease-free' rate of 34 per cent for the whole group is acceptable and it is not surprising that 48 per cent of the mixed T.2 group survived. Only a single T.4 case survived for 5 years.

In *Table II* the T.4 cases have been excluded and the results for the T.2 and T.3 groups are summarized. The survival of 89 out of 275 T.3 cases (32 per cent) happens by chance to be close to the survival of the whole series.

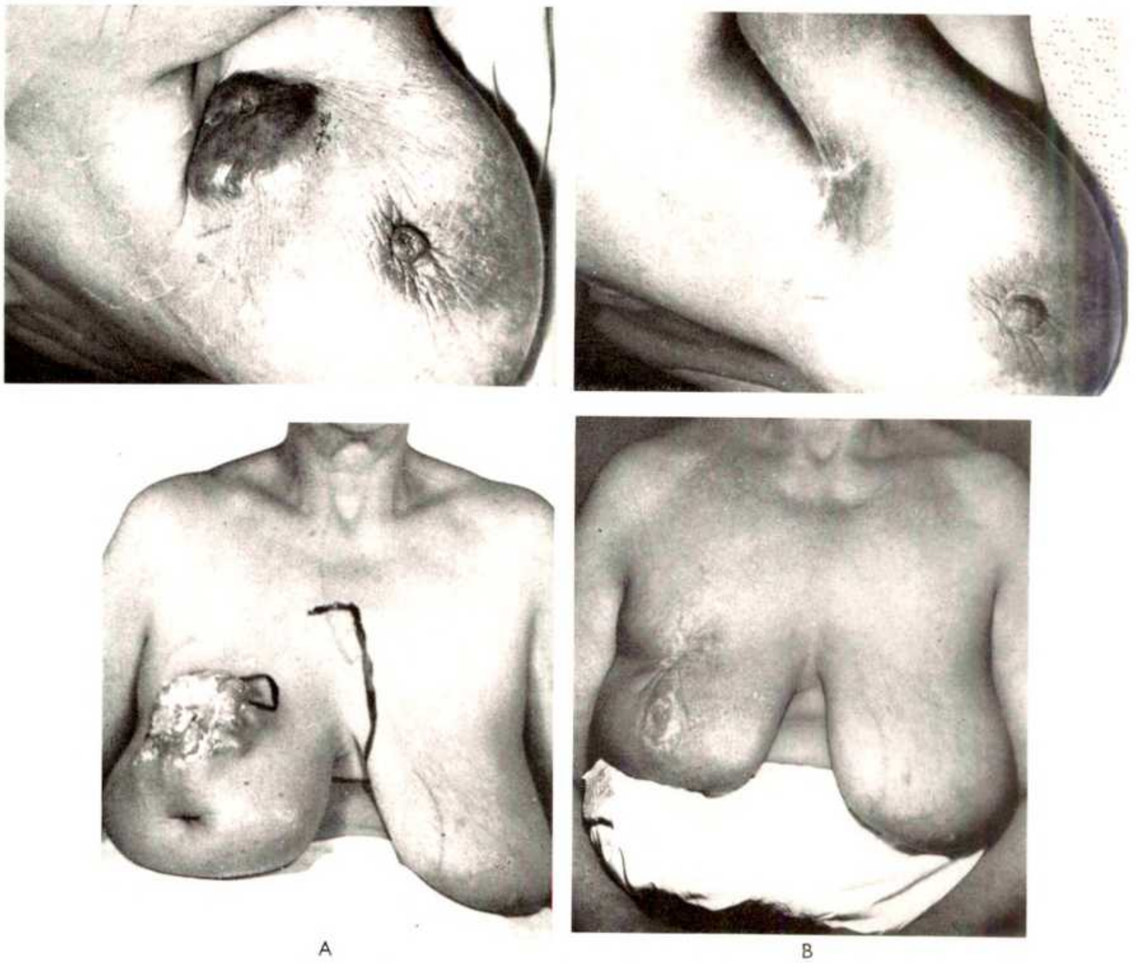

FIG. 4.—A, Typical advanced cases. B, The results 12 years later.

MORBIDITY OF TREATMENT

The price paid by the survivors is considerable. Soft-tissue deformity due to fibrosis is very common and may be severe. It starts within 6 months of completing the course of radiation and is progressive for 2 or 3 years. Fortunately it is usually painless even when the appearance is grotesque (*Figs.* 6, 7). In perhaps 20 per cent of this group the residual 'breast' is plastered on to the rib cage so firmly that when the remnant is grasped and moved, it is the patient who is rocked! The presence of large fibrous lumps and iron-hard plaques in and below the axilla closely mimic carcinoma and confuse the uninitiated.

Worrying inflammatory episodes may be seen in the irradiated breast for many years. As a result of minor trauma the breast becomes pink and painful, resembling one type of erysipelas which was so familiar to an earlier generation of surgeons. The condition settles down in a few weeks, despite rather than as a result of antibiotics, but it may recur several times. When there is no history of trauma or infection, and no constitutional disturbance or pyrexia—a common pattern—the signs are indistinguishable from massive local recurrence. In such circumstances, time must be allowed to decide.

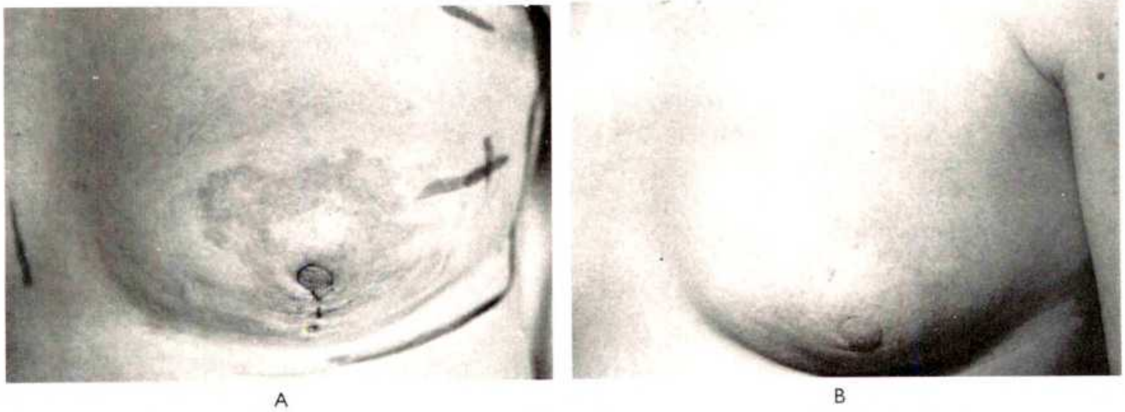

FIG. 5.—A, A patient of 29 years with fixity and severe skin involvement. B, Total regression of the primary tumour with good cosmetic result.

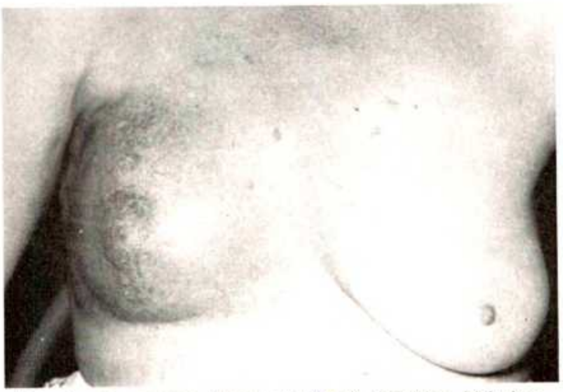

FIG. 6.—An average degree of fibrosis following high-dose radiation.

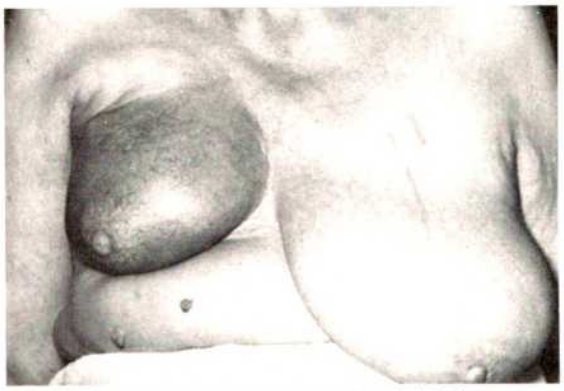

FIG. 7.—Severe painless fibrosis 16 years after the initial treatment.

Table I.—SURVIVAL OF PATIENTS WITH CARCINOMA OF THE BREAST AFTER HIGH-DOSE RADIATION

STAGE	NO. OF CASES	'DISEASE-FREE' AT 5 YEARS	
T.2 N.1a	27	14	48 per cent
T.2 N.1b	29	16	
T.2 N.2	27	11	
T.2 N.3	3	0	
T.3 N.1a T.3 N.1b	187	76	32 per cent
T.3 N.2	71	11	
T.3 N.3	17	2	
T.4 N.1a	—	—	
T.4 N.1b	—	—	
T.4 N.2 T.4 N.3	24	1	
Total	385	131	(34 per cent)

There is no correlation between breast deformity and local pain and stiffness. Acute local pain usually indicates the presence of rib fractures due to avascular bone necrosis, which in turn is due to post-irradiation endarteritis obliterans. Many ribs may sometimes be seen to be fractured as a chance finding on radiographic examination and it is as well not to inform the patient of this. Callus formation after fracture is usually good and healing is uneventful but some fractures produce no callus at all. In this series the sternum was fractured on two occasions and both cases healed uneventfully.

Late skin damage is usually trivial and is totally overshadowed by the soft-tissue changes. Lung damage is slight because only small volumes of lung parenchyma are caught in the X-ray beams. A few

Table II.—SURVIVAL OF PATIENTS WITH STAGE T.2 AND T.3 CARCINOMA OF THE BREAST AFTER HIGH-DOSE RADIATION

STAGE	NO. OF CASES	'DISEASE-FREE' AT 5 YEARS	PERCENTAGE 'DISEASE-FREE' AT 5 YEARS
T.2	86	41	48
T.3	275	89	32
Total	361	130	36

patients develop dyspnoea out of proportion to the extent of pleural thickening and pulmonary fibrosis may be shown on chest radiographs, but respiratory cripples as a result of treatment have not occurred. No satisfactory explanation of this disproportionate dyspnoea can be found. Some degree of lymphoedema is common but it is rarely severe; it is commonest in a plump arm and where the axilla has been extensively infiltrated. Its appearance several years after radiation often indicates active carcinoma though a symptomless axillary vein thrombosis may give an identical picture. Brachial neuritis is occasionally encountered and is quite resistant to treatment.

DISCUSSION

The justification for radical high-dose irradiation must lie in the balance between the cure rate and the damage done to the patient in securing it, which means that subjective judgement is inevitable. The patient's own opinions are important here. Most of these women would much sooner possess a small contracted breast than no breast at all, particularly if they have no pain in it. Therefore the aesthetic argument as judged by 'patient satisfaction' answers itself.

The disease-free rate of 36 per cent for all T.2 and T.3 cases is open to all the usual legitimate objections to 5-year survival figures in breast carcinoma; this figure certainly drops to 21 per cent at 10 years (51 survivors out of 245 cases treated for the years 1955–61 inclusive), which is still not negligible. What is often forgotten is the *quality* of survival, rather than its duration.

This group of women has advanced disease; those who do not perish from metastatic disease have an excellent quality of life, without discharge and fungation or any of the other signs of uncontrollable breast cancer. Their survival without mastectomy and their almost invariable knowledge of the true diagnosis add an extra dimension of sweetness to life that cannot be quantified. To hear such patients explaining this is a moving experience.

What high-dose radiation can almost always achieve is the *local* eradication of the majority of breast cancers, or at least their local arrest. During the first 5 years after treatment roughly one-half of the group die of distant metastases but without return of the primary growth. During the next 5 years a further number succumbs but the primary cancer, once arrested, does not recur.

In an important but neglected paper by Ross (1939) simple mastectomy was performed routinely in 50 patients after the radium implantation of their breast carcinoma by Keynes's technique. Careful histological analysis showed that 'about half of them contained carcinoma cells, the remainder showed only dense scar tissue and we noted that among the latter group there were several cases in which a heavy dose of radium had been used'. The radiation dose received by these tumours was not known accurately but it must have been substantially less than the doses quoted in the present report. As there is a roughly linear relationship between applied dose and tumour-cell death, it is not surprising that our local recurrence rate after the high doses used is so low. It is part of our deliberate policy that the breast should be conserved so we have to rely on the absence of macroscopic evidence of local recurrence over the course of time. Opportunities for autopsy have been few but these have usually failed to show viable carcinoma cells; even when clumps of apparently healthy cancer cells are found they are walled off in dense layers of mature fibroblasts and their ability to 'escape' is uncertain.

The high-dose technique described (about 6500 rad in 5–6 weeks) cannot be further increased without producing an unacceptable morbidity. Unfortunately breast cancer is a disease of limited radiosensitivity and there is no reliable way of assessing in advance those that will respond to lower doses. Thus, all the cases selected need a high dose and will therefore share in the morbidity.

After 17 years' experience of this technique it is clear that certain types of case which were formerly included should not be included in the future. A palpable supraclavicular node is nearly always a death sentence so that such patients should be excluded from 6 weeks' arduous radiation and treated more simply. The same is true if the primary cancer is large—10 cm. or more in diameter—since very few patients in this group survive even 5 years. If these two groups of cases are excluded in future, survival figures will be more encouraging.

Mastectomy is still carried out on many women who would be far better off left to the radiotherapist. Operation is contra-indicated not merely because it may disseminate tumour but because it is irrelevant, for example, in the management of sizeable inner-quadrant primary tumours, or large primary tumours anywhere, or where there is marked skin involvement or any degree of fixation to muscle. This is equally true when the topmost axillary nodes are hard or semi-fixed. The surgical management of breast cancer will rightly remain the mainstay of treatment for many years ahead, particularly if it is used more selectively than in the past.

Radical radiation provides a good alternative treatment in many cases and is the treatment of choice in many more. Low-dose radiation techniques achieve next to nothing, apart from the simple palliation of bleeding and fungating masses. High-dose radiation is an ordeal for most patients and carries a high rate of morbidity; for these reasons alone patients should be selected as rigidly for it as our imperfect criteria permit.

Acknowledgements.—I am indebted to the group of surgeons who have referred cases to me over many years and to Dr. Max Hulbert, St. Mary's Hospital, Paddington, for helpful criticism. I am obliged to Mr. R. N. Blake for the illustrations, Mrs. C. Hardstaff for secretarial help, and the staff of the Regional Radiotherapy Centre for the 100 per cent follow-up.

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BLADDER FUNCTION FOLLOWING ABDOMINOPERINEAL EXCISION OF THE RECTUM FOR CARCINOMA

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SUMMARY

Denervation of the bladder was demonstrated in 8 of 28 patients following abdominoperineal excision of the rectum. It is suggested that routine postoperative bladder-function studies be performed to detect this complication and thus to enable suitable postoperative care and long-term follow-up to be undertaken.

URINARY retention occurs in a significant number of patients following abdominoperineal excision of the rectum for carcinoma (Lockhart-Mummery, 1932; Buckwalter, Shropshire, and Joiner, 1955); its cause may be mechanical obstruction or neurological injury (Watson and Williams, 1952). It has been suggested that satisfactory voiding is regained spontaneously in the majority of cases (Watson and Williams, 1952; Roberts, 1961) and little attention has been paid to the need for routine bladder-function studies either in the immediate or late postoperative period.

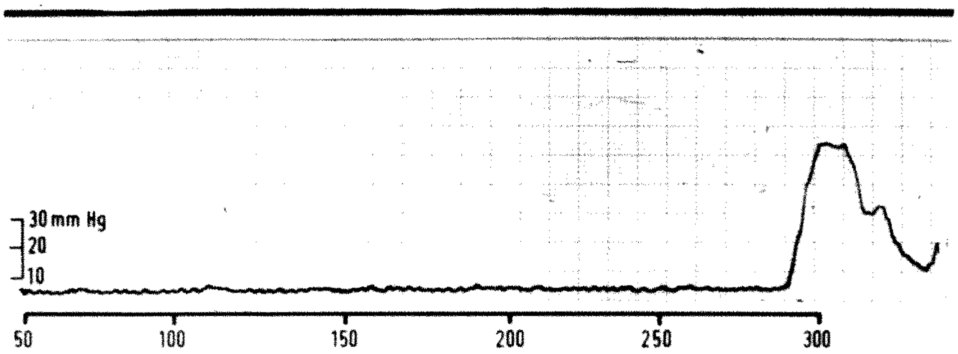

FIG. 1.—Cystometrogram of a normal innervated bladder.

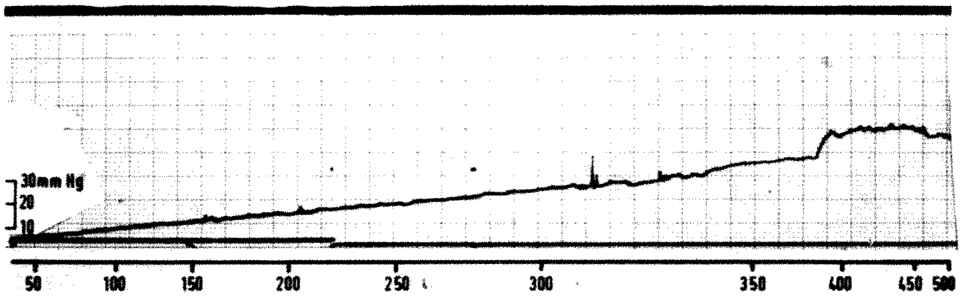

FIG. 2.—Cystometrogram of a denervated bladder.

During a period of 18 months 7 patients presented with urinary difficulties between 3 and 28 years after abdominoperineal excision. Investigation suggested that their bladder symptoms were occasioned by the operative procedure. For this reason routine screening of patients undergoing abdominoperineal excision of the rectum was instituted.

MATERIAL

Group A.—This group comprised 7 patients with long-term complications of excision of the rectum.

Group B.—Twenty-eight patients underwent vesical function studies. Fourteen patients were studied both pre- and postoperatively and the other 14 cases were investigated postoperatively only.

METHODS

Bladder symptomatology was noted. Intravenous pyelography, residual urine estimation, cystometrography, and (where indicated) cystoscopy were carried out. The cystometrogram was performed with a 16F three-way Foley catheter, using 1 : 5000 chlorhexidine as the irrigating fluid. The pressure changes were recorded via a transducer on a Devices recorder. The results were classified as normal (*Fig.* 1) or denervated (*Fig.* 2). No attempt was made to classify the subjective sensory changes. The postoperative cystometrogram was carried out on the day that the surgeon elected to remove the catheter. The three-way Foley catheter was used for postoperative drainage and thus avoided a catheter change before performing the cystometrogram.

RESULTS

Group A.—Group A consisted of 7 patients presenting 3–28 years (average 7–8 years) after abdominoperineal excision of the rectum for carcinoma. The case details are given in *Table I.*

Two male and 3 female patients were found to have denervated bladders. All had difficulty with micturition and urinary-tract infection; 4 of the 5 patients had significant residual urine. One male patient was admitted in renal failure due to prostatic hypertrophy and another patient was admitted with retention due to a prostatic abscess.

Table I.—Details of 7 Patients (Group A) presenting 3–28 Years after Abdominoperineal Excision of the Rectum for Carcinoma

Case	Age and Sex	Survival (yr.)	Difficulty with Micturition	Time of Onset after Operation	Urinary Infection	Additional Procedures	Residual Urine (ml.)	Cystometrogram
1. H. S.	83 M.	7	+	Immediate	+	Repeated bouginage	500	Denervated
2. L. P.	58 M.	28	+	Immediate	+	Bouginage; transvesical prostatectomy; cystotomy and removal of bladder stone	200	Denervated
3. E. C.	64 F.	4	+	2 yr.	+	Antibiotics	100	Denervated
4. E. W.	61 F.	6	+	Immediate	+	Antibiotics; pelvic floor repair	150	Denervated
5. E. McC.	49 F.	10	+	9 yr.	+	Antibiotics	Nil	Denervated
6. O. B.	71 M.	3	+	2½ yr.*	+	Dialysis; antibiotics	Anuric	Normal
7. H. C.	65 M.	4	+	4 yr.	+	Nil	500	Normal

* This patient had renal failure.

Group B.—Twenty-eight patients were studied prospectively. Denervation as demonstrated by a cystometrogram (*Fig.* 2) was present in 8 of the 28 patients (6 males and 2 females) after abdominoperineal resection.

The cystometrograms found to be abnormal were repeated at 2, 6, and 12 weeks and thereafter at 3-monthly intervals. No bladder showing denervation postoperatively has subsequently returned to normal.

All the patients with normal innervation voided spontaneously on the removal of the catheter.

Two male patients showed a significant residual urine 6 months after abdominoperineal resection and investigation by pyelography and cystoscopy demonstrated signs of prostatic obstruction. These patients were asymptomatic and had normal bladder innervation.

MANAGEMENT OF PATIENTS WITH A DENERVATED BLADDER

Patients in whom denervation was shown to have occurred were managed in the following way.

The catheter was removed after the cystometrogram had been performed and the patient was given carbachol (0·5–1 ml. 6-hourly) by injection. Residual urine estimation was carried out 12 hours later and parenteral carbachol was administered daily until the residual urine was shown to be less than 100 ml. The patient was then given oral cholinergic therapy (Myotinine, 5–10 mg. q.i.d.), the dose being reduced as a reduction in the residual urine occurred. Two male patients required transurethral resection as well as cholinergic therapy in order to obtain satisfactory voiding; no patient required further prolonged catheter drainage.

DISCUSSION

Retention of urine following combined excision of the rectum occurs in 17–50 per cent of patients (Watson and Williams, 1952; Buckwalter and others, 1955). This has in the past been attributed to bladder-neck obstruction and rarely to parasympathetic nerve injury. Rankin (1969) showed that nerve injury had occurred in 11 of the 45 patients in his series undergoing abdominoperineal excision of the rectum. Our own series shows that 5 of 7 patients with late vesical complications had a denervated bladder, and similar neurological damage was present in 8 of 28 patients in the prospective study.

The information obtained by investigation in the immediate postoperative period ensured that the correct treatment was instituted and avoided retention and its sequel of bladder overdistension. Long-term review of the patients to check for signs of urinary retention, especially in the male patients, will detect those developing significant prostatic obstruction.

Failure to recognize the primary neurological nature of the postoperative urinary difficulty may lead to these patients being subjected to unnecessary, repeated, and often major surgical procedures, as in *Cases*, 1, 2, and 3 (*Table I*). Urinary infection had been present in the patients in group A from the time of operation despite repeated courses of antibiotics.

The operative mortality and long-term survival following abdominoperineal excision of the rectum for carcinoma continues to improve (Morgan, 1965; Mann, 1969). Appreciation of the palliation achieved by the removal of a rectal tumour has led to more extensive procedures (Hughes, 1963; Moore, 1965). There are therefore an increasing number of patients who are liable in both the short and the long term to vesical complications, and it is incumbent upon surgeons carrying out such operations to remember the possibility of nerve damage and to minimize its consequences. In this way the patient will have an improved quality of life following operation.

Acknowledgements.—I am indebted to Mr. T. J. McNair, Mr. T. I. Wilson, Mr. P. Edmond, and Mr. J. W. W. Thomson for their help and encouragement in the preparation of this paper and to the surgical staff of the Royal Infirmary, Edinburgh, for permission to study their patients.

I am grateful to Miss Catherine Keil for undertaking the secretarial work involved.

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SHORT NOTES OF RARE OR OBSCURE CASES

THE OCCURRENCE OF CARCINOID TUMOUR IN TERATOMA OF THE TESTIS

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SUMMARY

The third reported case of a carcinoid tumour arising in a teratoma of the testis is presented. The points of difference between the present case and the 2 previously reported ones are discussed.

Unusual locations of carcinoid tumours are considered in the light of theories explaining their origins. The features of ovarian carcinoid tumours are reviewed and parallels drawn between them and the rarer testicular carcinoid tumours.

THE occurrence of a carcinoid tumour in a teratoma of the testis is a rare phenomenon. Only 2 similar reports have been found in the literature (Simon, McDonald, and Culp, 1954; Berkheiser, 1959) and in both instances the carcinoid tumour had occurred in a cystic teratoma in a patient in the sixth decade. Dixon and Moore (1953) made no mention of carcinoid tumour in their review of 990 cases of testicular tumour. Among 995 cases of neoplastic lesions of the testis studied by the Testicular Tumour Panel and Registry 3 examples of carcinoid tumour were encountered, none of which showed evidence of teratoma formation in the affected testis (Collins and Pugh, 1964). Two further cases of testicular carcinoid, not associated with teratomatous growths, were described by Kemble (1968) and Kermarec and Duplay (1968). The occurrence of a carcinoid tumour in a mainly solid teratoma of the testis in a 31-year-old man is therefore considered worth reporting.

CASE REPORT

A 31-year-old man was referred because of an enlarged left testis which had been noted during a medical examination for a pension scheme. The patient stated that he had had this enlargement for as long as he could remember and had neither noticed any recent increase in size nor experienced any discomfort at the site. Five years previously he had been investigated for infertility at another hospital, where he had been told that no abnormality had been detected, and subsequently he had fathered 2 children. He had not undergone surgery previously.

Physical examination revealed a fit man of athletic build, the positive findings being restricted to the scrotum. The left testis was enlarged to 6 cm. in its longest axis. It was firm and non-tender, normal testicular sensation being present. It could not be transilluminated. The right testis was not enlarged. Lymphadenopathy, abdominal masses, and gynaecomastia were not present. The E.S.R. was 5 mm. in 1 hour, the haemoglobin 14·8 g. per cent, and the white-cell count 4100 per c.mm. with a normal differential. The plasma urea and electrolytes were normal. Urine examination and chest radiography revealed no abnormality.

A diagnosis of teratoma of the testis was considered likely. The left testis was delivered through a scrotal incision. There was no fluid in the tunica vaginalis. The testis was enlarged and its posterior aspect felt abnormally firm. A wedge of tissue was removed for frozen section and the cut surface was noted to be yellow in colour. The frozen section was reported as being from a teratoma. The left inguinal canal was then opened through a groin incision and the spermatic cord was isolated, ligated, and divided at the internal ring. The cord, epididymis, and testis were removed through the scrotal incision. The inguinal canal was repaired and both wounds were closed.

Macroscopically a pale yellow tumour, measuring 4 cm. in its greatest diameter, was found to occupy the lower pole and posterior surface of the removed testis, abutting on to but not invading the tunica (*Fig.* 1). The cut surface showed mainly firm homogeneous tissue, apart from a few small cystic spaces in the lower part of the mass. The tumour was not encapsulated and merged somewhat irregularly with the surrounding testicular tissue.

Microscopically the tumour comprised three intimately mingled types of tissue all supported by a connective-tissue stroma. The small cystic spaces had a pseudo-stratified ciliated columnar epithelial lining (*Fig.* 2) and, adjacent, there were small islands and strands of poorly outlined cells with eosinophilic cytoplasm and pale uniform nuclei which had an irregularly whorled arrangement (*Fig.* 3). Some of these groups of cells were related to partially calcified spherical structures similar to psammoma bodies. The overall arrangement was that of a

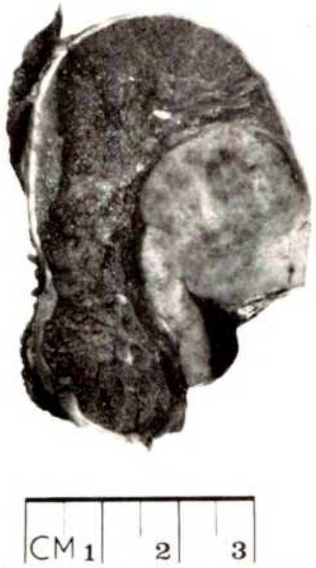

FIG. 1.—Macroscopic view of the testis with the tumour.

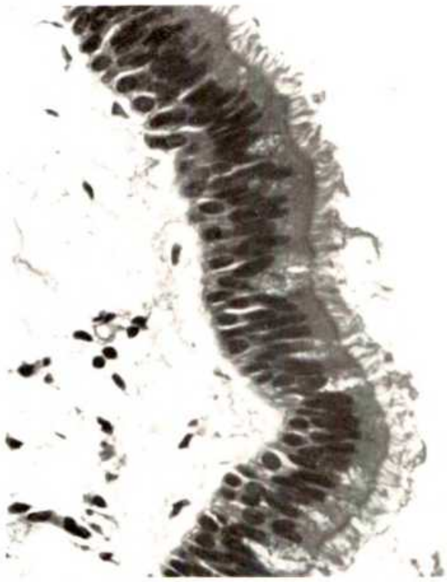

FIG. 2.—The respiratory-type epithelium which lined the cystic spaces. (× 400.)

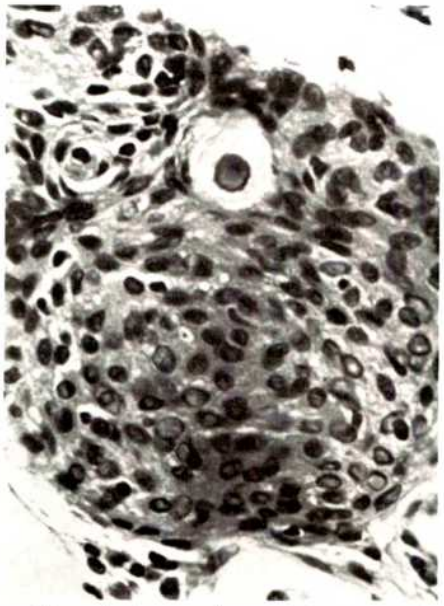

FIG. 3.—The meningiomatous element of the teratoma. (× 400.)

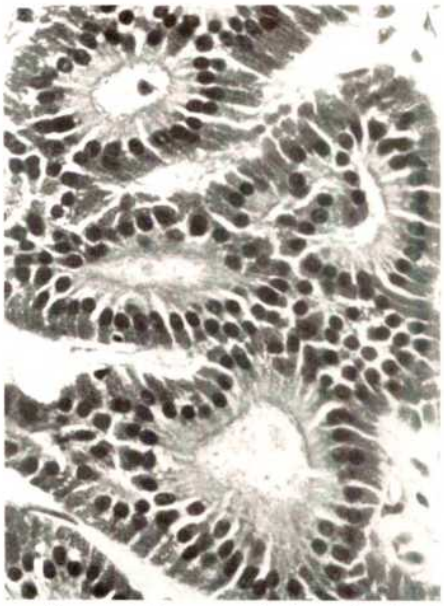

FIG. 4.—The carcinoid tumour showing cells with basally situated granules and acinar arrangement. (× 400.)

tissue intermediate in appearance between arachnoid and a meningioma. Lying next to these areas and extending to form the bulk of the tumour mass were varying sized and shaped clusters of regular cells, many with a distinctly acinar arrangement (*Fig.* 4). The pale eosinophilic cytoplasm contained abundant, basally situated, strongly eosinophilic granules. Specific staining by the Fontana-Masson method revealed them to be argentaffin granules which stained rust-red with the Diazo technique. The nuclei were oval, and mitotic figures were not seen. There was no capsular invasion but the carcinoid element extended in fine clusters into the surrounding testicular tissue. The spermatic cord, epididymis, and testicular tissue in the upper portion of the testis showed no significant abnormality.

Postoperatively the patient made an uneventful recovery. A lymphangiogram showed no filling defects in the abdominal nodes. The urinary 5-hydroxyindole-acetic acid was 5 4 mg. per 24 hours (normal 2–10 mg. per 24 hours) and the whole-blood 5-hydroxytryptamine was 174 mg. per ml. (normal 50–250 mg. per ml.). The patient denies having had any symptoms suggestive of either an abdominal carcinoid tumour or the carcinoid syndrome at any stage before or after his operation. He remains well 6 months after operation.

DISCUSSION

Carcinoid tumours in the appendix were first described by Obendorfer in 1907, and in 1914 Gosset and Masson showed that they originated from Kulchitsky cells. The ability of the cytoplasmic granules in these cells and in the tumours to reduce silver salts led to the use of the term 'argentaffin carcinoma'. While the terminal ileum and appendix are the commonest sites of tumour formation, they have also been found to arise in all parts of the alimentary canal from the oesophagus to the rectum (Cheek and Wilson, 1970). Similarly, they have been reported in appendages of the alimentary tract such as the gall-bladder (Porter and Whelan, 1939), the common bile-duct (Little, Gibson, and Kay, 1968), and the pancreas (Persand and Walrond, 1971). Their occurrence in alimentary areas is not unexpected in view of the presence of Kulchitsky cells at such situations (Morson, 1958). Carcinoid tumours have also been found in the nasopharynx (Jarvi, 1945), the larynx (Goldman, Hood, and Singleton, 1969), and the tracheobronchial tree (Logan, Sehdeva, Hatcher, and Abbott, 1970), which can be accounted for by the finding of normal argentaffin cells in the respiratory tract by De Muylder and Fayt (1954).

A significant number of carcinoid tumours have been reported in the ovary. Hoch, Lichtig, Peretz, Paldi, Pascal, Kuchs, and Brandes (1971) found 32 'primary' carcinoid tumours of the ovary in a recent review of the literature and in 27 of them the carcinoid tumour was part of a benign cystic teratoma. The multipotentiality of teratomas provides an explanation for the unusual location of these ovarian carcinoids and attempts have been made to determine whether they had arisen in relation to teratomatous gastro-intestinal or respiratory structures. In a review of 5 cases Peterson (1957) found that 2 had arisen in relation to the gastro-intestinal epithelium, while Climie and Heath (1968) noted that in 5 out of 9 other cases the carcinoid element was associated with respiratory structures. The ovary, of course, can be the seat of a metastasis from a primary carcinoid tumour in a conventional site such as the ileocaecal region, and 8 such cases have been reported by Shuster, Mendoza-Divino, and Joselson (1970). Brown and Richart (1969) were of the opinion that ovarian carcinoids which were neither associated with ovarian teratomas nor secondary to a primary carcinoid tumour elsewhere were examples of so-called 'simplified teratomas' in which one element outgrew all the others. Toker (1969), on the contrary, believed that they had originated *ab initio* from Kulchitsky cells in the ovary. Normal Kulchitsky cells, however, have not been found in the germinal organs.

Parallels can be drawn between ovarian carcinoid tumours and the few testicular carcinoid tumours that have been reported. In the 2 testicular cases recorded by Simon and others (1954) and Berkheiser (1959) the carcinoid tumour had arisen in a benign cystic teratoma and in each case the authors tried to determine whether it had originated from gastro-intestinal or respiratory teratomatous structures. A respiratory-tract derivation was decided upon by Simon and others and a gastro-intestinal tract origin by Berkheiser. No teratomatous component was seen in either of the cases described by Kemble (1968) and Kermarec and Duplay (1968). Kemble believed that the carcinoid tumour had arisen from argentaffin cells present *ab initio* in the testicle, while Kermarec and Duplay considered also the possibility of the tumour representing a simplified teratoma in which all the other teratomatous structures were absent. The further possibility of a testicular carcinoid tumour being a metastasis from a primary growth in the alimentary tract is illustrated by 1 of the 3 cases mentioned by Collins and Pugh (1964). This patient died a few months after orchidectomy with multiple carcinoid tumours in the peritoneum and mesentery; his appendix had been removed previously but had not been examined histologically. The importance of excluding an abdominal primary neoplasm whenever a carcinoid tumour is encountered within the scrotum is further emphasized by a case of metastatic involvement of the epididymis reported by Cope and Newcomb (1930) and another case described by Kemble (1968) in which a metastatic deposit was found on the serosal surface of the tunica vaginalis; in both instances the primary growth was situated in the small intestine.

The case described here is the third reported case of a carcinoid tumour arising in a teratoma of the testis. There are points of difference, however, between the present case and the 2 previously reported cases. The patient described by Simon and others (1954) was a 58-year-old man who had experienced 2 years of accelerated enlargement of a 14-year scrotal swelling. Berkheiser's (1959) patient was a 54-year-old man who complained of 1 year's painful enlargement of a testis that had been increased in size from birth. Our patient was a much younger man (31 years of age) without testicular symptoms, his lesion being detected at a routine medical examination. In both the previously reported cases the tumour was an essentially cystic teratoma in which the carcinoid component was relatively small—an 8-mm.-diameter nodule in a 5-cm.-diameter cyst in the former, and groups of carcinoid cells in the walls of the cysts in a multicystic tumour in the latter. In the case reported here the tumour was mainly solid and the major part of it comprised clusters of carcinoid cells. It was not possible to identify with certainty the tissue from which the carcinoid element had arisen. The epithelium in the teratomatous part of the tumour, however, was distinctly respiratory in type (*Fig.* 2). The tendency for a component tissue of a teratoma to proliferate has already been mentioned in connexion with the origin of carcinoid tumours. The small area of meningioma-like tissue (*Fig.* 3) represents a similar tendency towards cellular proliferation, which in this instance is overshadowed by that of the carcinoid component.

The carcinoid tissue and the other elements present in the testicular teratoma described here all appeared well differentiated on microscopic study. Collins and Pugh (1964), however, stated that even the most differentiated teratoma cannot be designated as benign. Similarly, Morson (1958) believed that there is no justification for the use of the term 'benign carcinoid'. In each instance the benign or malignant nature of the lesion is determined by its clinical behaviour. In the present case there was no clinical or radiological evidence of metastases from the testicular lesion, or of a primary neoplasm responsible for the latter.

None of the reported carcinoid tumours of the testicle has been a functioning tumour associated with the carcinoid syndrome or with biochemical evidence of endocrine secretion by the tumour cells. Of the ovarian carcinoid tumours reviewed by Kelley and Scully (1961), however, 37·5 per cent were considered to be functioning, and Brown and Richart (1969) stated that the carcinoid syndrome occurs relatively more frequently among patients with neoplasms of the ovary than in those with lesions of the gastro-intestinal tract, because the venous drainage from the ovary by-passes the liver where 5-hydroxytryptamine produced by the carcinoid cells is destroyed by monoamine oxidase. There was no evidence of flushing, diarrhoea, wheezing, or cardiac lesions in the case reported here. In the absence of such suggestive clinical features the preoperative diagnosis of a primary testicular carcinoid tumour is virtually impossible. Thus, in all the reported cases biochemical studies of endocrine activity have only been performed postoperatively. This was true of the present case as well, and the patient's postoperative whole-blood 5-hydroxytryptamine and urinary 5-hydroxyindole-acetic acid levels were within the normal range. Such postoperative estimations, however, may when abnormal indicate the persistence of further carcinoid tumour in the patient, as occurred in the case reported by Kemble (1968), where a carcinoid tumour nodule on the tunica vaginalis was secondary to an ileal carcinoid tumour and the postorchidectomy urinary 5-hydroxyindole-acetic acid level was high.

Acknowledgements.—We wish to thank Dr. R. J. R. Cureton and Dr. R. D. Ledray for the pathological details of this case.

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OMENTAL TRANSPOSITION IN THE TREATMENT OF RADIONECROSIS

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SUMMARY

A technique is described for the closure of chest-wall defects following radical excision for radionecrosis. Such defects are usually extensive with an avascular bed and often involve an opening into the pleural cavity; surgical closure poses significant problems. The method described here utilizes a transposed omental flap to provide a vascular bed for a skin-graft, whilst cephalad shifting of the origin of the diaphragm is used to close the pleural defect. This latter innovation has the dual advantages of simplicity and effectiveness, whilst greatly facilitating the passage of the omentum to the chest wall with minimal risk of omental strangulation.

THE ability of the greater omentum to adhere to inflamed and traumatized viscera, and thus to contribute to the resolution of intraperitoneal inflammation, is fundamental to the successful outcome of abdominal surgical procedures. The particular properties of mobility, vascularity, plentiful endowment with lymphatics, and powers of cellular proliferation bestow a unique status upon this structure. Surgical exploitation of these properties has been carried beyond the abdomen by transposition of the omentum for myocardial revascularization (Vineberg, 1969) and in the relief of lymphoedema (Goldsmith and De los Santos, 1966).

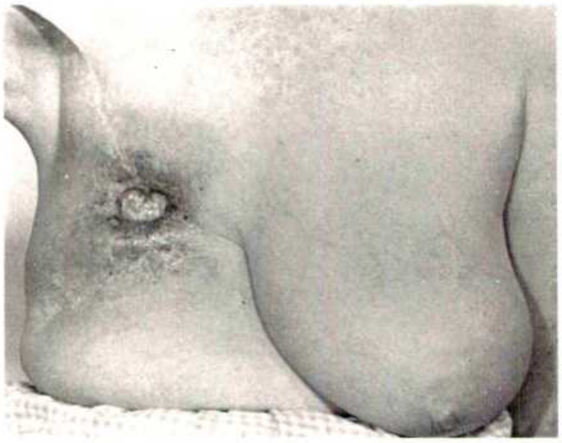

FIG. 1.—General tissue damage from irradiation with an ulcer to the right of the sternum.

The facility with which the omentum will support a split-skin graft was demonstrated by Kiricuta (1963), who used transposed omentum covered by a skin-graft in the treatment of a radionecrotic ulcer on the chest wall. Dupont and Menard (1972) reported 4 cases in which this principle had been used, with details of the operative techniques. Essentially, the omentum was transposed to an extra-abdominal site in the form of a flap pedicled upon the gastro-epiploic vessels, passing through a defect in the musculofascial layer of the abdominal wall and thence via a subcutaneous tunnel to the site of election.

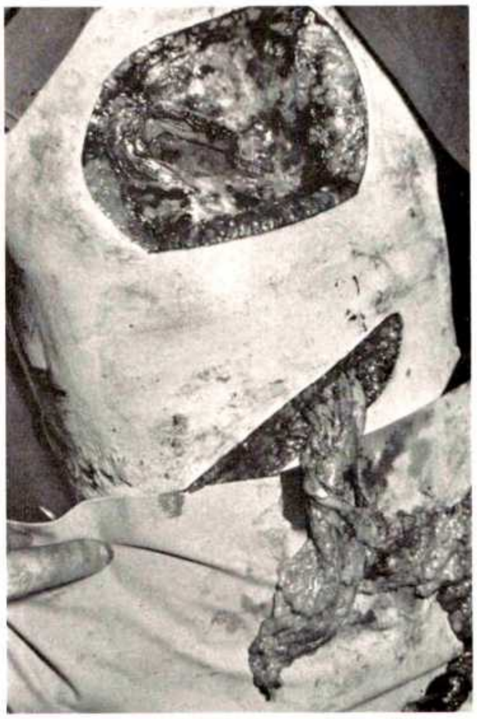

FIG. 2.—A wide excision of the tissue damaged by irradiation has been made. This has included excision of the fourth costal cartilage and a part of the adjacent fourth rib. A Kocher's incision has been made and the omentum delivered on to the surface before being taken up into the defect behind the costal margin.

We have recently applied this method in a similar clinical situation and report here certain further observations on the technique.

CASE REPORT

A 55-year-old Caucasian female presented with a radionecrotic ulcer on the right anterior chest wall (*Fig.* 1).

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Fourteen years previously she had undergone a classic right radical mastectomy for carcinoma of the breast, followed by postoperative irradiation (3000 r). Within 1 year of operation she had developed a local recurrence in the scar, which was treated successfully by further irradiation (5000 r). Thereafter, the area had remained quiescent, with no evidence of recurrence or metastasis, for 13 years. She had then suffered minor trauma to the irradiated scar, resulting in ulceration which failed to heal. Surgical exploration revealed radionecrotic costal cartilage, which was excised, and biopsy showed no evidence of recurrent tumour.

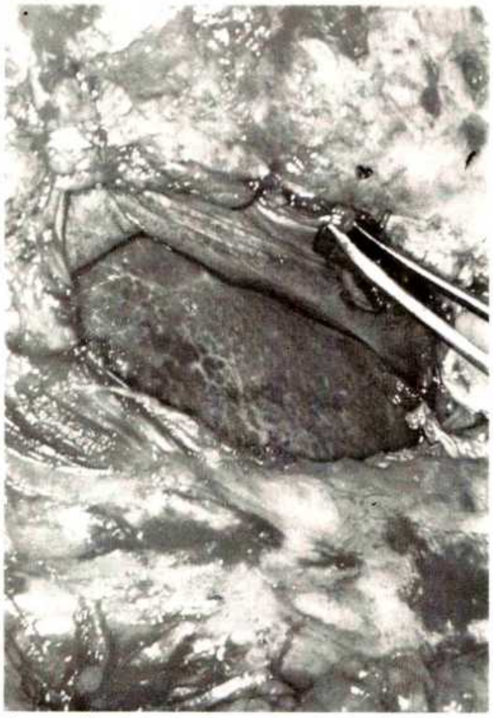
FIG. 3.—The defect in the anterior chest wall with the diaphragm sutured to its medial and lateral sides and the upper margin. The liver is seen in the base of the opening.

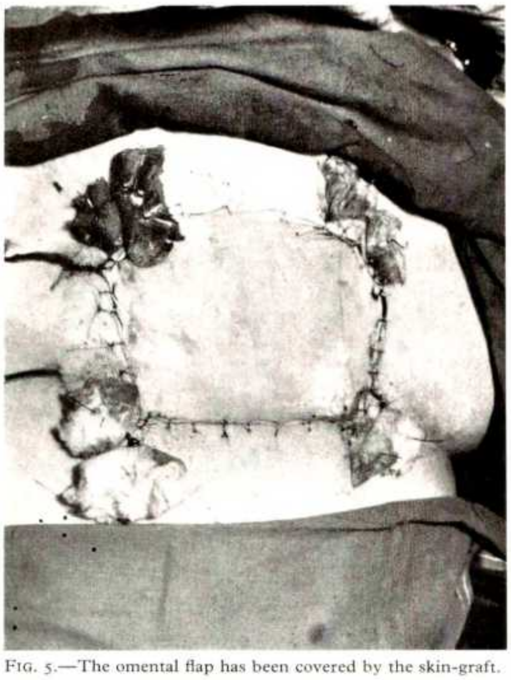
FIG. 5.—The omental flap has been covered by the skin-graft.

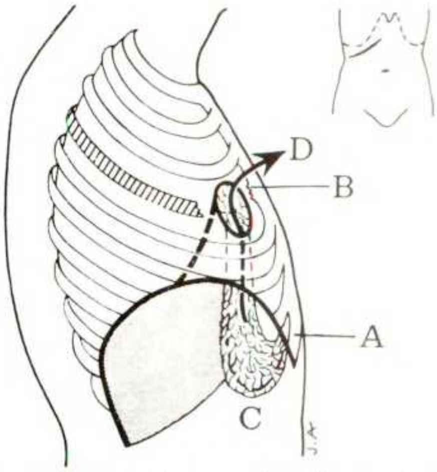

FIG. 4.—Diagrammatic representation of the procedure used. The diaphragm was freed from its anterior attachment (A) and raised to (B). This left the opening in the anterior chest wall excluded from the thorax and in free communication with the peritoneal cavity. The great omentum was brought up (C) behind the costal margin and delivered to the surface at D. The insert shows the Kocher's incision.

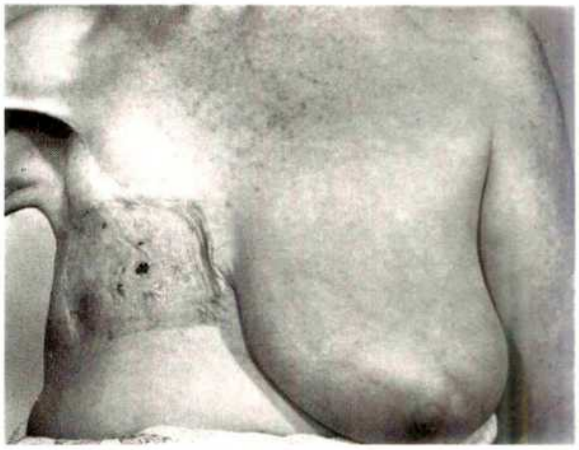
FIG. 6.—The wound soundly healed postoperatively.

The ulcer persisted, requiring daily dressings, and the patient requested definitive surgery to resolve this situation. Further biopsy was negative in respect of tumour, and a chest radiograph showed no gross change in the subjacent ribs. Wide excision of the ulcer and adjacent indurated tissues was clearly required, thus posing the problem of closure of an extensive defect in a heavily irradiated area.

A free graft of skin would not survive on the predicted wound bed, and a transposition flap from the upper abdomen was considered inadvisable in view of the size of the defect and the significant risk of partial loss of such a flap. Conventional repair by tubed pedicle or marsupial flap was rejected on account of the multiple stages involved.

The use of transposed omentum to provide a vascular bed for the reception of a free skin-graft was therefore selected as the only method which would permit excision of the ulcer and definitive closure of the defect at a single operative procedure.

OPERATIVE TECHNIQUE.—The ulcer was widely excised, down to the skeletal plane of the chest wall, revealing poorly vascularized tissues and a necrotic fourth costal cartilage. This was removed together with an adjoining portion of rib, thereby creating a defect in the parietal pleura (*Fig.* 2). The lung surface was free from intrapleural adhesion and was in consequence free to collapse down.

The abdomen was opened using a Kocher incision and the greater omentum was freed from old adhesions to a hysterectomy scar. Exteriorization of the omentum demonstrated an adequacy of tissue for the purpose intended, and further omental mobilization (in terms of creating a pedicle upon the right gastro-epiploic vessels) was not required in this case.

The diaphragm was detached from its insertion along the right anterior costal margin and the freed edge was moved cephalad and sutured to the muscle and periosteum along the superior border of the pleural defect (*Fig.* 3). (The pleural cavity was drained by means of a rubber tube and water seal.) In this manner the chest-wall wound was brought into communication with the peritoneal cavity via the orifice in the rib cage from where the piece of rib and costal cartilage had been removed, thus establishing a retrocostal route for the passage of the omentum from the abdomen to the site of repair (*Fig.* 4).

The margins of the chest-wall wound were then prepared for reception of the skin-graft. One of the problems of grafting a mobile surface on the trunk is the inevitable tendency for respiratory and postural movements to cause distortion of the wound edge, thereby transmitting a shearing force to the graft, and hence a high liability to haematoma formation and partial graft loss. This may in part be overcome by anchoring the wound margins to the deep fascia with a continuous pull-out nylon suture, passing between the subcutaneous tissue in the wound edge and the deep fascia, emerging at each end from the skin surface, and there locked by means of a bead and collar. One such suture was inserted along each of the four margins of the wound and secured in this manner.

The omentum was then drawn up into the chest wound and was seen to negotiate the route described without tension or torsion, and was fixed to the edges of the rib-cage orifice with fine catgut sutures; the abdominal wound was then closed. The transposed omentum was draped carefully over the base of the chest wound, and secured in position with multiple fine catgut sutures. Particular care was taken to avoid any impairment of the omental circulation during these manœuvres.

A split-skin graft was taken from the left iliac fossa, using a Padgett dermatome. This donor site was selected in preference to the conventional area on the thigh, because a large and relatively thick sheet of skin was required and under these circumstances there is considerable merit in using the trunk rather than a limb (Cort and Herbert, 1971). The graft was applied to the omental bed and sutured in place with a Redivac drain beneath the lower margin of the graft, emerging through a lateral stab wound (*Fig.* 5). Drainage was provided because there is reason to believe that omentum may produce a significant volume of transudate in the early postoperative phase, with a consequent risk of a serous effusion beneath the graft (McLean and Buncke, 1972). Gentle pressure and further fixation were established by tie-over sutures and a bolster dressing, care being taken to avoid excess tension on these sutures lest the delicate omental vessels be compressed.

The postoperative course was uneventful, with removal of the chest and abdominal drains at 48 hours. The graft-bed drain yielded 250 ml. of serous fluid in the first 72 hours and was removed at 96 hours. Graft inspection on the seventh day showed 100 per cent take, and the omental vessels were noted to be prominent beneath the graft. Healing of all areas was complete by the fourteenth day (*Fig.* 6), and histological examination of the resected tissue confirmed extensive radionecrosis with no evidence of recurrent tumour.

DISCUSSION

Previous authors have reported closure of defects in the rib cage and pleura using Marlex mesh overlaid by omentum and graft (Dupont and Menard, 1972). We suggest that the diaphragmatic manœuvre described here has considerable advantages when it is anatomically feasible. The need to implant foreign material is avoided and the method provides a retrocostal route for the omentum, thereby greatly reducing the risk of omental strangulation at the site of transgression of the abdominal wall or in a subcutaneous tunnel. In the present case the defect left by excision of the necrotic chest wall was not large and the incised diaphragm was brought to the upper margin of the defect with ease. It is considered that there would have been sufficient diaphragmatic tissue for the plan still to have been used if the third as well as the fourth costal cartilage had been affected. It is also felt that wider areas of chest wall could be excised and treated in the same way with careful planning for the individual case. The abdominal incision could be made lower and the posterior rectus sheath could be raised as a flap in continuity with the diaphragm.

We found no need to perform any specific omental mobilization in terms of a gastro-epiploic pedicle. This factor must be presumed to vary widely between individual patients, but it is worthy of note that a direct simple transposition may be practicable, thus simplifying the nature of the operation.

Acknowledgements.—We wish to thank Mr. Norman E. Winstone, Consultant Surgeon of Selly Oak Hospital, Birmingham, for providing details of the patient's previous treatment, and Mr. T. Dee, Chief Medical Photographer, Queen Elizabeth Hospital, for the photographs.

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HAEMANGIOPERICYTOMA OF THE PRE-SACRAL SPACE

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SUMMARY

A slowly growing tumour in the pre-sacral space is described. On surgical excision this proved to be a haemangiopericytoma which has since recurred locally. The difficulty and necessity of adequate removal are discussed.

A HAEMANGIOPERICYTOMA was first described by Stout and Murray (1942) as a vascular tumour in which the proliferating cell is a pericyte of Zimmerman (1923), which is a modified smooth muscle-cell surrounding small blood-vessels and normally being responsible for their contractility.

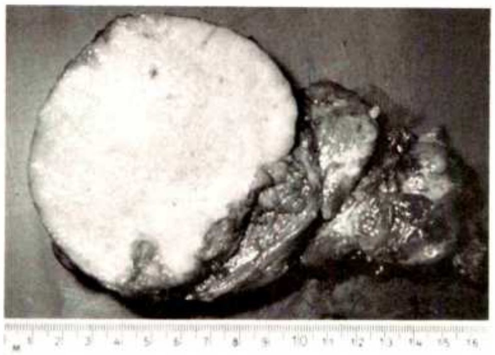

FIG. 1.—Cut surface of the specimen showing a white, whorled appearance.

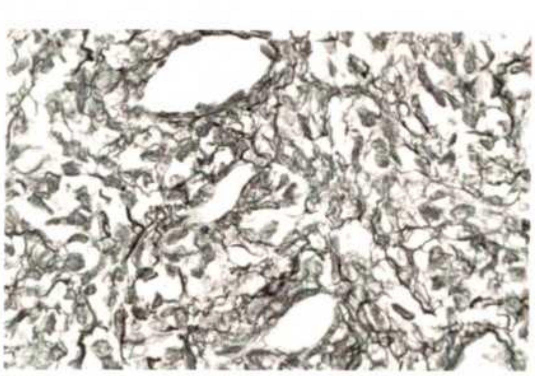

FIG. 3.—Section of the tumour stained with silver to show the reticulin-fibre supporting structure. (× 400.)

The essential characteristics of a haemangiopericytoma are that it consists of many capillaries, with or without lumina, lined by normal endothelial cells and surrounded by a delicate reticulin-fibre supporting structure. The space between these capillaries is filled with proliferating pericytes, which are spindle-shaped cells without myofibrils and having no organoid structure. This tumour is therefore distinguished histologically from haemangio-endothelioma, glomus tumour, vascular leiomyoma, vascular fibrosarcoma, and undifferentiated carcinoma (Harrison and Bulteau, 1972).

Haemangiopericytomas can occur anywhere in the body where there are capillaries, but approximately 45 per cent are found in the musculoskeletal system and 18 per cent in the intra- and retroperitoneal spaces (Backwinkel and Diddams, 1970).

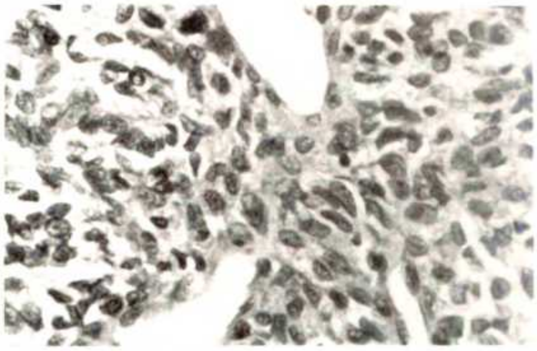

FIG. 2.—High-power view of a section of the tumour. H. and E. (× 400.)

Jackman, Le Mon Clark, and Smith (1951) described the pre-sacral space as a common site for masses of congenital, infective, or neoplastic origin, but of 64 neoplastic tumours from a total of 114 cases recorded at the Mayo Clinic from 1935 to 1948, no case of haemangiopericytoma was mentioned, accentuating the rarity of a pre-sacral haemangiopericytoma.

CASE REPORT

Mrs. C. T. was aged 23 in 1952 when she presented to the Queen Victoria Hospital, Melbourne, in her third pregnancy, on which occasion no abnormality was recorded. Subsequently she had three further normal pregnancies, but in 1959, when she was seen during her seventh pregnancy, she was found to have a pre-sacral mass of approximately 5 cm. in diameter attached to the sacrum. Plain radiographs showed a soft-tissue shadow only with no bony abnormalities. It was decided not to interfere at this time and the pregnancy resulted in a normal delivery. Her eighth and ninth pregnancies followed, the former being complicated by an unstable lie, but both ending in vaginal deliveries. Tubal ligation was performed in 1963 and she was followed by the Surgical Unit because of her pelvic tumour.

As the tumour was slowly growing, operation was undertaken in 1966. A full blood examination was normal, a Casoni test was negative, and a chest radiograph was clear. A barium-enema examination and intravenous pyelography confirmed that the tumour was displacing, but not involving, the rectum and ureters. Operation was performed by two surgeons using a synchronous combined approach. The tumour was fairly well encapsulated over most of its surface with no major feeding vessels found during dissection. However, there was a large amount of oozing from the surface of the tumour, as well as from the sacrum, and a blood transfusion of 17 pints was required during the procedure.

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Anteriorly the tumour 'capsule' was elongated downwards and intimately adherent to the posterior rectal wall. As complete removal was not possible without excision of the rectum, and the true nature of the tumour was not known, small firm remnants of the tumour capsule were left adherent to the rectal wall. Bleeding was eventually controlled with packs which were left in situ and removed 48 hours later.

The excised tumour was approximately 9 cm. in diameter (*Fig.* 1) with its cut surface exhibiting a white, whorled appearance, which can be explained by the absence of blood-filled capillaries due to compression of their lumina by the proliferating pericytes. The capsule was elongated in the direction of its rectal attachment just above the anal sphincter.

Microscopically, the tumour was seen to be a haemangiopericytoma (*Figs.* 2, 3) with numerous endothelial-lined vascular spaces separated by cords of fleshy pericyte cells.

Postoperatively the patient's convalescence was uneventful, but since that time there has been a gradual increase in size of the remnants, and in May, 1972, she had a semi-fixed nodular tumour of about 4 cm. in diameter lying in the retrorectal space. Otherwise the patient is well and remains symptomless.

DISCUSSION

At the time of surgery the true diagnosis was in doubt and therefore a frozen section was performed. This was of no assistance other than to confirm the presence of mitotic cells.

The extensive blood-loss during surgery indicated a vascular tumour of some type and indeed caused some concern in obtaining the amount of blood necessary for rapid replacement. When dealing with a possible haemangiopericytoma it is emphasized that adequate blood should be readily available to avoid this problem. Douglas, Mitchell, and Short (1966) described a case of retroperitoneal haemangiopericytoma in which the common and internal iliac arteries were controlled by tapes during surgery, both internal iliac arteries eventually being ligated. Despite this procedure there was still considerable bleeding from the pelvic floor.

Stout (1949) indicated that in a haemangiopericytoma, although the tumour appears well encapsulated, nests of dividing cells exist at the periphery of the 'capsule'. This is one reason why local recurrence occurs in 50 per cent of intra-abdominal cases and why wide excision is advocated by most authors (Slattery, Aronson, and Loman, 1956). Spiro, Brockunier, and Brumschwig (1964) have described a supraradical approach removing the anus, rectosigmoid, uterus, adnexae, and vagina for a recurrent tumour in a similar situation.

In the present case a clearance wide enough to prevent recurrence would involve excision of the anus and rectum, and it is the opinion of a consultative group of surgeons that this would not be justified in view of the absence of symptoms, the very slow progress of the tumour, and the low incidence of distant metastases.

The use of deep X-ray therapy alone or as an adjunct to surgery has not proved beneficial for large tumours of this kind, although Harrison and Bulteau (1972) reported a case of haemangiopericytoma of the nasal cavity which responded well to cobalt radiotherapy. The authors are not aware of any reported cases where cytotoxic therapy has been used.

Acknowledgements.—The authors wish to thank Dr. E. Abrahams and Mr. H. Berkshire for their assistance in the preparation of the illustrations.

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REVIEWS AND NOTICES OF BOOKS

Practice of Surgery. Current Review. Volume 1. By WALTER F. BALLINGER, M.D., St. Louis, and THEODORE DRAPANAS, M.D., New Orleans. 10 × 7 in. Pp. 321 + x. Illustrated. 1972. London: Henry Kimpton. £10·55.

THIS book consists of a series of reviews on specific subjects by members of the departments of surgery at the Tulane University School of Medicine in New Orleans and at the Washington University School of Medicine in St. Louis. The subjects are those in which, in the opinion of the editors, important advances are being made. These cover a wide range of general, vascular, traumatic, thoracic, and plastic surgery, so that the book will interest most surgeons. The chapters on fluid replacement in trauma, polyhormonal syndromes, and ventilatory failure after operation or injury are particularly good, while there is much of interest in most chapters. Each chapter has an excellent bibliography related to its subject.

The chapter on emergency medical transportation is of interest in describing the relatively backward position of the U.S.A. compared with the excellent service in this country thanks to such organizations as the St. John Ambulance Association, the local authorities, and the National Health Service.

The book can be recommended to all surgeons as a convenient method of keeping well informed over a wide range of surgery and as a source of references for further reading.

Recent Progress in the Study of Disorders of the Colon and Rectum. Edited by S. DROBNI and M. FEHER. 9½ × 6¼ in. Pp. 538. Illustrated. 1972. Budapest: Akademiai Diado. L.8.50.

THIS book publishes papers delivered at the International Congress of Hendrologicum Collegium held in Budapest in July 1970, and it consists of ninety-six papers by authors from twenty-six countries, with many contributions from surgeons in Eastern Europe and Russia. It is divided into sections on congenital anomalies, diagnostic procedures, polyposis, malignant disease, colitis, proctology, etc., the largest section of thirty-seven papers being on malignant disease, while seventeen papers are on various aspects of colitis.

There are some surprising omissions; for example, there is no contribution on the problems of rectal prolapse and there are only two contributions that deal with diverticular disease of the colon. Most of the papers are published in English, with a few in German and one in French. The printing and production are excellent, with the figures and illustrations (mostly black and white but a few in colour) clear and lucid.

Surgeons in England will not find anything very new to them in these papers, but many of the problems discussed are also subjects of controversy and slow advance in this country, and it is interesting to learn how surgeons in other lands are trying to solve them. Large-bowel malignancy and its many problems seem to be as common in Eastern Europe as in the Western world, and there also seems to be considerable division of opinion about the value and place of sphincter-preserving operations, both in low rectal cancers and in cases of ulcerative colitis. There are some useful contributions on amoebic infection, reminding us that its diagnosis may be difficult even when it is considered, and that the sigmoidoscopic appearances may closely resemble those of non-specific ulcerative colitis.

Unfortunately, not all the contributions have summaries and none of the chapters has any references at the end, even when references are mentioned in the text, an omission which rather detracts from the value of this book as a work of reference.

The Upper Cervical Spine. By DETLEF VON TORKLUS and WALTER GEHLE, Hamburg. 10½ × 7½ in. Pp. 101. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.48.

THIS is a useful book. It is not easy to read, but it presents very full information about the anatomy, anomalies, and pathology of the upper cervical spine. It is clearly based on a great deal of painstaking work. The text is very well illustrated throughout by diagrams and reproductions of radiographs, which greatly ease the reader's task and assist the understanding of this sometimes difficult region. Paediatricians will in particular welcome the sections dealing with development and anomalies, while all clinicians who have to treat necks will be grateful for this collection of reliable basic information. The authors have—rightly—dealt only very briefly with the matter of treatment. To do so would to some extent have lessened the value of the book. They have, instead, concentrated on bringing order to the description of situations at and below the occiput; most readers will think that they have succeeded in this considerable task. The figures are sensibly numbered and well arranged so that references to them in the text can instantly be followed. Many references are given, and these are conveniently listed. The index is short, but is adequate and reliable. The arrangement and heading of the sections could perhaps be sharper and more definite, and it is hoped that some errors of proof reading will be corrected in the next edition. Dr. Michaelis's translation of what may have been a difficult text on what certainly is a complex subject is good and clear. Most English readers will have cause to thank him for opening up this mine of information. The slim volume costs £7, but it is an important book and it should be seen by all who are concerned with the diagnosis and treatment of disorders of the cervical spine.

Abdominale Angiographie. By W. WENZ, with the co-operation of G. VAN KAICK, D. BEDUHN, and F.-J. ROTH. Pp. 226. Illustrated. 1972. Berlin: Springer-Verlag. DM.96.

THIS book in German is based on the authors' experience of abdominal angiography in 2804 adult and child patients and is meant as a guide to the non-specialist radiologist working in a small hospital, to trainee radiologists, and to general surgeons who wish to know what help can be obtained from specialized radiology. Renal angiography (except for trauma) has been omitted.

The vascular anatomy of the abdomen is described. There are detailed sections on the various forms of arterial and venous angiography with descriptions of the equipment and techniques needed.

There is unfortunately no discussion or illustration of photographic subtraction which has recently become cheap, very quick, and reliable. The authors prefer electronic and colour subtraction, neither of which would appear to be suitable for a small department.

There are detailed sections on the angiography of abdominal syndromes followed by discussion of the angiography of individual organs. Throughout the book the authors maintain a good balance between the relative value of clinical examination combined with the routine radiographic investigations, scintigraphy, and angiography. For example, the value of angiography in pancreatic disease is very fairly and soberly assessed.

The section on the morbidity of angiography is very good and describes the treatment of complications in detail. It is a sobering thought that 21 per cent of their patients had changes in the blood-flow to their legs following angiography.

The illustrations of 183 cases are small but demonstrate their points. The 21 colour illustrations are harder to understand than the black and white ones and add no further information.

The most useful part of the book for its users will undoubtedly be the up-to-date and very full bibliography of 790 references.

A textbook will never replace practical experience in angiography. However, with this proviso in mind this book succeeds as a guide to the investigator of abdominal diseases who is inexperienced in specialized radiology. It tells him the indications for angiography of the abdomen in a given situation; the technique of the procedure with its inherent dangers; it also indicates his chances of obtaining worth-while information unobtainable by other means and how to assess the findings. It will be a useful reference book on the bench.

Orthopaedics in Infancy and Childhood. By G. C. LLOYD ROBERTS, M.Chir. (Cantab.), F.R.C.S., London. 8½ × 5½ in. Pp. 337 + x. Illustrated. 1971. London: The Butterworth Group. £6·75.

THIS book is intended to be of value to both orthopaedic surgeons and paediatricians and is written by an orthopaedic surgeon with a wide experience in the care of children of all ages.

In its systematic arrangement consideration of the generalized disorders of the skeleton is followed by that of the effects of vascular, lymphatic, and metabolic anomalies and diseases, and discussion of bone cysts, tumours, and various infections. There is a chapter on the disorders of the central nervous system which owes much to the influence of Paul Sandifer in the part on cerebral palsy; in the section on the disabilities associated with myelomeningocele a commendably moderate and realistic attitude is taken towards the whole problem. There follows a short description of a variety of rare conditions. The remaining two-thirds of the book deal with the disorders of the different regions. Nothing seems to have been missed out, but with such a vast range of items it is obvious that many get only a short mention.

The many queer combinations of disturbances of growth and form in childhood provide a delightful ambience for the eponymously minded and no opportunity is lost here and much good it does us all in enlarging our diagnostic capacity and enjoyment; sometimes it is almost as good as the best dermatology, but may one protest, however, at 'acromionectomy'!

The many illustrations are good, but it is unfortunate that the name of the patient appears in some of the radiographs, and this should be avoided in the next edition.

This book deserves to be read by all orthopaedic surgeons who have to treat children and should be of much value to paediatricians when faced with a baby with a rare deformity.

Synopsis of Surgery. Second edition. Edited by RICHARD D. LIECHTY, M.D., Iowa, and ROBERT T. SOPER, M.D., Iowa. 7¾ × 4¾ in. Pp. 1108 + xiv. Illustrated. 1972. London: Henry Kimpton. £7.

IN spite of its title this is really a general surgical textbook for students compacted by listing and tabling some of the material. The 26 contributors come predominantly from the University of Iowa. This second edition has been expanded with chapters on total parenteral feeding, transplantation, and gynaecology. The number of illustrations has been increased but the diagrams remain clearer than the photographs and radiographs, some of which are darkly reproduced. The text is well written and on the whole well balanced, but clinical descriptions are sometimes too brief and therefore too generalized; for instance, mesenteric vascular occlusion is described as causing the rapid onset of abdominal distension and tenderness, with no mention of the frequent absence of signs. In contrast, operative detail is occasionally too lavish; a short treatise is devoted to the various forms of colostomy.

Its high price will put this book out of the reach of most students.

Orthopaedics and Accidents. By MARGARET MILLER, R.G.N., S.C.M., and JAMES H. MILLER, M.B., Ch.B., F.R.C.S. (Glas.), F.R.C.S. (Edin.). 8¼ × 5½ in. Pp. 256 + xiv. Illustrated. 1972. London: The English Universities Press Ltd. £1·35.

THIS pleasant little book is well worth browsing through since it contains a great deal of interesting information which is well set out.

It will be useful to senior students and house officers as well as to the nursing staff. The section on orthopaedic nursing will allow the young house-surgeon to have a new insight into nursing problems.

It is the sort of book that will be found on sister's desk in the orthopaedic ward or in the casualty department.

A few antique heresies, such as the value of electric heat in tennis elbow and the antiquated methods of applying traction, have crept in but probably this is no great disadvantage because the young have to develop their own critical faculty.

A good little book to be recommended and the authors are to be congratulated.

Reconstruction Surgery and Traumatology, Volume 13. Edited by G. CHAPCHAL, Nijmegen. 9½ × 6¾ in. Pp. 209 + ix. Illustrated. 1972. Basle: S. Karger. £10·80.

THE first part of this book occupies half the pages and is devoted to surgical and related methods of dealing with the effects of cerebral palsy. It deals in turn with the methods that can be recommended for the nervous system and the different deformities that occur in the limbs. It presents a useful summary of present practices in these fields and provides a fairly large bibliography.

The second section occupies 72 pages and deals with the treatment of spinal injuries, with particular reference to the need for careful handling of the patient as the best means of promoting recovery by avoiding further damage; the application of rigid fixation to the mandible by the use of the tension-band principle, the fate of exposed bone, and the management of pressure sores.

The third section includes a statement that the aetiology of idiopathic infantile scoliosis is not known and then offers an explanation based on the effects of different countries' customs with regard to the postures in which children are placed. The final chapter is on metabolic aspects of scoliosis.

The English is not very good and there are many spelling mistakes in this otherwise well-produced but very expensive review.

Prolactin and Carcinogenesis. Edited by A. R. BOYNS and K. GRIFFITHS. 8½×6 in. Pp. 230+viii. Illustrated. 1972. Cardiff: Alpha Omega Alpha Publishing. Price not given.

THE report of the proceedings of the Fourth Tenovus Workshop lives up to the high standard of its predecessors and is published just 8 months after the meeting itself. Prolactin was identified as a distinct hormone in man only 2 years ago but since then a large amount of work has been done on its chemistry, estimation, physiology, and pathology. Its special importance lies in the part it plays in the development and function of the breast, its undoubted role in supporting the growth of mammary carcinoma in experimental animals, and its possible similar function in human breast cancer. It appears also to influence the prostate in animals and may be involved in prostatic disease in man.

Much of the work on prolactin from both sides of the Atlantic is reported here, together with verbatim records of the critical and informed discussions. The emphasis, as the title indicates, is on its relation to cancer. The book should be in every large medical library and all endocrinologists, pathologists, and surgeons working in this field will find it indispensable reading and a useful source of references to earlier works.

Developments in Biomedical Engineering. Edited by MARTIN M. BLACK, School of Applied Sciences, University of Sussex. 9×6 in. Pp. 192+x. Illustrated. 1972. London: Sussex University Press, distributed by Chatto & Windus, London. £6.

THIS excellent book, which is perhaps highly priced for the general reader, contains much information about the rapidly developing field of biomedical engineering. The topics dealt with are divided into three groups: prosthetics and biological valves; membranes and pumps; biological simulation and measurements. Each section is subdivided into parts dealing with specific problems. The subsections include much detail but seem to the general reader to demand a considerable background of experience for full appreciation. Nevertheless, the book is so well written that it has a somewhat wider appeal than just to the specialist.

Plastics Materials in Surgery. Second edition. By BERNARD BLOCH, M.B., Ch.B., F.R.C.S., Sydney, and GARTH W. HASTINGS, Ph.D., B.Sc., Th.L., F.R.I.C., M.R.S.H., North Staffordshire Polytechnic, Stoke-on-Trent. 9×6 in. Pp. 273+ix. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $18.75.

WE badly need a book on the use of plastics in surgery, whether as implants or otherwise. In 1967 Bloch and Hastings produced the first edition of their book which was a catalogue of what had been used, where and how. It read like a railway timetable, but on the whole was less useful because it was uncritical. The second edition brings one up to date with source references, but times have changed. We have all used plastics and are bewildered by their variety. We now need an authoritative and critical account, with facts and figures, on which plastic to use and why. When a patient says, 'How long will it last, doctor?' we mumble something, but we still do not know. When a new plastic is produced everyone finds it ideal and discards the old one. As the authors state: 'Clinical use is in advance of experimental evidence of suitability.' It always has been, yet there is little guidance to be found in this book, even though the first chapter purports to discuss methods of assessment, and in chapter 5 toxicity and biological and mechanical evaluation are dealt with, but the treatment is too vague and non-specific.

For the tiro some of the information can be misleading, and much of it will lead to disaster; on p. 146 it is stated: 'Cartilage powder is found to accelerate wound healing.' If this is so, then we should all be using it; like detergents for washing up the dirty dishes, it saves time and effort. But is it true? All the ten publications about cartilage powder have come from one centre, even though only two are listed. Anyone picking up this book might expect guidance on which plastic to use; he will be disappointed, and perhaps overwhelmed by the 760 references in chapter 4.

For the practical surgeon this book has little to offer and is rather expensive.

Environmental Health Perspectives. Experimental Issue No. 2, October, 1972. 10×7¾ in. Pp. 128+iii. Illustrated. 1972. North Carolina: U.S. Department of Health, Education, and Welfare, National Institute of Environmental Health Sciences. Price not given.

THIS is a journal with prepared articles from a variety of sources, dealing specifically with the problems of environmental health. This issue includes such diverse subjects as the effects of noise and ototoxic drugs, aspects of microwave radiation, and susceptibility to lead toxicity. It is unlikely to appeal to the general reader and is a journal for the specialist.

Fundamentals of Anesthesia Care. By BETTY J. SMITH, C.R.N.A., New York. 9×6 in. Pp. 120+vii. Illustrated. 1972. London: Henry Kimpton (St. Louis: C. V. Mosby). $2.

IN her preface Miss Smith explains that her book has been written for student-nurse anaesthetists and that it is not intended as a single introduction to every part of anaesthesia. She provides a well-written and excellent account of many largely, but not entirely, technical aspects of anaesthesia, and some of surgery. She takes great care to emphasize those most important but often small points which collectively, and occasionally individually, make such a difference to the comfort and safety of the patient. There is splendid advice on behaviour in the presence of conscious and semiconscious patients in the induction and postoperative care rooms, and practical comment upon such matters as the care of the patient's lips and the insertion of a needle into a vein. Miss Smith's obvious dislike of conveyor-belt systems and her dedication to the patient as an individual deserve special commendation in this age of 'turnover' and 'cost effectiveness'. The limitations of the book for the physician anaesthetist are entirely outweighed by its obvious advantages as a carefully prepared account of routine technical procedures that every junior doctor in anaesthesia should know about. Too many anaesthetists take these for granted nowadays and they are rarely described in scientific texts.

Head and Neck Surgery. By P. M. STELL, F.R.C.S., Liverpool, and A. G. D. MARAN, M.D., F.R.C.S., Dundee. 8½×6 in. Pp. 454+x. Illustrated. 1972. London: William Heinemann. £7·75.

ONE of the privileges of increasing age is that it provides an opportunity for writing textbooks and criticizing the young! Although the value of the former is doubtful, there may well be grounds for suspecting that many younger surgeons are more concerned with surgical expertise than case selection or patient care.

This particular book is in many ways exceptional. The authors are certainly youthful, although vastly experienced in the problems of head and neck surgery. In addition, they have avoided the all-too-common pitfall of producing just another 'Atlas of Surgical Techniques'.

For several years they have been jointly responsible for a highly successful surgical course and this book is largely based on the course syllabus. The first half is devoted to basic principles and the remainder to a fairly detailed and didactic account of the various operative procedures necessary for the eradication of disease in the various sites which make up the head and neck.

No claim is made that this is anything but an introduction to this particular surgical specialty, and as such it succeeds admirably. Naturally, experienced surgeons will disagree with some of the more detailed sections, for uniformity of opinion is not a characteristic of practising surgeons. However, it is all good sense, clearly written and tolerably well illustrated, considering the small pages provided by the publishers.

Buy it, read it, and read it again.

Surgical Emergencies. Diagnosis and Management. Edited by T. SCHRIRE, M.A., M.B., F.R.C.S., F.R.S.S.Afr., Cape Town. 8½ × 5½ in. Pp. 286. Illustrated. 1972. London: William Heinemann. £4·15.

THIS book is intended to give guidance to those who organize casualty departments and to give instruction to casualty officers. There are helpful suggestions concerning lay-out, equipment, and management of the casualty department. The clinical chapters are variable in their potential value to the junior casualty officers, but those on hand infections, on the repair of superficial wounds, and on the emergency care of chest and head injuries are practical. As a reference book on the casualty department shelf it merits purchase, but it has less value as a medium of basic instruction for the junior casualty officer.

Abdominal and Vaginal Hysterectomy. By S. JOEL COHEN, M.B., B.Ch., F.R.C.S., F.R.C.O.G., Johannesburg. 9¾ × 7½ in. Pp. 170 + xii, with 153 illustrations. 1972. London: William Heinemann. £3·50.

As indicated in the foreword by Sir Norman Jeffcoate, Mr. Joel Cohen is an acknowledged surgical master. In this monograph he describes his techniques of hysterectomy in considerable detail. The text is well and liberally illustrated to emphasize the relevant operative steps. Both abdominal and vaginal hysterectomies are described, with the latter being given the most space. The author makes the case for vaginal hysterectomy as the best means of removing the uterus even when there is no prolapse present. An interesting and useful 'appendix' section is housed separately inside the back cover and describes the role of the operating nursing sister. Here again the author describes in detail the 'routine' as it affects the theatre sister taking the case.

This book should be of interest both to the experienced and to the trainee in gynaecological surgery.

Bile Salts in Health and Disease. By K. W. HEATON, M.D., M.R.C.P., Bristol. 8½ × 5½ in. Pp. 252 + x. Illustrated. 1972. Edinburgh: Churchill Livingstone. £3·50.

IN 1937 Baillière, Tindall & Cox published the *Physiological Chemistry of the Bile* by H. Sobotka. This book was to become a kind of bile bible for the next 30 years, wherein could be found much information on the bile-salts in the human and in many animal species. In the past 20 years research into the physicochemical properties of the bile-salts has explained their role and that of lipoproteins in the carriage of cholesterol in the aqueous bile, thus providing a basis for the understanding of the formation of gall-stones. More recently, gas/liquid chromatography has provided the technological advances necessary for studying the enterohepatic circulation of bile-salts and hepatic bile-acid pools in health and disease, and there has been a supernoval explosion of research.

Dr. Heaton's book is about all of these developments, and includes chapters referring to his own special contribution in the role of the diseases of the intestine affecting the enterohepatic circulation of bile-acids with reference to gall-stone formation.

It is a very useful, smallish book with over 700 references, and is ideal for the specialist surgeon interested in gastro-enterology.

Functional Anatomy and Histology of the Lung. By CHUZO NAGAISHI, M.D., Kyoto. 11¾ × 8½ in. Pp. 295 + xxviii. Illustrated. 1972. Baltimore: University Park Press. $49·50.

IN this book nine eminent men in nine forewords have chosen to extol the high qualities of the author as a surgeon, scholar, and anatomist.

To break into the book one may think of an anatomical subject and then look it up. For instance, under the heading of 'The Relationship between Pulmonary and Bronchial Vascular Systems' will be found a history of investigations since 1937 to the present time. The findings are grouped and described. Controversial points are highlighted. The bearing of an anatomical or histological point upon pathology is often observed. This same thoroughness applies throughout the book. The references are full and there is a good proportion of Japanese studies fitting in with, and elaborating, those of the West. The reproduction and diagrams are excellent and there are many instructive electron-microscopy photographs. The English is good, although in a few places one may have to read the text several times to get the feel of a sentence. This is a unique and outstanding book. The reviewer is minded to repeat the words of a tourist to his wife after leaving a Botticelli room in the Uffizi: 'That room is full of very good paintings.'

Acute Inflammation. By J. V. HURLEY, M.D., Ph.D. (Melb.), F.R.C.Path., Melbourne. 8½ × 5½ in. Pp. 144 + vii. Illustrated. 1972. Edinburgh: Churchill Livingstone. £2·50.

THIS short monograph aims at describing current views on the morphology and mechanism of acute inflammation and its sequelae. It gives an admirably succinct account of these subjects including basic ultrastructural changes and recent work on the chemical control of the phenomena of inflammation. In these respects the monograph provides a most convenient summary of recent research and will be valuable to those working for examinations or merely wishing to bring their knowledge up to date. It is to be noted, however, that the book does not deal with immunological mechanisms, which are now known to be intimately concerned with the initiation and persistence of many previously unexplained phenomena in the field of inflammation.

Praktische Anatomie, Volume 1, Part 4. **Bein und Statik.** By J. LANG and W. WACHSMUTH, Würzburg. 12 × 9½ in. Pp. 473 + xii. Illustrated. 1972. Berlin: Springer-Verlag. DM.640.

IN this book the descriptive and applied anatomy of the lower limb is celebrated—perhaps that is one of the few words suitable for describing this immaculately produced volume. Even those with no knowledge of German will be impressed by the range of material covered but above all by the illustrations, many of which are among the most outstanding of all contemporary representations of the human body. There is only one snag to this beautiful example of book production—at about £80 for this one volume (or about £70 as a subscription price, for there must be several more to come to complete the whole body) even libraries will require rich uncles.

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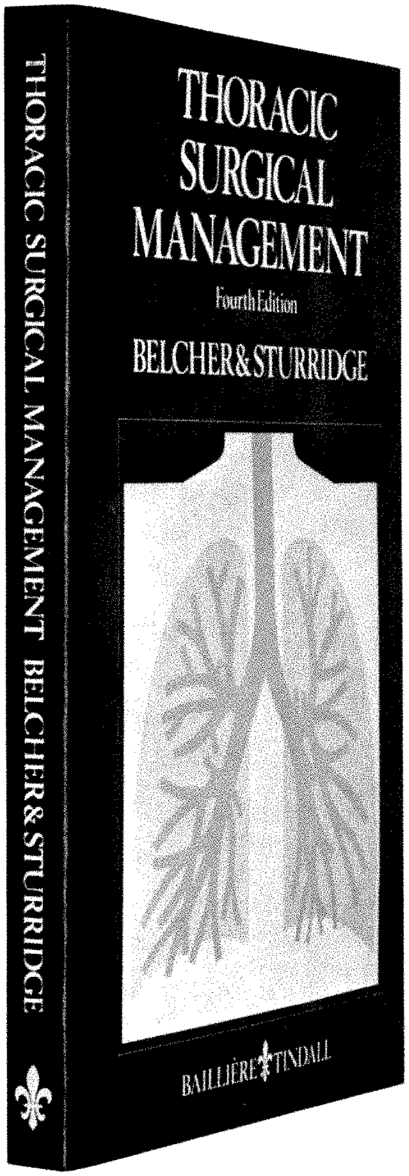
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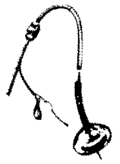

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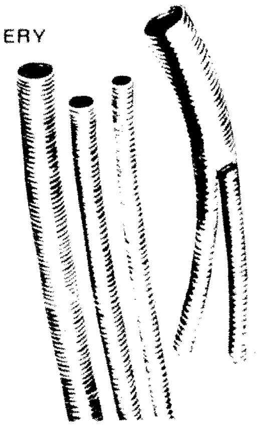

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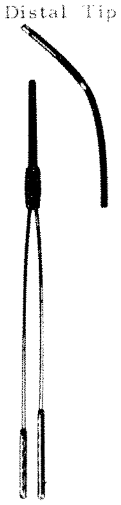

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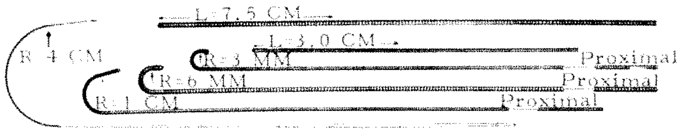

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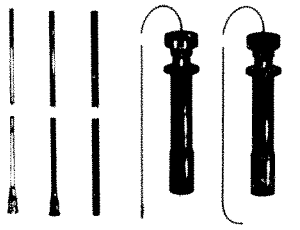

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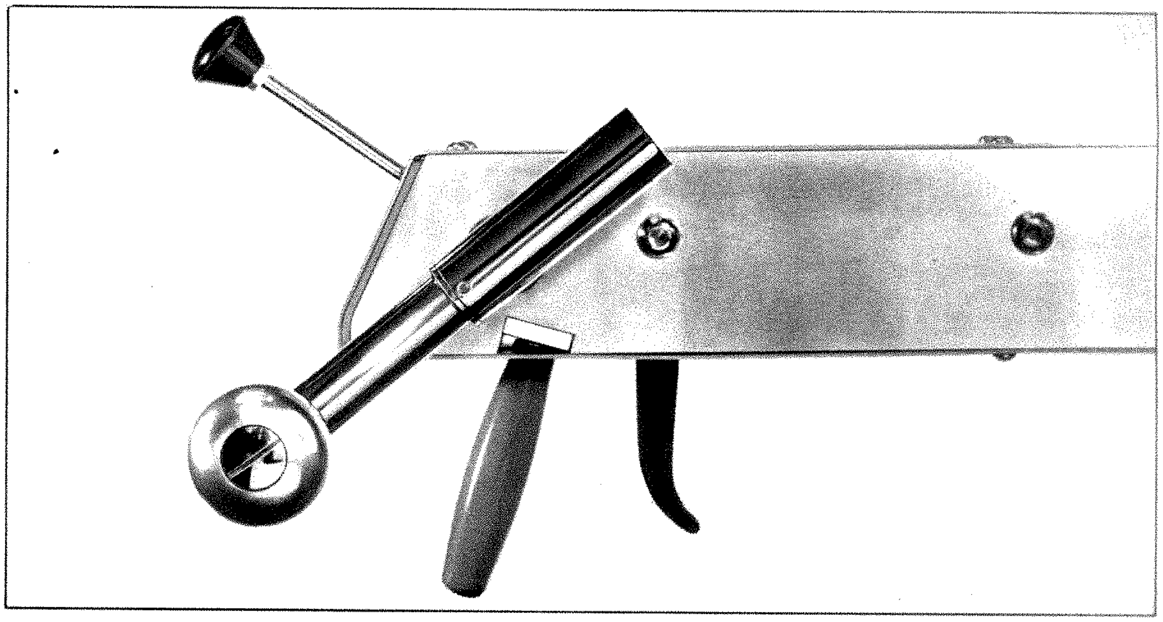

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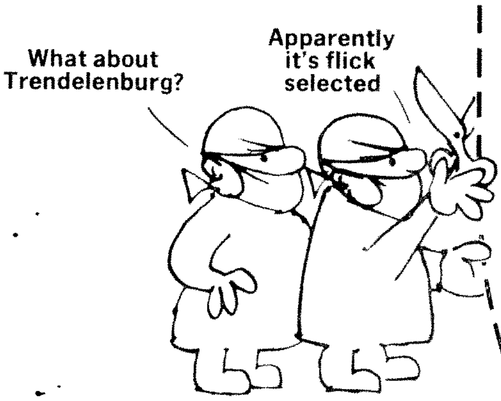

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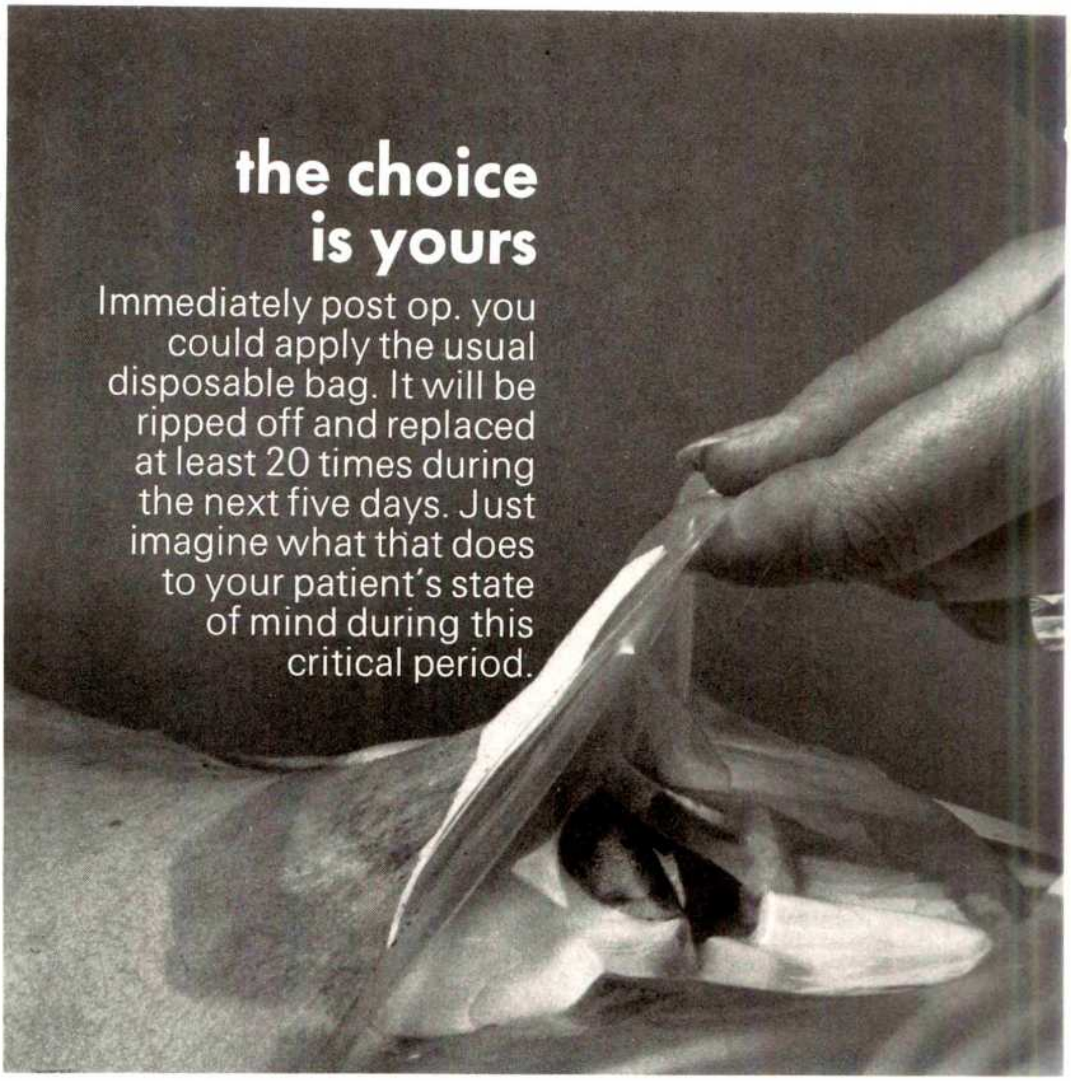

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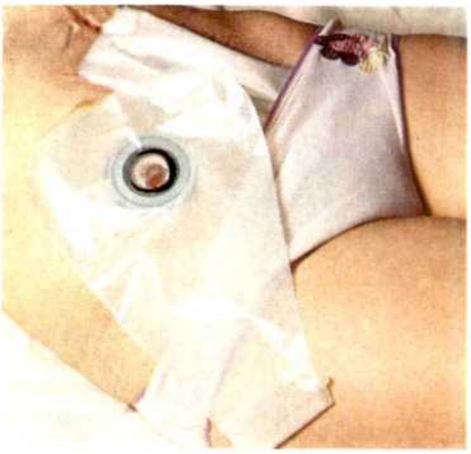

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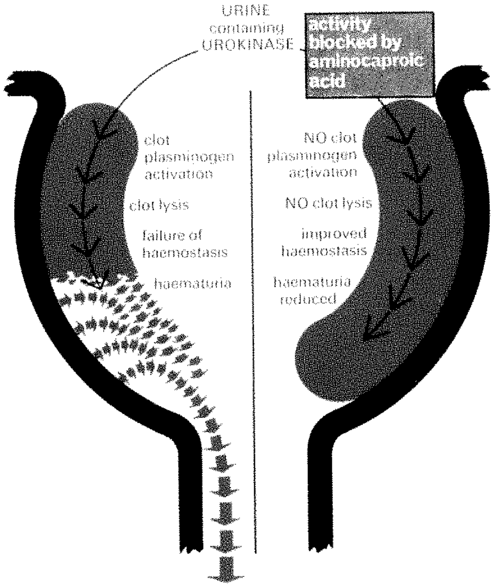
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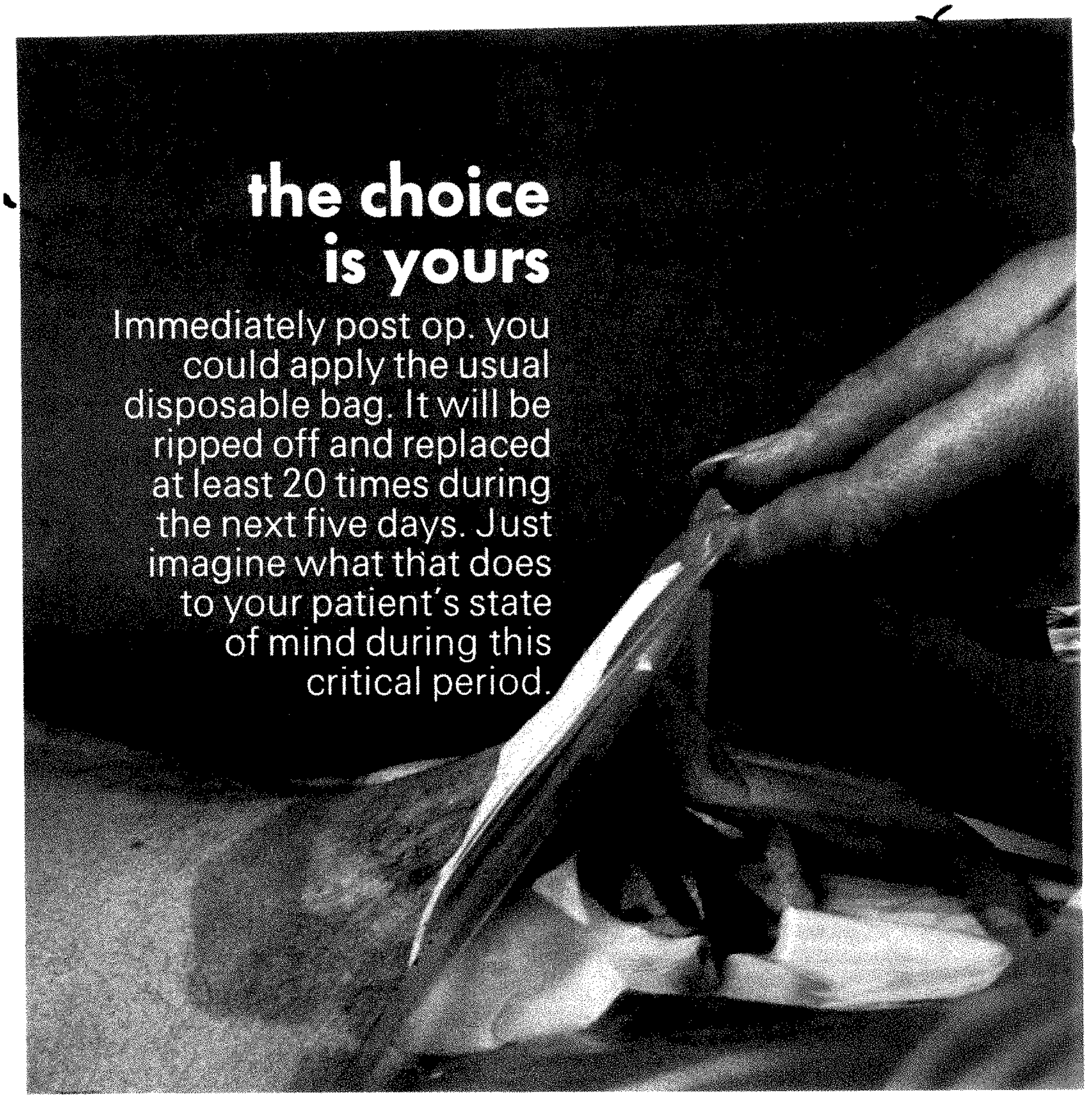

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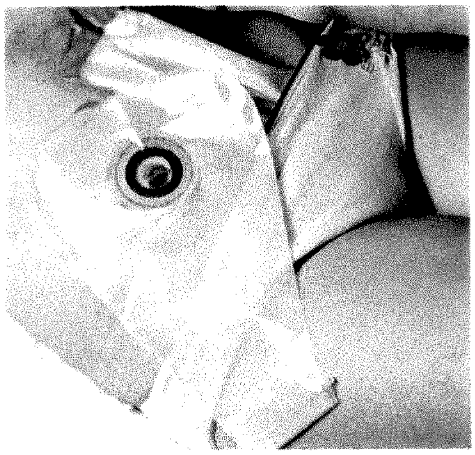

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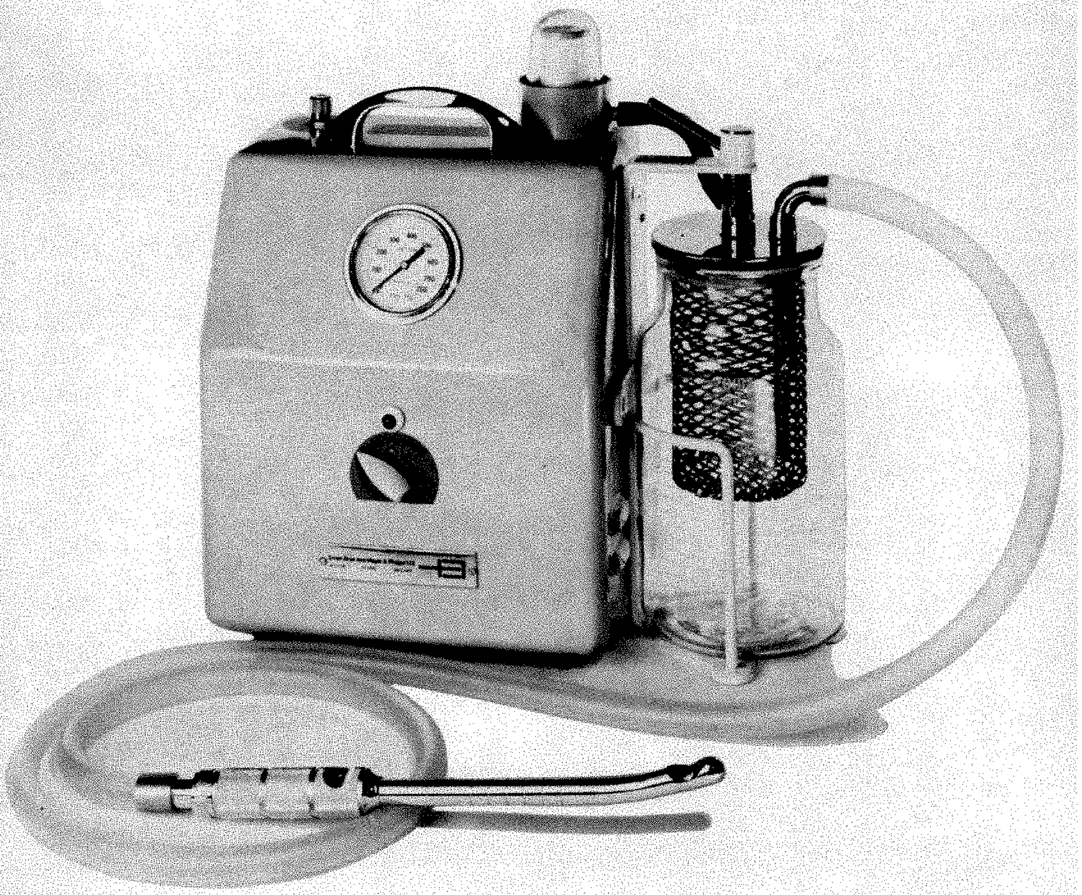

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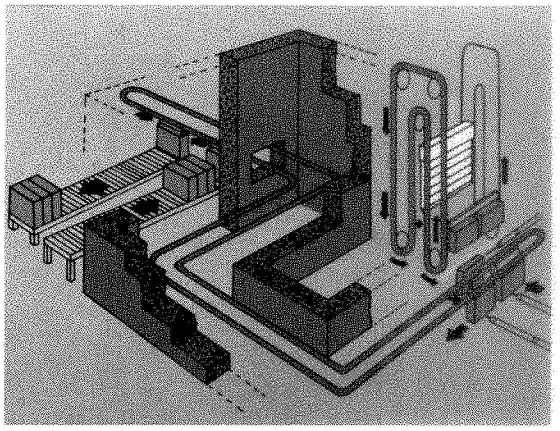

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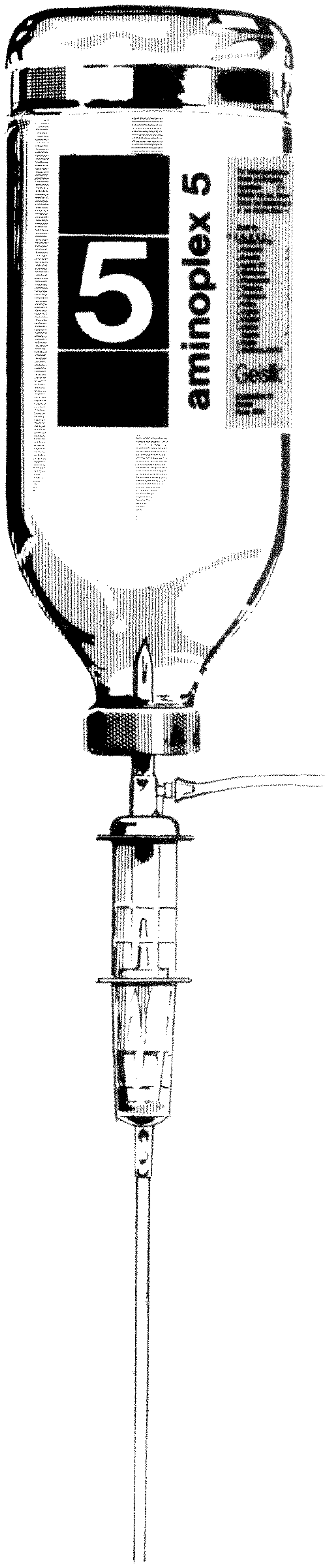

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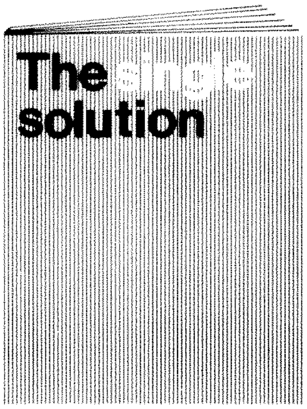

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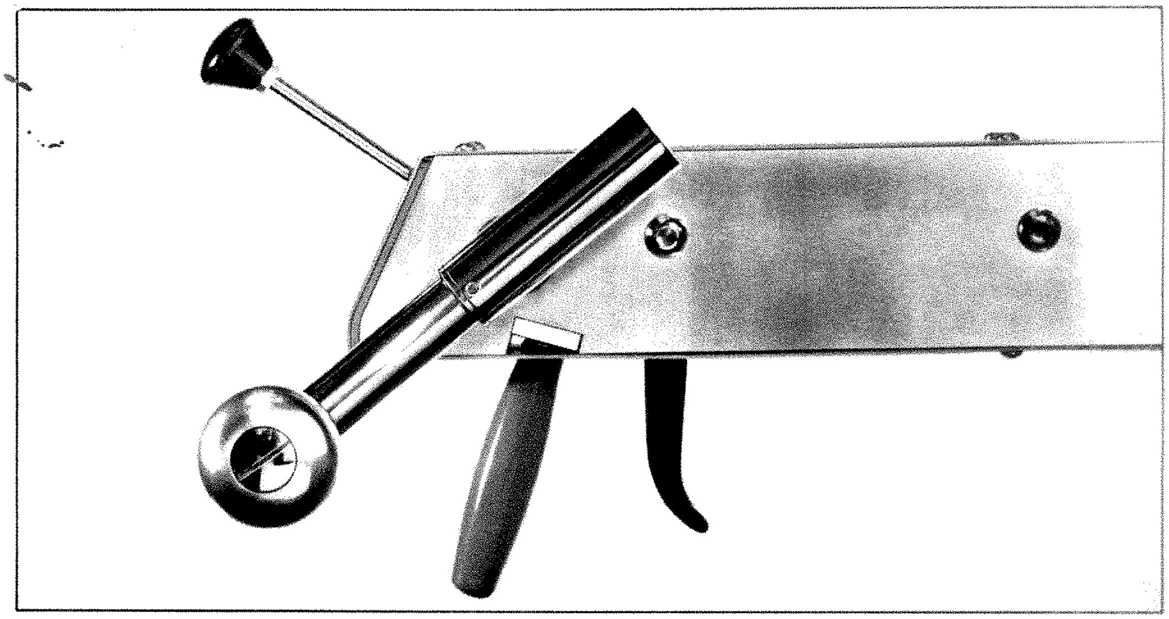

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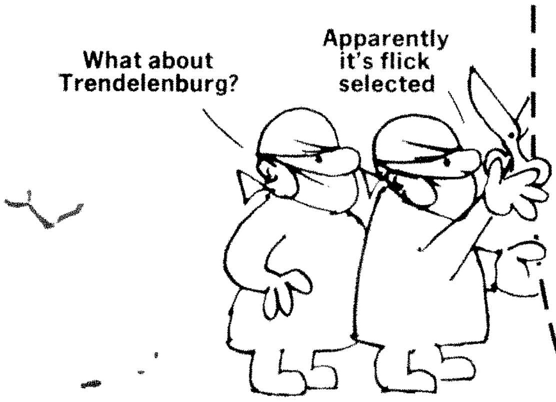

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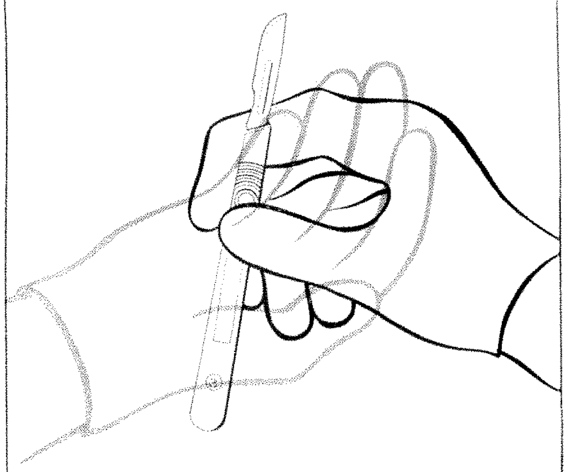

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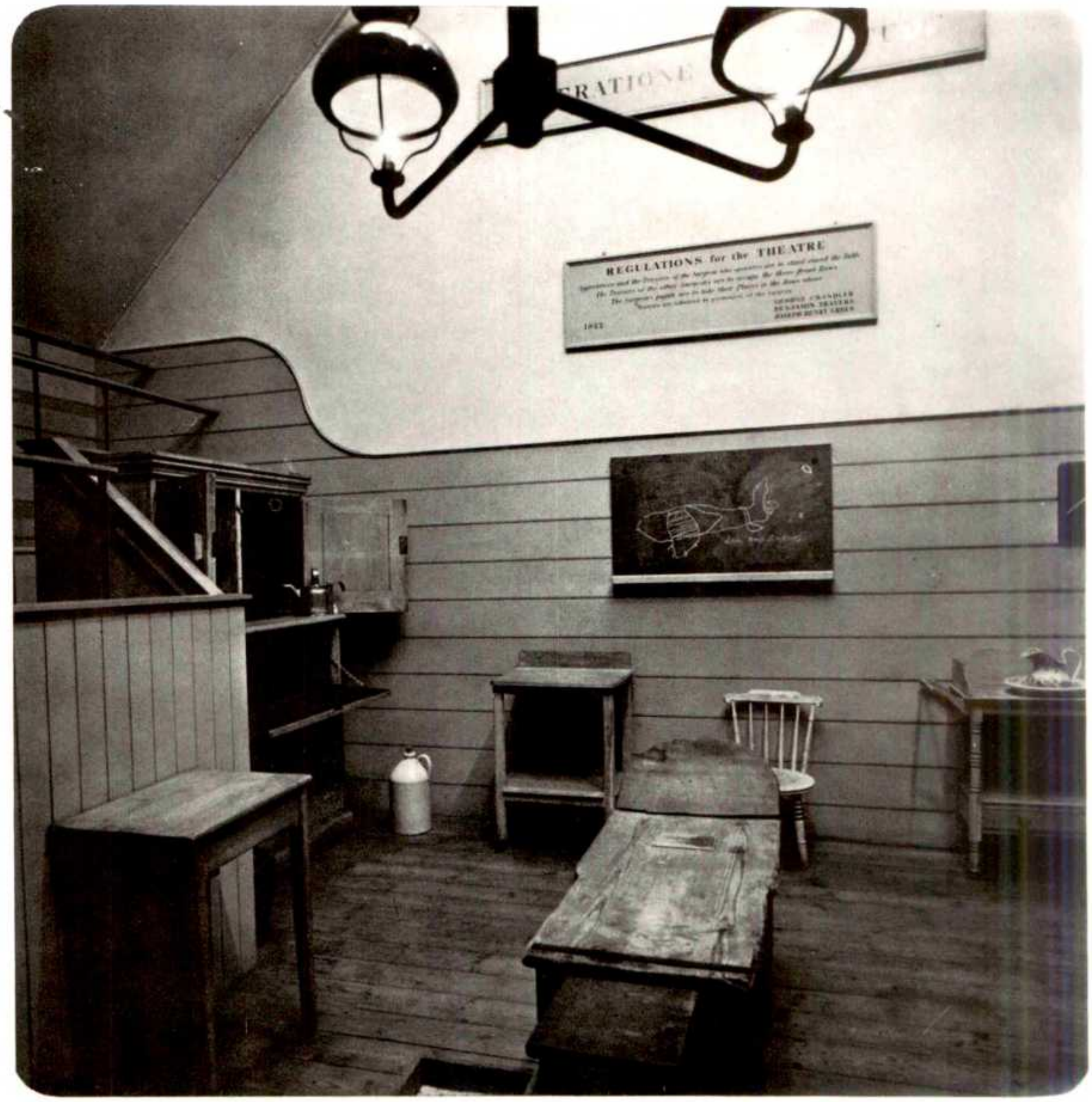

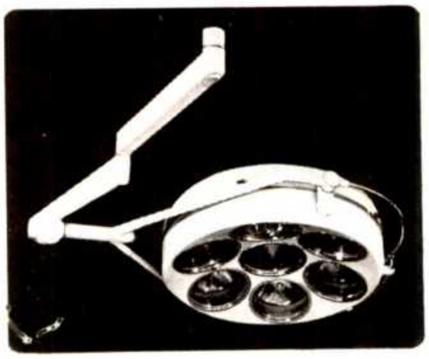

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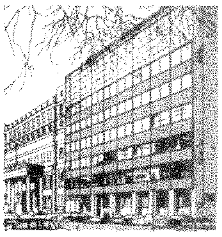

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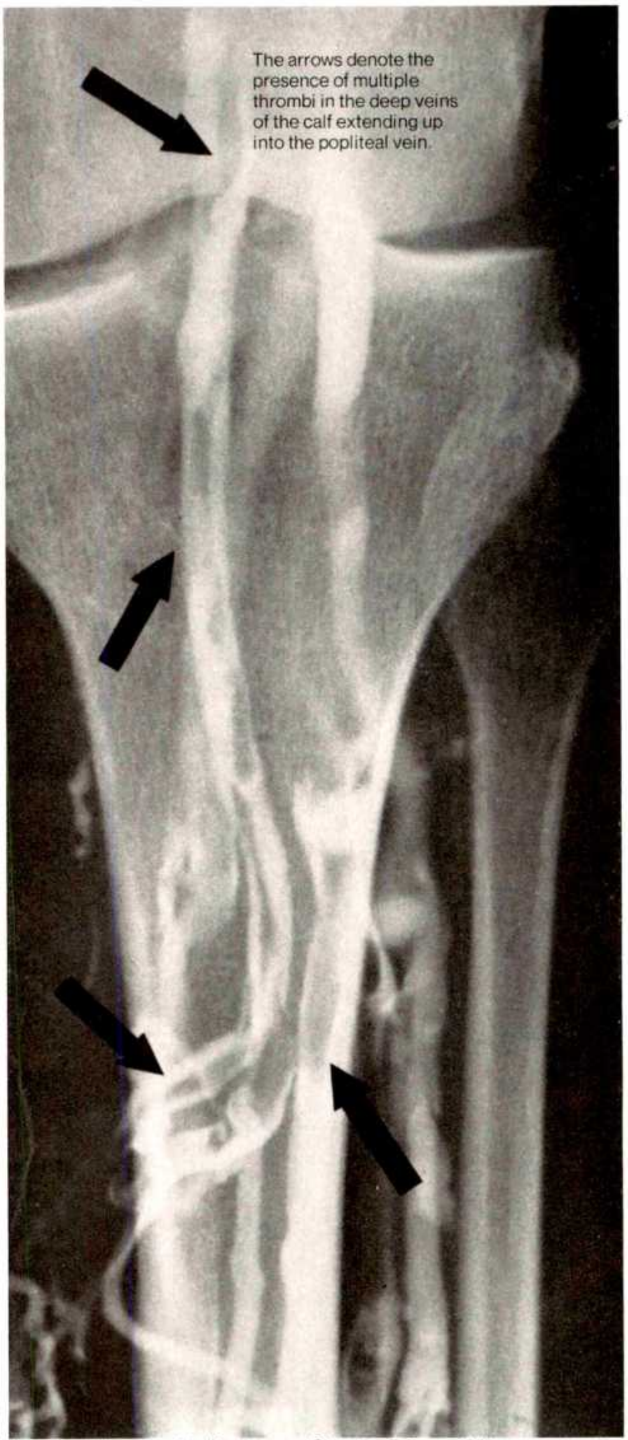
“. . . the infusion of 1 litre of dextran 70 over a period of six hours starting at the induction of anaesthesia markedly decreases the incidence of post-operative thrombosis without any evidence of an increase in bleeding complications . . .”[3]



The arrows denote the presence of multiple thrombi in the deep veins of the calf extending up into the popliteal vein.

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THE
BRITISH JOURNAL OF SURGERY

Vol. 60 AUGUST, 1973 No. 8

ORIGINAL PAPERS

THE EFFECTS OF INTRAVENOUS AND INTRADUODENAL FEEDING ON NITROGEN BALANCE AFTER SURGERY

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SUMMARY

To assess the value of nutrition in the first week after surgery, total nitrogen balance was determined in three groups of patients (two experimental, one control) undergoing vagotomy and pyloroplasty from 1 day before to 8 days after operation. In the experimental groups nutrition was maintained postoperatively by the intravenous route in one and intraduodenally in the other at a level adequate for normal non-postoperative subjects. Water and electrolyte intakes were similar in the three groups, but patients in the control group received no calories or nitrogen in the immediate postoperative period.

With respect to nitrogen economy, the group fed largely by the intraduodenal route fared best. Nevertheless, nitrogen balance did not reach equilibrium until day 5 in any group, probably indicating a relative increase in protein catabolism in the early postoperative period.

MANY investigators have shown that the administration of calories and protein derivatives to patients in the immediate postoperative period can reduce the negative nitrogen balance consequent upon the operative procedure, although the extent of the reduction has varied considerably. There is also controversy whether the intravenous (i.v.) or the intraduodenal (i.d.) route is the better way to feed the postoperative patient. Thus, Koop, Riegel, Grigger, and Barnes (1947) reported that nitrogen is more readily spared postoperatively when nutrients are given i.d., whereas Abbott and Albertsen (1963b) took the opposite view. Many factors, including age (Walker, Watt, Morgan, and Parker, 1971), sex (Abbott and Albertsen, 1936a), body-weight, debilitating disease, postoperative complications, degree of surgical trauma (Moore and Ball, 1952), and environmental temperature (Campbell and Cuthbertson, 1967), are known to affect the metabolic response to trauma.

In the present study of nitrogen balance postoperatively we compared results of feeding by the i.v. and i.d. routes, eliminating as far as possible any intergroup differences possibly attributable to factors known to affect the metabolic response. Thus only healthy male subjects undergoing one particular operation were studied, they were matched by age and weight, and the same surgeon performed all the operations. Any subject in whom postoperative complications developed was excluded from the study.

PATIENTS AND METHODS

The subjects of our study, who were undergoing total perabdominal vagotomy and Heineke-Mikulicz pyloroplasty for chronic duodenal ulceration, were nursed at an ambient temperature of 23 ± 2° C. and a relative humidity of 40–60 per cent. They were divided into three groups (two experimental and one control) which were closely matched by such factors as age ($P > 0{\cdot}2$, Kruskal-Wallis test) and weight ($P > 0{\cdot}2$, t-test). The study consisted of nine balance periods, each of 24 hours' duration, starting at 8 a.m. on the day before operation (day -1) and ending at 8 a.m. on day 8.

Group 1 (8 patients).—Nutrition was given i.v. only during the first 3 days postoperatively (days 1–3), then partly i.d. and partly by mouth during days 4–6, the amount of the i.d. infusion being reduced and of the oral diet increased so that by day 7 feeding was wholly oral with a diet similar to that taken on the day before operation (day -1). The parenteral nutrients used were Aminosol 10 per cent (a casein hydrolysate), Intralipid 10 per cent, and fructose and

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glucose solutions. The amino-acid solution and fat emulsion were infused simultaneously into a T-piece attached to an i.v. cannula; heparin (1000 U. per 500 ml.) was added to the former solution immediately before infusion in order to hasten fat clearance. Intraduodenal infusions were given via a gastrostomy tube (Kay, 1964) inserted at operation.

Table I.—DAILY INTAKE OF DIETARY CONSTITUENTS OF THE THREE GROUPS

DIETARY CONSTITUENT	DAY −1	DAY 0 (Operation)	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	GROUP
Water (ml.)	2500	100	3250	3500	3500	2800	2500	2300	2500	1
	2500	100	3000	3300	3300	2800	2500	2300	2500	2
	2500	100	2500	2500	2500	2500	2500	2500	2720	3
Sodium (mEq.)	100	0	160	160	160	95	93	85	100	1
	100	0	95	95	95	95	93	85	100	2
	100	0	100	100	100	100	100	100	100	3
Potassium (mEq.)	65	0	50	50	50	88	93	88	65	1
	65	0	82	82	82	88	93	88	65	2
	65	0	60	60	60	60	60	85	65	3
Nitrogen (g.)	12·5	0	12·7	12·7	12·7	13·5	15·9	18·4	12·5	1
	12·5	0	10·9	10·9	10·9	13·5	15·9	18·4	12·5	2
	12·5	0	0	0	0	5·2	10·4	15·6	15·6	3
Total calories* (Cal.)	1660	0	2130	2130	2130	2015	1995	2000	1660	1
	1660	0	2015	2015	2015	2015	1995	2000	1660	2
	1660	0	0	0	0	550	1100	1650	1660	3

* Including energy potentially derived from protein and its derivatives.

Group 2 (7 patients).—The diet was given entirely by i.d. infusion during days 1–3, employing a jejunostomy feed of our own composition (Hindmarsh, 1971). Feeding was as in group 1 during days −1 and 4–7.

Group 3 (11 patients).—The patients in the control group had a water and electrolyte intake similar to that in the experimental groups throughout the study. They received no calories or nitrogen during days 1–3 but increasing amounts of these on days 4–6. On day 7 solely oral feeding was re-established with a diet similar to that taken by all the patients on day −1.

The water, Na, and K intake of all three groups and the calorie and nitrogen intake of the two experimental groups differed only in relation to the difficulty in arranging dietary régimes containing the desired amount of each substance; for example, the large Na content of Aminosol meant that group 1 received more of this ion than did the other groups on days 1–3. The calorie, water, nitrogen, Na, and K intake of patients in the experimental groups were maintained postoperatively at levels sufficient to produce equilibrium or a positive balance when given by mouth to resting, non-traumatized patients (*Table I*). For ease of management all the patients in any one group received the same feeding régime without any attempt to relate intake to individual body-weight. Mean energy and nitrogen intakes per kg. of body-weight were 30·6 Cal. and 180 mg. respectively in group 1 and 30·2 Cal. and 163 mg. in group 2.

Total nitrogen losses were determined in the urine, faeces, and gastric aspirates. We measured Na and K in the faeces and gastric aspirates and faecal fat to determine the proportion of feed given i.d. lost by these routes. The gastric aspirates of all the patients who were fed i.d. were inspected for cloudiness as an extra check that the feed had not refluxed. Urine carbohydrate losses also were measured throughout the study.

Total nitrogen was measured by the micro-Kjeldahl method (Varley, 1967a), Na and K by flame photometry (Varley, 1967b), and faecal fat by the method of van de Kamer, Huinink, and Weyers (1949). The daily nitrogen balance was calculated by subtracting from the intake the nitrogen losses in the urine, faeces, and gastric aspirate, and the cumulative nitrogen balance of each patient was calculated by totalling his daily nitrogen balances. Group mean daily and cumulative nitrogen balances were calculated.

RESULTS

The negative nitrogen balance was smaller in the groups fed postoperatively than in the control group in the early postoperative period (*Table II*). However, neither group 1 (i.v.) nor group 2 (i.d.) achieved nitrogen equilibrium at this time despite their receiving nitrogen and calorie intakes that were adequate in all three groups the day before operation. Group 2 fared somewhat better than group 1 with respect to nitrogen economy, the mean daily negative nitrogen balances of the former being somewhat less than those of the latter during days 1–3; the difference was highly significant ($P < 0·001$) on day 2. The differences between the nitrogen balances of the three groups are clearly apparent in their mean daily cumulative nitrogen balances (*Fig.* 1); with respect to nitrogen economy, group 2 fared best, group 1 achieving an intermediate position between group 2 and group 3 (control).

In all three groups only small amounts of carbohydrate (mean $\leqslant 3·2$ g. per day) were recovered from the urine, and Na and K losses in the gastric aspirates and Na, K, and fat losses in the faeces were slight. These findings have been reported in detail (Hindmarsh, 1971).

DISCUSSION

The studies of Cuthbertson (1930, 1932, 1936) in the United Kingdom and Howard, Winternitz, Parson, Bigham, and Eisenberg (1944) and Howard, Bigham, Eisenberg, Wagner, and Bailey (1946) in the United States showed that after such major trauma as fracture of the long bones the administration of normally sufficient amounts of nitrogen and calories did not prevent a negative nitrogen balance at the height of the catabolic phase. Furthermore, even increasing the daily intake of calories to 5400 and of nitrogen to 34 g. did not invariably produce nitrogen equilibrium. At the other extreme Krieger, Abbott, Levey, and Holden (1958) and Abbott, Levey, and Krieger (1959) reported that in some of their female patients nitrogen equilibrium was maintained after relatively minor trauma, such as cholecystectomy, on as little as 170 mg. of nitrogen per kg. of body-weight and about 23 Cal. per kg. per day. After partial gastrectomy, nitrogen equilibrium was achieved over a 5-day period with the i.v. administration of about 270 mg. of nitrogen and 35 Cal. per kg. per day (Abbott and Albertsen, 1936a, b).

Data from 23 published studies of the effect of calorie and nitrogen administration on nitrogen balance in the immediate postoperative period are summarized in *Fig.* 2, which relates daily nitrogen intake to nitrogen balance at three levels of calorie intake. In most cases the charted nitrogen balance is the cumulative balance of days 0–3. When calorie and nitrogen intakes were not related to body-weight and the weight was not stated, we assumed a weight of 70 kg. for men and 60 kg. for women. Most of these patients were fed i.v. and a few intrajejunally or orally. Data from patients undergoing such minor operations as inguinal herniorrhaphy or very traumatic surgery were excluded; therefore, the results shown relate to surgery levels 3–6 in the trauma scale (Moore and Ball, 1952), mostly level 3 or 4. The regression lines cover only reported values, i.e., they were not extrapolated. All of the correlation coefficients showed a highly significant relationship ($P < 0·001$) between daily nitrogen intake and nitrogen balance.

Analysis of the data from which *Fig.* 2 was constructed shows that an intake of less than 20 Cal. per kg. of body-weight per day never provided equilibrium in males or females. With an energy intake of 20–40 Cal. per kg. per day, nitrogen equilibrium could be achieved with a nitrogen intake

Table II.—MEAN DAILY NITROGEN BALANCES OF THE THREE GROUPS

DAY	MEAN DAILY NITROGEN BALANCE (g.)									*P*		
	Group 1			*Group* 2			*Group* 3			*Group* 1 v *Group* 3	*Group* 2 v. *Group* 3	*Group* 1 v *Group* 2
	Mean	S.E.M.	*n*	Mean	S.E.M.	*n*	Mean	S.E.M.	*n*			
−1	+0·9	0·8	8	+0·5	0·8	7	+0·4	0·8	11	>0·05	>0·05	>0·05
0	−4·0	1·1	8	−4·5	0·6	7	−5·8	0·9	11	>0·05	>0·05	>0·05
1	−8·3	2·1	8	−2·4	1·8	7	−12·9	1·3	11	>0·05	<0·001	>0·05
2	−10·9	0·9	8	−4·2	0·9	7	−14·3	0·9	11	<0·05 >0·01	<0·001	<0·001
3	−5·6	1·4	8	−3·9	1·1	7	−13·5	0·6	11	<0·001	<0·001	>0·05
4	−4·3	0·9	7	−3·3	1·3	7	−8·8	0·8	11	<0·01 >0·001	<0·001	>0·05
5	0	1·1	7	+0·4	1·5	7	−3·1	1·0	11	>0·05	>0·05	>0·05
6	+2·2	0·5	7	+4·5	1·3	7	+1·1	0·5	11	>0·05	>0·05	>0·05
7	−5·1	1·8	7	+0·1	1·1	7	−1·6	0·7	11	>0·05	>0·05	<0·05 >0·01

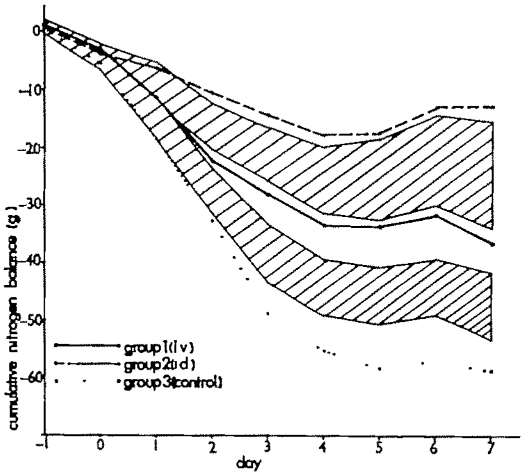

FIG. 1.—Mean daily cumulative nitrogen balances in the three groups. Shaded areas indicate the range of 2 S.D. of the mean differences. (Where the lines that join the means are outside these areas, the means are significantly different ($P < 0·05$).)

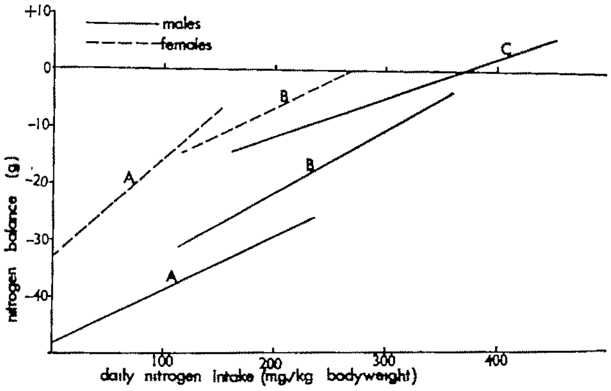

FIG. 2.—The relationship between the reported daily nitrogen intake and nitrogen balance after surgery at three energy intakes: A, <20; B, 20–40; and C, >40 Cal. per kg. of body-weight per day.

Data from the following studies were employed to construct the figure: Brunschwig, Clark, and Corbin, 1942; Gardner and Trent, 1942; Mulholland, Co Tui, Wright, and Vinci, 1943; Co Tui, Wright, Mulholland, Carabba, Barcham, and Vinci, 1944; Werner, 1947; Riegel, Koop, Drew, Stevens, and Rhoads, 1947; Wilkinson, Billing, Nagy, and Stewart, 1950; Beal, Cornell, and Gilder, 1954; Van Itallie, Moore, Geyer, and Stare, 1954; Abbott, Davis, Benson, Krieger, and Levey, 1955; Abbott and others, 1957; Beal, Payne, Gilder, Johnson, and Craver, 1957; Holden, Krieger, Levey, and Abbott, 1957; Krieger, Abbott, Levey, and Holden, 1957; Levey, Krieger, Benson, Davis, and Abbott, 1957, Krieger and others, 1958; Abbott and others, 1959; Gilder, Moody, Cornell, and Beal, 1961; Abbott and Albertsen, 1963a, b; Brøckner, Larsen, and Amris, 1964; Larsen and Brøckner, 1965; Johnston, Marino, and Stevens, 1966.

of about 280 mg. in females and probably about 400 mg. per kg. per day in males. It would be unwise, however, to assume from these data that nitrogen equilibrium postoperatively can be achieved with a lower nitrogen intake in females than in males; most of the females had undergone cholecystectomy, whereas most of the males had had partial gastrectomy or a similar operation, and it is possible (although unlikely) that the former operation is less traumatic than the latter. With an energy intake greater than 40 Cal. per kg. per day, nitrogen equilibrium could be achieved in males given 370 mg. of nitrogen per kg. daily; no female subjects reached this energy intake.

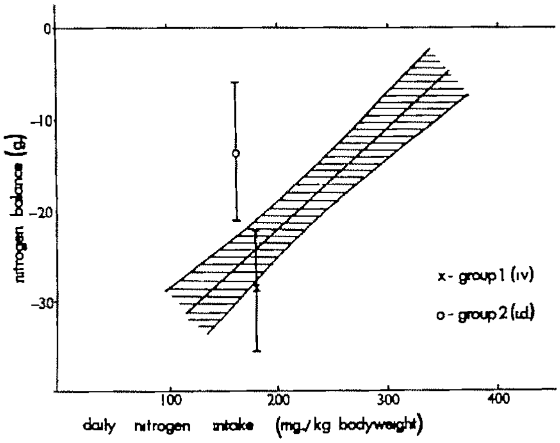

FIG. 3.—Cumulative nitrogen balance in groups 1 and 2 during days 1–4 compared with the regression line (from *Fig.* 2) of the relationship between daily nitrogen intake and postoperative cumulative nitrogen balance of male patients with an energy intake of 20–40 Cal. per kg. of body-weight per day. Bars indicate the range of ±2 S.E.M., shaded area encloses the 95 per cent confidence limits of the regression line.

We compared the results obtained in our groups 1 and 2 with the reported results for male subjects in the early postoperative period (*Fig.* 3). Because nutrition was not given to patients in the present groups 1 and 2 on day 0, the cumulative nitrogen balances shown are those of days 1–4 only. Only group 1 (Aminosol i.v.) values are close to the regression line constructed from the other authors' reports, group 2 (i.d.) values evidencing significantly more nitrogen sparing ($P < 0{\cdot}05$).

Although Krieger and others (1958) and Abbott and others (1959) showed that nitrogen equilibrium could be maintained in some subjects, particularly females after cholecystectomy, on as little as 170 mg. of nitrogen and 23 Cal. per kg. of body-weight per day, and Spivey and Johnston (1972) and Johnston (1972) reported this state postoperatively on 240 mg. of nitrogen and 40 Cal. per kg. per day, in most previous studies (*Fig.* 2) equilibrium could not be achieved on an intake adequate for normal non-postoperative circumstances. As the results of our group 1 were close to the regression line constructed from the results of previous studies, this group is used as an example of the 'typical' patient in the subsequent discussion.

A possible explanation for our failure to achieve postoperative nitrogen equilibrium in group 1 could be that trauma increases energy requirements temporarily; if so, a normally adequate calorie intake would result in an energy deficit and impaired nitrogen utilization. Cuthbertson (1932) and Cope, Nardi, Quijano, Rovit, Stanbury, and Wight (1953) stated that basal metabolism increases after trauma, including surgery. However, Kinney, Zarem, and Rogers (1959), Kinney (1960), and Levey, Czarnecki, Krieger, and Abbott (1960) have shown that, although basal energy expenditure increases by about 10 per cent after operations similar to those undergone by our patients, total energy expenditure differs little from the 'normal' amount of healthy males at rest (about 2000 ± 200 Cal. per day) because of reduced activity in the early postoperative period. Therefore, the daily intake of 2100 Cal. by our group 1 patients should have been sufficient to meet their postoperative energy requirements.

It could be argued that the infused fat emulsion or carbohydrate may not have been properly utilized. This is unlikely to be the case since infused Intralipid is well utilized by man (Reid, 1967a, b); further, there can be no question about the metabolism of fructose and glucose, and there were no excessive losses of these carbohydrates in urine. However, nitrogen equilibrium was not achieved, which leads us to question whether these patients' nitrogen intake was adequate.

To have reasonable certainty of nitrogen equilibrium from an oral diet a healthy adult male should receive not less than 850 mg. of good-quality protein (136 mg. of protein nitrogen) per kg. of body-weight per day, the protein calories providing between 7 and 15 per cent of the total energy intake (Davidson and Passmore, 1969). Our group 1 patients (i.v. feeding) had a daily nitrogen intake of about 180 mg. per kg. (nitrogen calories = 15 per cent of the total energy intake) postoperatively. *Fig.* 3 indicates that, assuming proportionally increased utilization, approximately twice this intake would have been required to achieve equilibrium.

Four possible explanations for the apparently greater nitrogen requirements of these postoperative patients than of normal subjects are:—

1. The protein derivative Aminosol might not be of high biological value. If this were the case it would be utilized inefficiently.
2. Aminosol infusion might be associated with high urinary losses of amino-acids and/or peptides.
3. Nutrients given parenterally might be less efficiently utilized than their counterparts given orally.
4. Nitrogen catabolism might be increased relative to anabolism postoperatively.

1. Biological Value of the Infused Protein.—Aminosol and most of the amino-acid preparations employed in the studies cited in *Fig.* 2 are casein hydrolysates whose composition differs little from the reference pattern adopted by the F.A.O./W.H.O. (1965) as ideal for human nutrition. Therefore, it is unlikely that the amino-acid composition of Aminosol was responsible for the negative nitrogen balance in group 1.

2. Urinary Loss of Amino-acids and Peptides.—The greater loss of α-amino-nitrogen by group 1 than by group 2 patients amounted to only about 2·5 per cent of the nitrogen infused (Hindmarsh, 1971).

Urinary peptide losses were not specifically measured, but in other studies in which Aminosol was infused at a similar rate urinary peptide-amino-nitrogen losses amounted to less than 7 per cent of the total amino-nitrogen infused (Lidström and Wretlind, 1952; Póka, Csóka, Czirbusz, Foldi, and Tőrők, 1967). Therefore, these losses can be discounted as a major cause of the negative nitrogen balance in group 1. This applies also to the studies analysed in *Fig.* 2, most of these patients having received nitrogen in the form of Aminosol or Amigen. Abbott, Krieger, Holden, Bradshaw, and Levey (1957) reported that patients given 12·5 g. of nitrogen i.v. daily as Amigen excreted only 6–12 per cent unchanged in the urine.

3. Comparative Utilization of Nitrogen given Orally and i.v.—Normal daily calorie and nitrogen requirements of healthy resting subjects fed orally and those fed i.v. may be different. Few studies have been made of normal subjects fed wholly parenterally, but Artz and Williams (1957) showed that their resting normal subjects were easily maintained in nitrogen equilibrium by the daily i.v. administration of 1600 Cal. and 13·6 g. of nitrogen. Results obtained in the present group 2 provide further evidence that poor utilization of nutrients given parenterally is not the only factor responsible for the lack of nitrogen equilibrium; these patients failed to achieve nitrogen equilibrium while being fed i.d. in the early postoperative period (although this was achieved with an identical diet given i.d. some 6 weeks later (Hindmarsh, 1971)).

It is not certain whether the calorie : nitrogen ratios of the diets contributed to the different nitrogen excretion rates of the group 1 and group 2 patients. The diet ratio (Cal. per g.) of the former group on days 1–3 was 168 : 1 and of the latter was 185 : 1. Calloway and Spector (1954) showed that optimal nitrogen utilization could be achieved when the diet ratio exceeded about 170 : 1, and Dudrick and Ruberg (1971) considered a ratio of 150 : 1 sufficient for optimal assimilation of nitrogen given i.v.; therefore our different diet ratios should not have had this effect. It may be, however, that the postoperative patient requires a greater calorie : nitrogen ratio, and that a minimum of 200 : 1, as used by Spivey and Johnston (1972), might have reduced the difference in nitrogen excretion by our two experimental groups. Alternatively, nitrogen may be better utilized when given as whole protein than as individual amino-acids and small peptides (Rose, Coon, and Lambert, 1954), or the calorie : nitrogen ratio may need to be greater for i.v. than for oral feeding to produce equivalent nitrogen assimilation. Part of the difference in nitrogen losses in groups 1 and 2 could be attributed to the Aminosol-induced urinary excretion of amino-acids and peptides. However, the subtraction of 10 per cent of the total nitrogen excretion of group 1 to allow for this loss (Lidström and Wretlind, 1952; Póka and others, 1967) still gave figures greatly in excess of those in group 2 patients during days 1 and 2.

4. Comparative Nitrogen Catabolism and Anabolism in the Immediate Postoperative Period.—Normal subjects on an energy-sufficient but nitrogen-free diet lose about 7 g. of nitrogen per day, largely in the urine (Calloway and Spector, 1954). This 'endogenous nitrogen loss', which results from the irreversible breakdown of some proteins during cellular metabolism, must be countered in the diet if nitrogen equilibrium is to be maintained. If the breakdown rate of tissue protein is increased, endogenous nitrogen losses and, therefore, the minimal daily nitrogen requirement will increase. There is much evidence to suggest that this is the case after trauma. Thus, in their experiments with ^{15}N-labelled glycine, Levenson, Braasch, Mueller, and Crowley (1959) showed that the rate of catabolism of plasma protein was increased after burning in the rat, and others have reported similar findings in man (Owen, 1967; Davies, Liljedahl, and Birke, 1969; Davies and Liljedahl, 1970). Further, an increased loss of isotopically labelled nitrogen from muscle protein containing the label in dogs and rats after burns and surgical operations has been reported (Levenson, Pulaski, and Del Guerico, 1964; Muto, Koyama, Kagamihuchi, Hara, Sekiya, and Sakai, 1967).

An increase in protein catabolism relative to anabolism seems, therefore, the most likely explanation for our failure to achieve nitrogen equilibrium postoperatively in the experimental groups, although the somewhat less efficient utilization of nutrients given intravenously than intraduodenally no doubt contributed to the greater negative nitrogen balance in group 1 (Aminosol i.v.).

Acknowledgements.—We are grateful to Paines & Byrne, Ltd., Greenford, Middlesex, for supplies of Aminosol and Intralipid; to Mr. R. A. Dixon, Sheffield University, and Dr. K. L. Weldon, Dalhousie University, for help with the statistics; to Miss Norma Lauder, departmental dietitian, for help with the diets; and to Miss U. F. Matthews, Director of the Editorial Service to the Faculty of Medicine, Dalhousie University, for assistance with the manuscript. The Endowment Fund of the United Sheffield Hospitals kindly gave us financial help.

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THE USE OF THE ARTERIAL SLING TOURNIQUET IN SURGICAL PRACTICE

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SUMMARY

An inflatable sling tourniquet has been developed to control arteries during surgical procedures and has been assessed clinically and experimentally. It has been found to give precise and reliable control over normal and arteriosclerotic arteries and to be extremely atraumatic in practice. It is particularly useful when catheters or shunts are to be passed up the occluded artery.

THE danger of applying a conventional clamp across an atheromatous artery is well recognized by arterial surgeons. Unless a satisfactory 'soft' portion of the artery can be found there is a danger of cracking an intimal plaque with a risk of subsequent thrombosis or dissection.

The design of present metal clamps allows a high pressure to be exerted on a narrow area of artery and only permits deformation of the artery in one direction. It is flattened from side to side between the clamp blades.

Clamps designed specifically to be atraumatic to diseased arteries have been described previously by Brown (1961) and Fogarty, Raible, and Krippaehne (1966). These authors discussed the specifications for the ideal arterial clamp and suggested designs which fulfil these.

The idea of using an inflatable sling to control arteries during clinical surgery has already been published (Dunn, 1971). A number of prototype slings have now been manufactured and used clinically over the past 2 years. They consist of an elongated balloon with a stiff backing which is threaded around the artery and secured by passing a ring around the two ends. The balloon is inflated through a tube attached to one end using a medical syringe. The stiff backing results in the inflated balloon compressing the artery in the line of least resistance (*Fig.* 1).

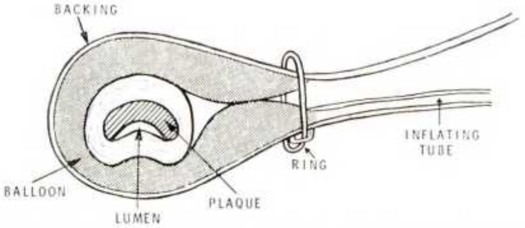

FIG. 1.—Tourniquet applied to an arteriosclerotic artery. Inflation occludes the lumen without cracking the intimal plaque.

The tourniquet has significant advantages over other clamps in that it is cheap and easy to manufacture and has no fixed 'side-to-side' occlusion plane and no handles protruding in the wound.

MATERIALS AND METHODS

Experimental Assessment.—In one experiment in a dog the sling was applied to the upper aorta and a conventional Atraugrip clamp (Down Bros., London) below it, and an arteriotomy was made between them, Both clamps were then applied at maximum pressure and the aorta was then removed and examined.

In a rabbit a miniature tourniquet and a clamp were applied to the aorta with sufficient pressure just to control the blood-flow in the isolated segment as assessed by making an arteriotomy between them. The clamps were left in place for 30 minutes, during which time the animal was heparinized to prevent distal thrombosis. The arteriotomy was then closed and the heparin reversed with protamine. Twenty-four hours later the segment of aorta was removed and examined microscopically for signs of damage and thrombus formation.

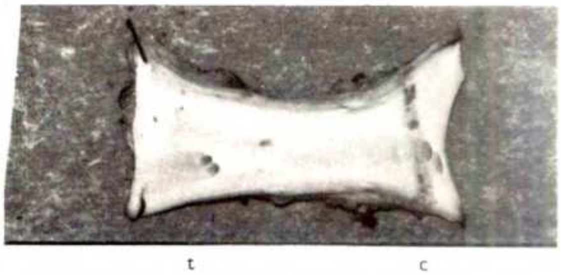

FIG. 2.—Dog's aorta removed after occlusion by both a clamp (c) and a tourniquet (t). The metal clamp has bruised the artery lining. The tourniquet has left no mark.

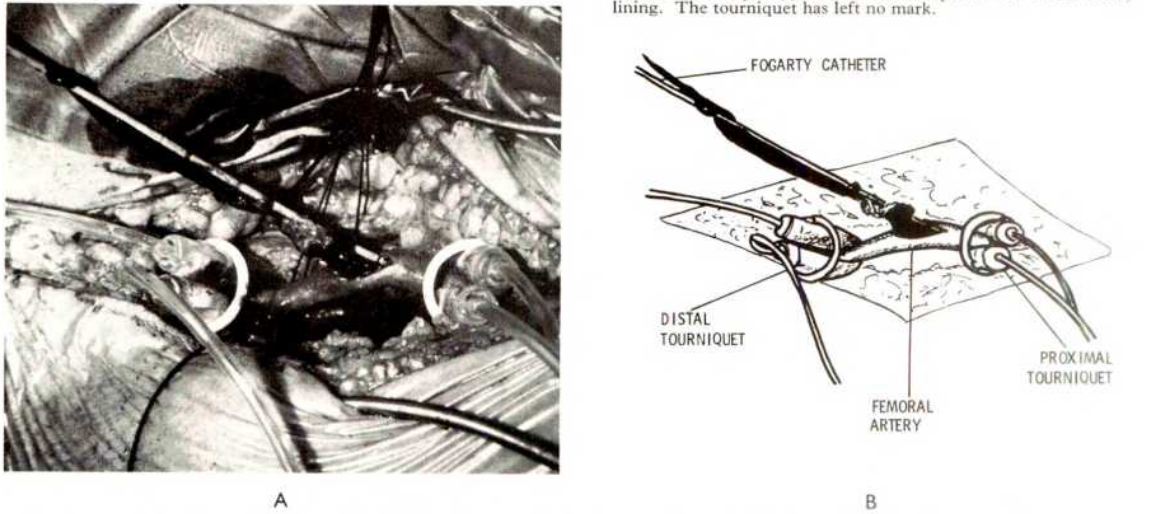

FIG. 3.—Femoral artery embolectomy. The assistant deflates the proximal tourniquet to allow the passage of the thrombus. Control is complete throughout the procedure.

Clinical Assessment.—The sling has been used in place of conventional clamps in five kidney transplant operations (where it was applied to the external iliac artery above the arterial anastomosis), in two femoral artery embolectomies, and in three operations for arterial insufficiency due to atheromatous disease. One of the renal transplant patients had severe atheromatous disease of the external iliac artery at the site of occlusion.

The sling was also assessed by applying it to an atheromatous artery removed from a limb after amputation for distal gangrene. The way in which it compressed the artery was observed and the degree of control was assessed by forcing saline under pressure through the artery.

RESULTS

Experimental.—The aorta of the dog is shown in *Fig.* 2. The injury due to the clamp is clearly seen. Histology was non-contributory as pathological changes did not have time to develop.

In the rabbit experiment the aorta was removed 24 hours after clamping. The mark of the conventional clamp was clearly seen with fresh red mural thrombus attached to it. There was no mark or thrombus at the tourniquet site. Histology showed an area of complete necrosis of the whole arterial wall at the site of the conventional clamp. There was neutrophil polymorph infiltration at this point and haemorrhage into the adventitia. At the tourniquet site there were occasional dead cells visible in the media with a few polymorphs between the medial fibres. No other evidence of necrosis of the arterial wall was seen. Some adventitial haemorrhage was noted.

Clinical.—Satisfactory and reliable control of the vessels was achieved in all the cases, even in the presence of atheroma.

The renal transplant patient with atheromatous disease of the external iliac vessel died 23 days postoperatively from myocardial infarction. Post-mortem examination of the iliac artery confirmed the presence of brittle plaques of atheroma in the iliac vessel at the clamp site. These were undamaged. Other arteries which had been occluded showed no signs of damage either at operation or postoperatively.

The sling had marked advantages over conventional clamps in femoral artery embolectomy (*Fig.* 3). The Fogarty catheter could be passed through the occluded artery and haemostasis maintained during embolectomy by inflating the sling and compressing the arterial walls on to the catheter. The degree of control and 'grip' on the catheter could be precisely controlled by the assistant with the inflating syringe.

Four different surgeons found the sling easy to apply. Slightly more arterial length had to be mobilized than for a conventional clamp. The absence of protruding clamp handles which could catch on arterial sutures was appreciated. The tourniquet was rather bulky but this did not present serious difficulties. Early models tended to slide along the artery in the direction of the blood-flow, but the addition of roughening to the surface of the balloon has largely overcome this difficulty. In the experimental situation loss of control due to accidental deflation of the balloon proved easy to overcome by pulling on the sling until a conventional clamp could be applied. The deflated sling gives the same degree of control as the conventional rubber sling has done in the past. The balloon is tough and not easy to penetrate with a suture needle. Once the anastomosis was completed the blood-flow through the artery could be precisely controlled by an assistant applying pressure to the inflating syringe. This made any leaks in the suture line easy to identify and close by suture without excessive blood-loss.

Application of the clamp to an excised atheromatous artery confirmed that the artery was satisfactorily occluded and compression did not split the intimal plaque.

DISCUSSION

The clinical and experimental work described in this paper confirms that the arterial sling tourniquet can satisfactorily control blood-vessels and is much less traumatic than conventional arterial clamps. It has been shown that the sling can occlude atheromatous arteries both gently and securely without damaging them.

The disadvantages of the instrument, namely that it is more bulky than a normal clamp, requires more mobilized length of artery for its application, and has a less fierce grip on the arterial wall, are much outweighed by its advantages. It is extremely atraumatic, has no handles to catch on sutures, and the control of the blood-flow within the artery is precise and can be carried out by an assistant at a distance. It is the author's instrument of choice in femoral artery embolectomy, kidney transplantation, and for occluding arteries with atheromatous plaques on their walls.

Since publication of the first paper about this sling (Dunn, 1971), there have been reports (Kountz, 1972) on similar balloon occlusion devices which have been used in experimental situations, mainly in the United States. The clinical potential of such devices has not previously been realized or reported on.

The tourniquet will soon be in production by A. Franklin and Sons, England.

Acknowledgement.—I am grateful to Professor R. Y. Calne and the staff of the Department of Surgery, University of Cambridge, and also Mr. W. A. B. Smellie and Professor G. W. Taylor, St. Bartholomew's Hospital, London, for help in the assessment of this device.

A patent has been granted.

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SURGICAL TREATMENT OF ANEURYSM OF THE THORACIC AORTA UNDER A TEMPORARY EXTERNAL BY-PASS SHUNT

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SUMMARY

Twenty-eight patients were operated upon for aneurysm of the thoracic aorta using a temporary external by-pass shunt. Four early deaths occurred, the cause of which could not be related to the by-pass procedure itself. The temporary long external by-pass from the left subclavian artery or from the ascending aorta to the femoral artery was preferable for resection of an aneurysm of the descending aorta or the distal aortic arch which required cross-clamping of the aorta.

DURING resection and replacement with a graft in the treatment of an aneurysm of the thoracic aorta the blood-supply to the distal organs has to be maintained in order to prevent ischaemic damage and heart failure. A temporary external by-pass shunt or a mechanical by-pass such as a cardiopulmonary by-pass (Cooley, DeBakey, and Morris, 1957; Austen and Shaw, 1960), a left heart by-pass (Cooley and others, 1957; Gerbode, Bainbridge, Osborn, Hood, and French, 1957), and a femorofemoral by-pass (Neville, Thomason, Peacock, and Colby, 1966; Dillon, Young, and Sealy, 1967; Bloodwell, Hallman, and Cooley, 1968) is usually applied for this purpose.

In the present series of 45 patients with thoracic aneurysms who have been treated surgically a cardiopulmonary by-pass was used in 13 patients, whereas various external by-pass shunts were employed in 28 patients. In the remaining 4 patients resection of the aneurysm was performed without any supportive measure. This paper presents the results of resection of aneurysm of the thoracic aorta using a temporary external by-pass shunt.

Table I.—SUMMARY OF THE DATA FOR LEFT SUBCLAVIAN TO DESCENDING AORTA, COMMON ILIAC, AND FEMORAL ARTERY BY-PASSES

TYPE OF BY-PASS	NO. OF PATIENTS	BY-PASS GRAFT		BY-PASS TIME (RANGE AND MEAN) (min.)	COMPLICATION	EARLY DEATH	LATE DEATH
		Diameter (mm.)	Length (cm.)				
Left subclavian to descending aorta	3	10–14	20–40	65–107 82	0	1*	0
Left subclavian to common iliac	3	12–14	50	80–100 91	1†	1‡	1§
Left subclavian to femoral	16	10–16	50	30–110 58	0	0	1§

* Rupture of concomitant abdominal aneurysm.
† Acute renal failure.
‡ Rupture of aneurysm during dissection.
§ Sudden death from unknown origin.

MATERIAL AND METHODS

Twenty-eight patients underwent operation for an aneurysm of the thoracic aorta under a temporary external by-pass shunt during the period from June, 1966, to December, 1971, at the Keio University Hospital, Tokyo. There were 24 males and 4 females, ranging in age from 20 to 73 years.

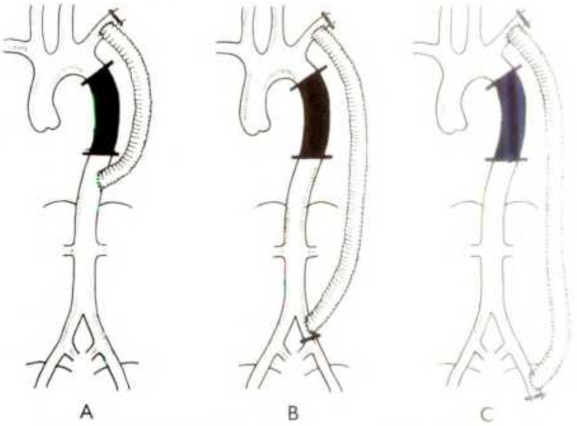

FIG. 1.—Diagrams showing temporary external by-pass shunts from the left subclavian artery to the descending aorta (A), to the left common iliac artery (B), and to the left femoral artery (C).

Twenty-four patients had an aneurysm of the descending thoracic aorta, 3 patients had an aneurysm of the aortic arch, and 1 patient had an innominate artery aneurysm. A dissecting aneurysm was found in 10 patients, a chronic fusiform enlargement in 9, and a saccular aneurysm in 9. The aneurysm was related to atherosclerosis in 13 patients, to cystic medial necrosis in 10, to syphilis in 4, and to trauma in 1.

A woven Teflon graft was used as a temporary external by-pass shunt without heparinization in all the patients during cross-clamping of the aorta.

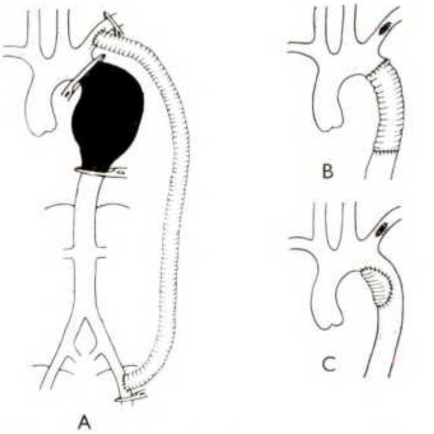

FIG. 2.—Diagrams showing the techniques of operation for an aneurysm of the descending thoracic aorta. A, Temporary long external by-pass from the left subclavian artery to the left femoral artery during occlusion of the aorta. B, After removal of the aneurysm the aorta was replaced with a Teflon tube graft. C, The defect of the aorta was covered with a Teflon patch after aneurysmectomy.

Various by-passes were used, including descending aorta to aorta, descending aorta to femoral, left subclavian to descending aorta, left subclavian to common iliac or femoral, and ascending aorta to femoral by-pass shunt.

RESULTS

1. Left Subclavian to Descending Aorta, Common Iliac, or Femoral By-pass Shunt (22 cases).—Twenty-two patients with an aneurysm of the descending thoracic aorta distal to the origin of the left subclavian artery were operated upon with the aid of an external by-pass shunt from the left subclavian artery to the descending thoracic aorta (3 cases), to the left common iliac artery (3 cases), and to the left femoral artery (16 cases) (*Fig.* 1). The by-pass graft ranged between 10 and 16 mm. in diameter and from 25 to 50 cm. in length. The by-pass time ranged from 30 to 110 minutes, with an average of 66 minutes (*Table I*).

After resection of the aneurysm the aorta was replaced with a woven Teflon graft in 21 of the 22 patients, while a Teflon patch was used to cover the defect of the aorta in the remaining 1 (*Fig.* 2).

Table II.—SUMMARY OF THE DATA FOR DESCENDING AORTA TO AORTA AND FEMORAL BY-PASSES

TYPE OF BY-PASS	NO. OF PATIENTS	BY-PASS GRAFT		BY-PASS TIME (min.)	COMPLICATION	EARLY DEATH	LATE DEATH
		Diameter (mm.)	Length (cm.)				
Descending aorta to aorta	1	14	20	90	Cerebral thrombosis	0	0
Descending aorta to femoral	1	12	50	99	0	0	0

Two of the 22 patients died in the early postoperative period. The causes were massive haemorrhage due to rupture of the aneurysm during dissection and rupture of a concomitant abdominal aneurysm on the second postoperative day. Late death occurred in 2 patients with a dissecting aneurysm, the cause of which remains unknown.

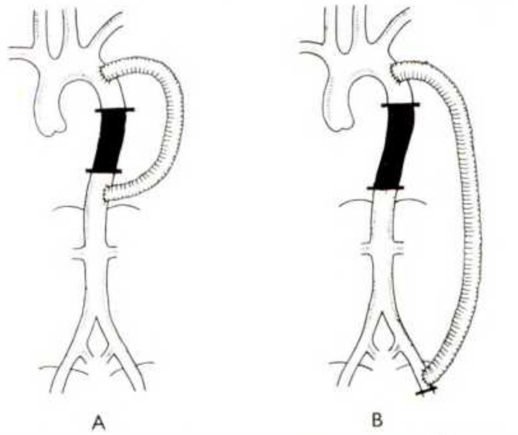

FIG. 3.—Diagrams illustrating temporary external by-pass shunts from the descending aorta to the distal thoracic aorta (A) and to the left femoral artery (B).

In spite of the by-pass time of 110 minutes, the length of the shunt of 50 cm., and no heparinization, no thrombus was recognized in any by-pass graft. Postoperative acute renal failure occurred in 1 patient with a dissecting aneurysm which was associated with complete obstruction of the left renal artery preoperatively.

2. Descending Aorta to Aorta or Femoral By-pass Shunt (2 cases).—The left subclavian artery was too small for the proximal anastomosis of the by-pass graft in 2 patients. In each case the descending aorta proximal to the aneurysm was used as an alternative. The distal anastomosis was with the descending aorta distal to the aneurysm in one patient and with the femoral artery in the other; the position of this anastomosis depended on the site and extent of the aneurysm (*Fig.* 3).

Aneurysmectomy and replacement with a graft were successfully performed in these 2 patients. Both of the by-pass grafts were 14 mm. in diameter with a length of 20 and 50 cm., respectively (*Table II*).

3. Ascending Aorta to Carotid or Femoral By-pass Shunt (4 cases).—For the 1 patient with an aneurysm of the innominate artery a by-pass shunt (10 mm. in diameter, 25 cm. in length) from the ascending aorta to the right common carotid artery was utilized to provide distal perfusion while the blood-flow in the innominate artery was interrupted (*Fig.* 4 A). Following resection of the aneurysm the by-pass graft was left in place as a permanent conduit after being shortened.

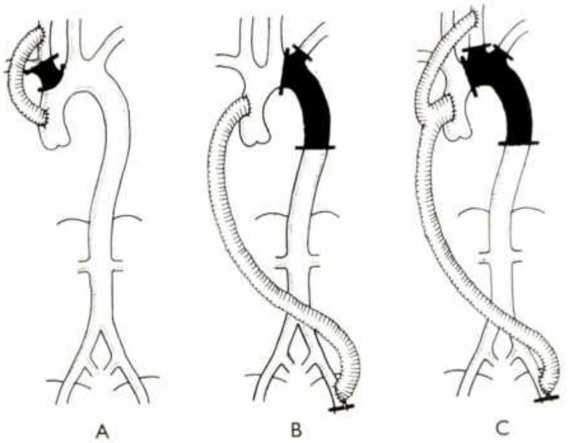

FIG. 4.—Diagrams indicating temporary external by-pass shunts from the ascending aorta to the right common carotid artery (A), to the left femoral artery (B), and to both the femoral and the left common carotid arteries (C).

An ascending aorta to femoral by-pass (14 mm. × 50 cm.) was applied in 2 patients with an aneurysm of the distal aortic arch which required clamping of the aorta proximal to the origin of the left subclavian artery (*Fig.* 4 B). In the remaining patient with an aneurysm of the aortic arch distal to the origin of the innominate artery an ascending aorta to femoral by-pass (20 mm. × 50 cm.) with a branch to the left carotid artery (10 mm. × 25 cm.) was utilized (*Fig.* 4 C). After resection of the aneurysm the aorta was replaced with a graft in 1 patient and was repaired with a Teflon patch in the other 2 patients (*Fig.* 5).

Table III.—SUMMARY OF THE DATA FOR ASCENDING AORTA TO FEMORAL AND COMMON CAROTID BY-PASSES

TYPE OF BY-PASS	NO. OF PATIENTS	BY-PASS GRAFT		BY-PASS TIME (min.)	COMPLICATION	EARLY DEATH	LATE DEATH
		Diameter (mm.)	Length (cm.)				
Ascending aorta to right common carotid	1	10	25	50	0	0	0
Ascending aorta to femoral	2	14	50	30, 70	1*	1†	1*
Ascending aorta to femoral and left common carotid	1	20 10	50 25	60		1‡	

* Infection.
† Rupture of aneurysm during dissection.
‡ Acute obstruction of superior mesenteric artery.

By-pass time ranged between 30 and 70 minutes. Early postoperative death occurred in 2 patients, and was related to acute obstruction of the superior mesenteric artery and to massive haemorrhage due to rupture of the aneurysm during dissection, respectively (*Table III*).

DISCUSSION

Since Cooley and DeBakey successfully removed an aneurysm of the ascending aorta by utilizing a cardiopulmonary by-pass in 1956 a total cardiopulmonary by-pass has been widely employed in the resection of an aneurysm of the ascending aorta or the aortic arch.

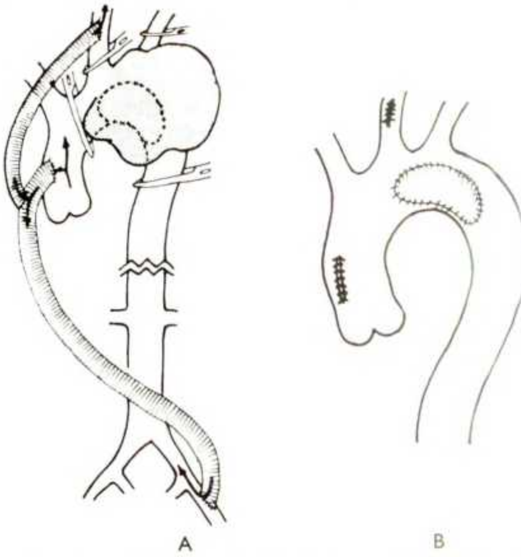

FIG. 5.—Diagrams showing the techniques of operation for an aneurysm of the distal aortic arch. A, Temporary long external by-pass with a carotid branch during clamping of the aortic arch. B, After excision of the aneurysm the aortic defect was covered with a Teflon patch.

On the other hand, a left-heart by-pass with a pump (Cooley and others, 1957; Gerbode and others, 1957) or a femoral vein to femoral artery partial by-pass with a pump oxygenator (Neville and others, 1966; Dillon and others, 1967; Bloodwell and others, 1968) is usually used during the resection of an aneurysm of the descending thoracic aorta. A mechanical by-pass, however, requires systemic heparinization, which may cause excessive bleeding from the prosthetic graft and the dissected surrounding tissues. An additional disadvantage of the left-heart by-pass is the difficulty in the control of blood-flow from the left atrium, which may result in atrial hypertension (Kahn, Vathayanon, and Sloane, 1968; Hug and Taber, 1969).

Clinical application of a temporary external by-pass between the left subclavian artery and the descending thoracic aorta has been reported (Adams, 1955; Stranahan, Alley, Sewell, and Kausel, 1955; Storey, Nardi, and Sewell, 1956; DeBakey and Cooley, 1961). Nagel and Williams (1966) utilized a temporary external by-pass from the left subclavian artery to the descending thoracic aorta with a Dacron graft 12 mm. in diameter. Kahn and others (1968) and Kirsh, Kahn, Crane, and others (1970) reported the use of an external shunt employing two metal cannulae connected by Tygon tubing placed on the aorta proximal and distal to the aneurysm, with an excellent result. Valiathan, Weldon, Bender, Topaz, and Gott (1968) described the use of a left subclavian to femoral by-pass with a GBH-coated polyvinyl catheter for the resection of an aneurysm of the descending thoracic aorta in 2 cases.

Since 1966 the present authors have applied a temporary external by-pass shunt without heparinization during cross-clamping of the descending thoracic aorta. A woven Teflon prosthetic graft was chosen as the by-pass material in order to avoid thrombus formation in the shunt. After using several short by-pass shunts, such as a left subclavian to descending aorta or a descending aorta to aorta by-pass, shunts from the left subclavian to the common iliac or to the femoral artery have been employed. This method has previously been reported as the 'temporary long external by-pass method' (Inoue, Kawada, Tanaka, Sohma, Fukuda, and Koyanagi, 1972). Thus, using the diseased aorta as the anastomosis site to the by-pass graft is avoided and the operating field is left free. Moreover, the by-pass flow rate is controlled by the cardiac output of the patient, and therefore artificial regulation of the by-pass flow is unnecessary. Neither thrombosis nor heart failure occurred during by-pass in our series of 24 patients with a descending thoracic aortic aneurysm. Furthermore, postoperative paraplegia due to spinal cord ischaemia or renal failure did not occur except in 1 patient who had a dissecting aneurysm with obstruction of the left renal artery.

Mahorner and Spencer (1954) reported a temporary external by-pass with a homograft for the resection of an aneurysm of the innominate artery. In 1971 Murray, Brawley, and Gott described a temporary by-pass with a GBH-coated cannula from the ascending aorta to the right carotid artery during reconstruction of the innominate artery.

In 1955 Cooley and DeBakey (1955) performed a complete reconstruction of the aortic arch during bridging with a homograft from the ascending to the descending aorta. In Japan Kimoto, Wada, Ueno, Suzuki, Harada, and Maruyama (1960) and Wada, Tashiro, Ueda, and Suda (1960) successfully resected an aneurysm of the aortic arch using the method described by Cooley and DeBakey (1955). However, it may not always be easy to expose the descending aorta as the site for distal anastomosis in this short by-pass. Moreover, the by-pass itself may disturb the operating field. Therefore, we prefer to employ a long by-pass from the ascending aorta to the femoral artery with or without a carotid branch. However, a sufficient distance of normal aortic wall from the aortic annulus to the aneurysm is absolutely necessary for the attachment of the by-pass graft. A pump oxygenator should be prepared for immediate use when this procedure is found to be inadequate.

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SELECTION OF OPERATION FOR DUODENAL ULCER BASED ON ACID SECRETORY STUDIES—A REAPPRAISAL

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SUMMARY

The incidence of recurrent duodenal or jejunal ulceration was assessed 5–10 years after selective surgery for duodenal ulceration in 253 patients after vagotomy and drainage and in 55 patients after vagotomy and antrectomy.

In the vagotomy and drainage group 8·6 per cent of the patients developed proven or highly suspected recurrent duodenal or jejunal ulcer. None of these patients had preoperative maximal acid output (M.A.O.) values less than 25 mEq. per hour. No recurrent jejunal ulcers occurred in the vagotomy and antrectomy group despite the fact that they had the same incidence of incomplete vagotomy by Hollander's criteria as the vagotomy and drainage group.

It is suggested that a policy of selection of patients for vagotomy and drainage based on a preoperative M.A.O. of 25 mEq. per hour seems more justified and realistic than the previously used level of 40–50 mEq. per hour. Vagotomy and antrectomy should probably be employed if the M.A.O. is greater than 25 mEq. per hour.

THE ideal operation for patients with duodenal ulceration remains elusive. Partial gastrectomy (Visick, 1948; Goligher, Moir, and Wrigley, 1956; Goligher and Franz, 1964; Goligher, Pulvertaft, and Watkinson, 1964), vagotomy without drainage (Dragstedt, Camp, and Fritz, 1949; Tanner, 1950, 1964), gastro-enterostomy alone (Lewisohn, 1925; Leiff, 1929; Tanner, 1964), vagotomy and gastrectomy with either Billroth-I or -II anastomosis (Herrington, 1963; Goligher and others, 1964; Bryant, Klein, and Griffin, 1967; Goligher, Pulvertaft, de Dombal, and others, 1968a, b; Jordan and Condon, 1970), a variety of vagotomy and drainage procedures (Weinberg, Stempien, Movius, and Degradi, 1956; Edwards, Classen, and Sawyers, 1960; Goligher and others, 1964, 1968a, b) and, more recently, parietal cell vagotomy without drainage (Amdrup and Jensen, 1970; Johnston and Wilkinson, 1970; Interone, 1971) have been employed in an attempt to reduce mortality and morbidity, but the long-term morbidity remains of the order of 10–15 per cent.

One of the most serious complications is the inability to cure the ulceration or to prevent recurrent ulceration after surgery. The finding that most patients with recurrent ulceration after gastrectomy had high levels of postoperative acid secretion led various groups of workers to advocate a policy of 'tailoring the operation' to the preoperative basal (Orr, 1962) or histamine-stimulated acid secretory status (Bruce, Card, Marks, and Sircus, 1959; Louw, 1964; Small, Bruce, Falconer, Sircus, and Smith, 1967). Systematic trials of the 'tailoring procedures' and, in effect, the role of gastric acid secretion in operative selection were interrupted, however, by the advent of vagotomy and drainage. Indeed, the relative simplicity and lower mortality of vagotomy and drainage resulted in the almost universal adoption of this procedure for almost a decade.

It soon became apparent that vagotomy and drainage applied to all patients was associated with a high recurrent ulcer rate (Goligher and others, 1964, 1968a, b; Bryant and others, 1967), and Bank, Marks, and Louw (1967) confirmed that the procedure was associated with an inadequate or 'safe' reduction in acid secretion in the majority of patients.

The purpose of the present paper is to reassess the value of preoperative acid secretory studies with regard to recurrent ulceration and to suggest a policy of 'tailored surgery' to the currently popular operations.

MATERIAL AND METHODS

Three hundred and eight patients submitted to elective surgery for chronic duodenal ulceration at the Groote Schuur Hospital were reassessed 5–10 years later with regard to the incidence of recurrent ulceration. A loosely applied policy of selection for surgery was practised in these patients, vagotomy and antrectomy being used for many patients with M.A.O. values greater than 40 mEq. per hour and vagotomy and drainage for the remainder. Thus, 253 patients had vagotomy and drainage, the vagotomy being either truncal or selective. Selective vagotomy was aimed at preserving both the hepatic and coeliac branches and the routine drainage procedure employed was a pyloroplasty of the Heineke-Mikulicz type. Gastro-enterostomy was reserved for the cases in which pyloroplasty proved technically hazardous. A few patients had gastroduodenostomies of the Jaboulay or Finney type. The remaining 55 patients were submitted to truncal vagotomy and antrectomy with a Billroth-II type reconstruction in all cases.

A preoperative augmented histamine or pentagastrin test (A.H.T.) (Bank and others, 1967) was performed in all the patients and 262 patients were available for postoperative studies. Postoperative insulin tests were performed on 138 patients (Bank and others, 1967); 127 after vagotomy and drainage and 11 after vagotomy and antrectomy.

CLINICAL ASSESSMENT

Recurrent Ulceration.—Recurrent ulceration has been grouped into duodenal (or jejunal) and gastric, and in view of the difficulty experienced in some instances in confirming the diagnosis of recurrent duodenal ulceration these patients have been further subdivided into 'proven' and 'highly suspected' groups. (Recurrent gastric uleration was less of a diagnostic problem with routine fibre-optic gastroscopy.) The 'proven' group comprised those patients in whom an ulcer was found at subsequent surgery. The 'highly suspected' group consisted of 11 patients with a clinical history associated with radiological, gastroscopic, or acid secretory data which were strongly suggestive of recurrent ulceration but in whom further surgery was not carried out because of a satisfactory response to medical therapy and reluctance to reoperate at that stage. Of these 11 patients, 10 gave a classic history of ulcer-type dyspepsia (2 having gastro-intestinal bleeding as well) and 1 was admitted with a gastro-intestinal haemorrhage. The reinstitution of ulcer therapy resulted in an abatement of the symptoms in all the patients. Two of the 11 patients had an ulcer crater demonstrated on barium-meal examination and 8 had acid secretory studies after histamine and insulin which indicated a 'high risk to recurrent ulceration'. The study was undertaken before duodenoscopy became a routine practice in the clinic.

Interpretation of the Insulin Test.—Insulin test results were interpreted by Hollander's criterion, i.e., an increase of 20 mEq./l. over basal levels (10 mEq./l. if the basal level was anacid) following the administration of insulin was taken as a positive response and indicative of incomplete vagotomy (Hollander, 1946, 1948).

Table I.—RECURRENT ULCERATION AFTER VAGOTOMY AND DRAINAGE AND AFTER VAGOTOMY AND ANTRECTOMY FO DUODENAL ULCER

OPERATION	DUODENAL/JEJUNAL ULCERATION						GASTRIC ULCERATION		TOTAL ULCERATION	
	Proven		*Suspected*		*Total*					
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Vagotomy and drainage (253 cases)	11	4·3	11	4·3	22	8·6	8	3·2	30	11·8
Vagotomy and antrectomy (55 cases)	0	0	0	0	0	0	1	1·8	1	1·8

Table II.—EFFECT OF VAGOTOMY AND DRAINAGE AND OF VAGOTOMY AND ANTRECTOMY ON THE GASTRIC ACID SECRETORY RESPONSE TO HISTAMINE (PENTAGASTRIN) AND INSULIN

OPERATION	A.H.T.							INSULIN				
	No. of Tests	*Mean Preoperative Value* (mEq. per hr.)		*Mean Postoperative Value* (mEq per hr.)		*Mean Percentage Reduction*		*No. of Tests*	*Multiple Criteria Positive*		*Hollander Positive*	
		B.A.O.	M.A.O.	B.A.O.	M A O.	B.A.O.	M A.O.		No.	Per cent	No.	Per cen
Vagotomy and drainage	253	5·1	27·3	1·8	9·0	64·7	67·0	127	28	22	52	40·9
Vagotomy and antrectomy	55	10·3	41·6	0·7	2·3	93·2	94·5	11	0	0	4	36·4

In addition, the multiple criteria suggested by Bank and others (1967) were employed. These criteria are: (*a*) an increase of free acid of 20 mEq./l. or more over basal values (10 mEq./l. if the basal level was anacid) (Hollander, 1948); (*b*) a basal level in excess of 2 mEq. per hour (Bachrach, 1962); (*c*) an increasing volume after insulin (Waddell, 1957); (*d*) whether the Hollander response occurs within 60 minutes or not, i.e., whether the vagotomy is 'adequate' or not (Ross and Kay, 1964; Johnston, Thomas, Checkells, and Duthie, 1967); (*e*) an increas of 1·5 mEq. per hour of free acid or 2 mEq. pe hour of total acid over the basal hour secretion occurring during any hour after insulin (Bank and other 1967). Three or more of these criteria occurrin together were assessed as signifying a high risk t recurrent ulceration.

RESULTS

Incidence of Recurrent Ulceration.—*Table* shows that 8·6 per cent of patients after vagotom and drainage had proven (4·3 per cent) or highl suspected (4·3 per cent) duodenal or jejunal ulce recurrence while *none* of the small number of patient in the vagotomy and antrectomy group develope jejunal ulceration.

Eight of the 253 patients subjected to vagotom and drainage developed gastric ulceration, an incidence of 3·2 per cent. One case of recurrent gastri ulceration (1·8 per cent) was encountered in th vagotomy and antrectomy group. The differenc between the two groups was not statistically significant ($P > 0·05$).

Pre- and Postoperative Acid Secretory Studie (*Table II*).—

Augmented Histamine (Pentagastrin) Test.—Th mean preoperative maximal acid output (M.A.O. in the vagotomy and drainage group was 27·3 mE per hour. Patients submitted to vagotomy an antrectomy had a very much higher mean preoperative M.A.O. (41·6 mEq. per hour). Basal aci output (B.A.O.) was 5·1 and 10·3 mEq. per hou respectively.

Vagotomy and antrectomy resulted in a reductio of the preoperative B.A.O. and M.A.O. levels o over 90 per cent. This reduction was significantl greater than the 64·7 per cent for basal and 67·0 pe cent for maximal acid output after vagotomy an drainage.

Insulin Test.—Of the 127 patients in the vagotomy and drainage group who had insulin tests done, 52 (40·9 per cent) had a positive response using Hollander's criterion, and of 11 patients who had a vagotomy and antrectomy, 4 (36·4 per cent) had a positive Hollander test.

Table III.—Comparison of Recurrent Ulceration Rates in Patients with a Preoperative M.A.O. greater than 25 mEq. per Hour and in those with a Preoperative M.A.O. less than 25 mEq. per Hour who were submitted to Vagotomy and Drainage

M.A.O. Group	Total No. of Patients	Duodenal/Jejunal Ulceration						Proven Gastric Ulceration		Total Ulceration	
		Proven		*Suspected*		*Total*					
		No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
>25 (mEq. per hr.)	143	11	7·7	7	4·9	18	12·6	2	1·4	20	14·0
<25 (mEq. per hr.)	110	0	0	4	3·6	4	3·6	6	5·5	10	9·1

Table IV.—Comparison of the Gastric Acid Secretory Response to Histamine/Pentagastrin and Insulin in Patients with a Preoperative M.A.O. greater than 25 mEq. per Hour and in Those with a Preoperative M.A.O. of less than 25 mEq. per Hour who were submitted to Vagotomy and Drainage

M.A.O. Group	Total No. of Patients	A.H.T.						Insulin				
		Mean Preoperative Level (mEq. per hr.)		*Mean Postoperative Level* (mEq. per hr.)		*Percentage Reduction*		*Total No. of Tests*	*Multiple Criteria Positive*		*Hollander Positive*	
		B.A.O.	M.A.O.	B.A.O.	M.A.O.	B.A.O.	M.A.O.		No.	Per cent	No.	Per cent
>25 mEq. per hr.	143	6·8	35·8	2·2	11·3	67·6	68·4	60	17	28·3	26	43·3
<25 mEq. per hr.	111	3·4	17·9	1·4	5·8	58·8	67·6	42	4	9·5	13	30·9

When multiple criteria were used as an index of positivity, the proportion of incomplete vagotomies was much lower than when Hollander's criterion alone was used. Twenty-two per cent of the vagotomy and drainage group and none of the vagotomy and antrectomy group had three or more positive criteria.

Relationship of Preoperative M.A.O. to Recurrent Ulceration after Vagotomy and Drainage.—In examining the augmented histamine test (A.H.T.) data in the vagotomy and drainage group it was found that no patient with a preoperative M.A.O. less than 25 mEq. per hour had a proven duodenal ulcer recurrence (*Table III*). There was a tendency for 'suspected ulcer' to occur in patients who secreted less than 25 mEq. per hour, but there was no significant difference in this respect between the patients who secreted more and those who secreted less than 25 mEq. per hour.

On the other hand, gastric ulcer recurrence occurred more frequently in the patients who secreted less than 25 mEq. per hour, but the difference was not significant ($P > 0{\cdot}05$).

Comparison of Acid Secretory Data in Patients subjected to Vagotomy and Drainage with Preoperative Acid Secretory Values greater or less than 25 mEq. per Hour.—*Table IV* shows that the percentage reduction in acid output in the two groups of patients was similar after operation, but that the B.A.O. and M.A.O. values were very much lower in the patients who secreted less than 25 mEq. per hour.

Insulin Tests.—Twenty-six (43·3 per cent) of the 60 patients in the over-25 mEq. per hour group who had insulin tests had a positive result using Hollander's criterion as compared with 13 (30·9 per cent) of 42 insulin tests in the under-25 mEq. per hour group. The difference was not statistically significant ($P > 0{\cdot}05$). When multiple criteria were used as the method of interpretation the over-25 mEq. per hour group had a significantly higher proportion of positive results (28·3 per cent) than the under-25 mEq. per hour group (9·5 per cent; $P < 0{\cdot}05$).

Comparison of Ulcer Recurrence Rates in Patients with Preoperative M.A.O. of greater than 25 mEq. per Hour after Vagotomy Operations (*Table V*).—

Vagotomy and Drainage.—One hundred and forty-three patients (56·5 per cent) had a preoperative M.A.O. of greater than 25 mEq. per hour and among these, 18 proven and suspected recurrent duodenal ulcers were found and 2 gastric ulcers (1·4 per cent).

Vagotomy and Antrectomy.—Forty-seven (84·5 per cent) of these patients secreted more than 25 mEq. per hour and none of them had either proven or suspected recurrent duodenal ulceration. One patient presented with recurrent gastric ulceration. There is an obviously significant difference between these patients and the vagotomy and drainage group with regard to recurrent duodenal ulceration but not gastric ulceration.

DISCUSSION

Recurrent 'proven' or 'suspected' duodenal or jejunal ulceration is the single most important complication after vagotomy and drainage and most authors cite an incidence ranging from 10 to 15 per cent (Weinberg and others, 1956; Edwards and others, 1960; Goligher and others, 1964, 1968a, b; Bryant and others, 1967; Bank, Marks, Louw, and Cobb, 1970; Jordan and Condon, 1970). Based on this high recurrence rate Small and others (1967) embarked on a programme of selective surgery for duodenal ulceration aimed at eradicating jejunal ulcer.

Their policy of selection entailed submitting patients with an M.A.O. greater than 50 mEq. per hour to vagotomy and antrectomy, while those with values below this were subjected to either standard two-thirds gastrectomy or vagotomy and gastro-enterostomy. The results in this group of patients, who were followed up prospectively over 5 years, were compared with a group of patients who had been subjected to partial gastrectomy. Although the results were inconclusive the authors felt that perseverance with the policy was justified. Orr (1962) and Louw (1964) had previously reported favourable results following a policy of selection based on similar preoperative A.H.T. levels, whereas other authors (Holt and Lythgoe, 1961; Clark, Murray, Slessor, and Wyllie, 1964) were of the opinion that preoperative acid testing had little prognostic significance. All these reported series, however, used an arbitrarily selected M.A.O. value of 40 or 50 mEq. per hour as the indication for the more extensive operation. The fact that proven recurrent duodenal ulceration was still occurring in 4·3 per cent of our vagotomy and drainage patients and that a further 4·3 per cent had suspected recurrence in spite of these selective criteria indicated that a lower preoperative M.A.O. value than 40 mEq. per hour might be a better discriminatory 'hypersecretor level' above which recurrent ulceration was more likely to occur. None of the 11 unequivocally proven recurrent duodenal or jejunal ulcers in the present series occurred in patients with a preoperative M.A.O. value of less than 25 mEq. per hour and the lowest M.A.O. value among these patients was 26·9 mEq. per hour. A similar trend was found in patients with 'highly suspected' evidence of ulcer recurrence. It is of interest to note that re-examination of the data of Clark and others (1964) reveals that of their 6 recurrent ulcers only 1 had a preoperative acid secretion of less than 25 mEq. per hour.

Vagotomy and drainage can be expected to reduce preoperative acid values (both basal and maximal) by 65–70 per cent irrespective of their magnitude. Thus, the postoperative acid output of patients with a low preoperative output will obviously be lower than that of patients with a high preoperative value. In the present series patients with a preoperative M.A.O. value of less than 25 mEq. per hour had a mean postoperative value of 5·8 mEq. per hour compared with 11·3 mEq. per hour in the group with a preoperative M.A.O. of more than 25 mEq. per hour. To date no recurrent jejunal ulcers (proven or suspected) have been found among patients undergoing vagotomy and antrectomy, the majority of whom (85 per cent) had an M.A.O. value in excess of 25 mEq. per hour, whereas 12·6 per cent of patients with an M.A.O. greater than 25 mEq. per hour subjected to vagotomy and drainage developed proven or suspected recurrent duodenal ulceration. The significantly better results after vagotomy and gastric resection are hardly surprising in view of the greater percentage reduction of the preoperative acid output. It would appear that an M.A.O. in the region of 5–6 mEq. per hour after vagotomy and drainage is desirable to protect against ulcer recurrence. It should be noted that the insulin test is suspect at these low levels. Insulin tests performed on a group of hyposecretors who had not been subjected to gastric surgery or vagotomy, with pentagastrin-stimulated M.A.O. values of less than 6 mEq. per hour, yielded variable results, particularly in the form of false negatives when Hollander's or multiple criteria were used for interpretation. Previously published results of the insulin test in patients with intact vagi have usually been of patients with duodenal ulcer who tend to be high acid secretors (Ross and Kay, 1964; Gillespie, Gillespie, and Kay, 1969). Nevertheless, the overall incidence of positive insulin tests (by Hollander's criteria) among the vagotomy and drainage patients of 40·9 per cent lies at the upper limit of the range presented by many authors (Ross and Kay, 1964; Kay, 1969). All the tests in the present series were done at least 3 months, and in the vast majority over 6 months, after surgery. In fact, the time interval was more than 4 years in 60 per cent of the cases. The negative-to-positive insulin test conversion which is known to occur in the first 3 months after vagotomy (Gillespie and others, 1969; Bank and others, 1970) can therefore be disregarded in the present series.

Interpretation of the insulin test results in the two groups of vagotomy and drainage patients with a preoperative M.A.O. value of greater or less than 25 mEq. per hour revealed an insignificant difference in the incidence of incomplete vagotomy when Hollander's criterion alone was used. However, the group with a preoperative M.A.O. of less than 25 mEq. per hour had a significantly lower incidence of positive results when the multiple criteria were employed. The use of the latter was therefore regarded as a more accurate index of liability to recurrent ulceration than Hollander's method, albeit empirically. Hollander's criterion would seem to be far more accurate with regard to whether the vagi are in fact intact or not. It is also of interest to

Table V.—Comparison of Recurrent Ulceration Rates in Patients with a Preoperative M.A.O. greater than 25 mEq. per Hour after Vagotomy and Drainage and after Vagotomy and Antrectomy for Duodenal Ulcer

Operation	Total No. of Patients	No. of Patients with M.A.O. >25 mEq. per hr.		A.H.T. Mean Preoperative Value (mEq. per hr.)		Recurrent Ulceration: Duodenal/Jejunal, Proven		Duodenal/Jejunal, Suspected		Gastric, Proven	
		No.	Per cent	B.A.O.	M.A.O.	No.	Per cent	No.	Per cent	No.	Per cent
Vagotomy and drainage	253	143	56·5	6·8	35·8	11	7·7	7	4·9	2	1·4
Vagotomy and antrectomy	55	47	84·5	12·5	47·8	0	0	0	0	1	2·1

compare the incidence of incomplete nerve section in the patients undergoing vagotomy and antrectomy and in the vagotomy and drainage group. Admittedly very few (11) tests were done in the former group, but the 36·4 per cent incidence of incomplete vagotomy by Hollander's criterion is similar to that in the vagotomy and drainage group; however, none of the tests was positive by the multiple criteria in the patients submitted to vagotomy and antrectomy.

If a positive Hollander test is taken as being indicative of a significant degree of residual vagal innervation after vagotomy it seems that in the presence of a preoperative M.A.O. of less than 25 mEq. per hour residual vagal fibres are relatively unimportant when vagotomy and drainage are performed. On the other hand, with a preoperative M.A.O. value greater than 25 mEq. per hour the persistence of vagal innervation assumes far greater importance. Insulin tests done on the vagotomy and antrectomy patients suggest a similar incidence of incomplete vagotomy. The absence of recurrent jejunal ulceration in this group indicates that the addition of antrectomy when vagal denervation is incomplete can sufficiently reduce gastric acid output to provide adequate protection against recurrent jejunal ulceration. The report by Small and others (1967) that no recurrent jejunal ulcers occurred in their patients who had been treated by gastro-enterostomy without vagotomy and who had had a preoperative M.A.O. of less than 30 mEq. per hour tends to corroborate the findings in this study. However, this favourable outcome has not been our experience using this level of secretion (Bank and Marks, 1971) and it is well known that recurrent ulceration after gastro-enterostomy alone may be delayed for many years.

Gastric ulceration after the vagotomy operations occurred independently of the level of acid secretion or completeness of vagotomy and no single aetiological factor could be incriminated as the mechanism of gastric ulceration in all the patients. It is likely that one or more of the 'risk factors', e.g., gastric retention, inadequate pyloroplasty, gastritis, antral hyperfunction, and poor acid reduction, singly or in combination, are operational in any individual case. We have now encountered 31 gastric ulcers after vagotomy and drainage for duodenal ulcer, many of which were at the proximal end of the pyloroplasty, and such ulcers have possibly been previously erroneously diagnosed in other series as recurrent duodenal ulcer on the basis of radiological studies alone (Bank, 1971).

Intra-operative testing for completeness of vagisection using the Burge technique (Burge and Vane, 1958; Burge, 1970a, b; Inberg, 1970) has not been found to be universally applicable and it would appear to be impossible to achieve complete vagotomy in all patients even in the hands of surgeons experienced in its use. The results of this study imply that a policy of selection of patients for vagotomy and drainage based on a preoperative M.A.O. of 25 mEq. per hour seems more justified and far more realistic than the previously used level of 40–50 mEq. per hour. Vagotomy and antrectomy is thus suggested for patients with a preoperative M.A.O. in excess of 25 mEq. per hour, and vagotomy and drainage should be reserved for those with a lower M.A.O. value.

Acknowledgement.—This study was supported by the Medical Research Council of South Africa.

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THE BUERGER SYNDROME IN JAVA

A DESCRIPTION OF THE CLINICAL SYNDROME AND SOME ASPECTS OF ITS AETIOLOGY

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SUMMARY

A case control field survey was carried out on 106 Indonesian patients with spontaneous peripheral gangrene. In 101 patients the disease was a four-limb youthful type of peripheral vascular disease occurring in young male smokers. Migratory superficial thrombophlebitis was present in 38 patients. This constellation of signs and symptoms was similar to that described for the Buerger syndrome.

Of the aetiological factors studied, tobacco, cold injury, familial aggregation, and a past history of mycotic infection may be of significance.

ALTHOUGH patients with spontaneous gangrene of the extremities were described in the Indonesian literature 50 years ago (Aalsmeer, 1922; Van Dijk and Oudendal, 1923) they were not recognized as forming a distinct clinical entity. At that time patients presenting with peripheral gangrene in Indonesian hospitals and clinics were variously diagnosed as suffering from Raynaud's disease, leprosy, diabetes, or syphilis.

In the early 1930's Professor E. P. Snijders from Amsterdam toured through Sumatra and Java, inquiring from hospitals about the incidence of patients presenting with gangrenous extremities. His report (Snijders, 1933) described in detail the case histories of 11 Indonesian young male smokers presenting with spontaneous gangrene of the extremities, and he recognized this group as forming a distinct clinical entity. He called this Von Winiwarter–Buerger's disease. Six of this group of patients were from Java.

Other papers describing 'Buerger's disease' in Indonesia have appeared but they are few and those that are available are mainly concerned with the treatment of the condition (Lodder and Müller, 1937; Van Leeuwen, 1938; Van Ouwerkerk, 1946; Kiagoes Agoess, Husni Hasbullah, and Djamaloeddin, 1971).

At the present time the vast majority of patients presenting with peripheral spontaneous gangrene in hospitals throughout Indonesia are diagnosed as 'Buerger's disease'. The clinical syndrome in these patients has not been described, its clinical course has not been documented, and no systematic study has been made into its pathogenesis or aetiology.

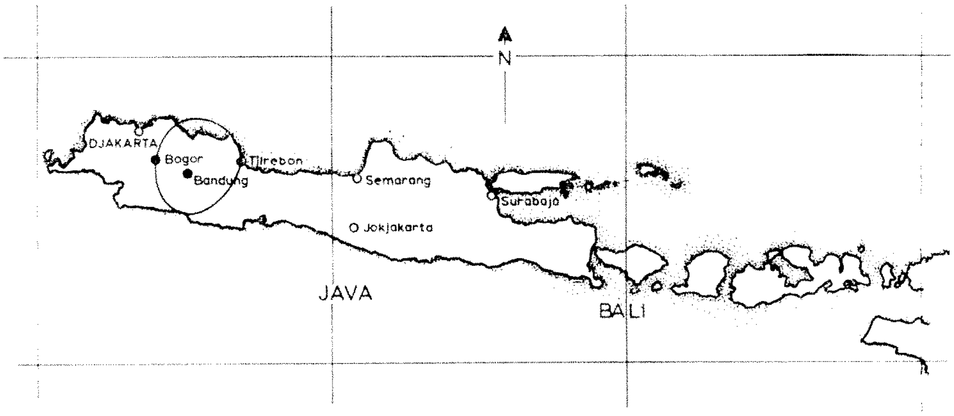

FIG. 1.—Map of the island of Java, Indonesia. The survey area is enclosed by the circle.

In this paper the results of a field survey of 106 Indonesian patients presenting with gangrene of the extremities is presented.

MATERIAL AND METHODS

Geographical and Sociological Setting.—The field survey was conducted in the eastern half of the province of West Java, Indonesia (*Fig.* 1). The area included the Bandung Plateau (2000 feet above sea-level) which is surrounded by hills and mountains ranging up to 8000 feet above sea-level. Also included were the cities of Bogor, which is noted for its excessive rainfall, and Tjirebon, which is an extremely hot city on the northern coast. Climatic limits within the area studied are shown in *Table I.*

The population and geographical centre of the area is the city of Bandung (1·5 million), but the area studied included the cities of Bogor, Tjirebon, Garut, and Tasikmalaja, as well as numerous small villages and towns. The population within the study area is not accurately known but is between 8 and 12 millions.

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Most of the patients and the control subjects were living a rural type of life and even those living geographically in the cities were sociologically rural. The predominant ethnic group in West Java is the Sundanese, although Chinese, Javanese, and smaller numbers of other Indonesian ethnic groups are found.

Sampling.—It was intended to study the patients within the survey area who had been diagnosed as suffering from Buerger's disease. A quota sampling technique was used in which the survey area was stratified into regions each based on a population centre. Quotas of patients were drawn from every region.

For each patient in the study a closely matched control subject was obtained, who was matched for place of residence, age, sex, race, and socio-economic status. The closeness of this matching is shown in *Table II*. In practice the controls were the young men who fulfilled the above criteria and lived in close proximity to the patient. The validation of this sampling technique is discussed more fully elsewhere (Hill, 1972).

Table I.—THE CLIMATE IN THE SURVEY AREA

AREA	HEIGHT ABOVE SEA-LEVEL (m.)	AVERAGE YEARLY TEMPERATURE (°C.)	MEAN DAILY RANGE OF TEMPERATURE (°C.)	ABSOLUTE MINIMUM TEMPERATURE WHICH OCCURRED IN THE SAME YEAR AS MAXIMUM RANGE RECORDED	YEARLY RAINFALL (cm.)	NO. OF MONTHS PER YEAR WITH RAINFALL GREATER THAN 100 mm.
Bandung	730	22·6	9·3	11·3	178	8
Tjirebon	2	27	7·2	22·8	236	7
Bogor	266	25	8·3	17	423	12
Pangalengan	1585	16·8	7·5	8·1	288	9

Table II.—AGE, SEX, SOCIO-ECONOMIC STATUS, AND ETHNIC GROUP IN THE PATIENTS AND CONTROL SUBJECTS IN THE PRESENT SERIES

	Patients	*Controls*
Age (years ± S.D.)	41·5 ± 8·9	41·3 ± 8·5
Sex	105 males	100 males
Socio-economic status	Poor	Poor
Ethnic group		
Sundanese	84	80
Javanese	12	14
Chinese	6	4
Other	4	2
Total	106	100

The Field Survey.—The survey team travelled from village to village looking for patients within the quota regions. The patients and their controls were examined and interviewed in their homes by the survey team. The survey team consisted of a final-year medical student, a senior social science student, and a medically trained field supervisor. After gaining the confidence of the respondent and his family the medical student carried out a complete interrogation and physical examination on the respondent and followed this with a complete non-directive interview covering the clinical manifestations of the disease as well as the following large list of possible aetiologies: age, sex, race, heredity, occupation, socio-economic status, diet, tobacco, geography, past illness, cold and climate, immersion foot, mycotic infection, ergot, allergy, syphilis, trauma, and alcoholism.

This interview was followed by a separate directive interview carried out by the social science student who filled out a comprehensive precoded interview schedule concerned with possible environmental and sociological aetiological factors.

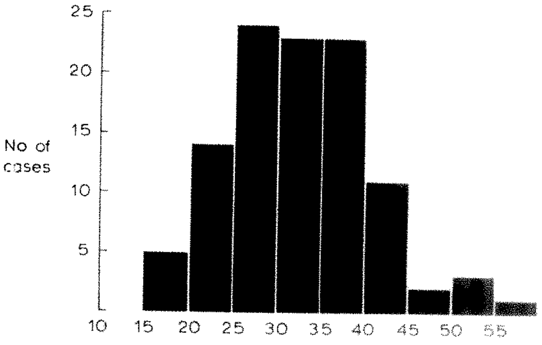

FIG. 2.—The age of onset of the disease in 106 patients.

The non-directive interview was used as an internal control for the directive interview and the field co-ordinator sought out and reinvestigated inconsistencies.

The information gained from both interviews was coded by one of the field supervisors (G. L. H.) and the results were analysed by the computer at the University of Otago, Dunedin, New Zealand.

RESULTS

The Clinical Syndrome.—The age distribution of the 106 patients at the time of the onset of their disease is shown in *Fig. 2*. The mean age of the group was 32 years and only 6 patients developed the disease after the age of 45 years.

Of the 106 patients studied, only 1 was a woman and she developed the disease at the age of 46 years. All the patients were cigarette smokers who had begun smoking before the onset of their disease and have continued to smoke.

Thirty-five patients had four-limb involvement (involvement was recorded when there was a missing distal pulse other than the dorsalis pedis + signs of ischaemia such as amputation, cyanosis, or pulp atrophy). A further 25 patients had three-limb involvement. In only 9 patients was the disease confined to one limb (*Table III*). In 22 patients one or both femoral pulses were impalpable, but 48 patients had normal femoral and popliteal pulses with absent posterior tibial pulses. Thirty patients had one or both radial pulses impalpable but all the patients had normal brachial pulses.

In 82 patients the disease commenced in the lower limbs. The initial symptoms are shown in *Table IV*.

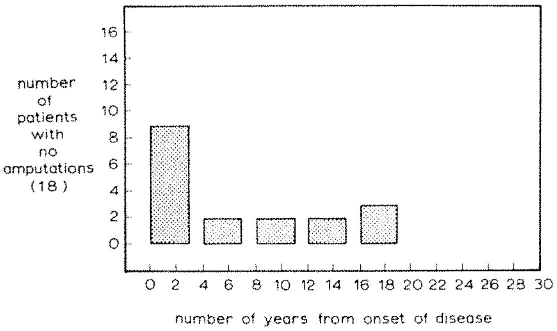

FIG. 3.—Patients without an amputation compared with the length of history.

Table III.—NUMBER OF LIMBS INVOLVED

No. of Limbs	*No. of Patients*
2 legs and 2 arms	35
2 legs and 1 arm	25
2 arms and 1 leg	2
2 legs	29
1 leg and 1 arm	6
1 leg	9
Total	106

Table IV.—INITIAL SYMPTOMS

Symptoms	*No. of Patients*
Numbness in feet	35
Tiredness and weakness in legs	33
Calf claudication	30
Foot claudication	27
Burning pain in foot	22
Cold feet	22
Ulceration and infection of digits	15
Thrombophlebitis	8
Cold hands	8
Hand claudication	6
Pain in fingers	6
Raynaud's phenomenon	2

The disease commenced peripherally and extended proximally. In 18 patients who had severe symptoms and clinical limb involvement, amputation had not been performed. The proportion of patients without amputation was higher among those with shorter histories (*Fig.* 3).

If the patients who had had an amputation are taken as a group the proportion with a major amputation as compared with those with only a digital amputation is higher among the patients with a longer history of the disease (*Fig.* 4). The patients with a longer history also tended to have more limbs with an amputation (*Fig.* 5).

Thirty-eight patients gave a history of superficial migratory thrombophlebitis and in the majority this was confined to the superficial tributaries of the long saphenous vein in the leg. Eight patients had superficial migratory thrombophlebitis as their initial symptom.

Twenty-eight patients complained of Raynaud's phenomena and in 24 this was confined to the hands.

Twenty-eight patients complained of hyperhidrosis of the hands and feet.

Other Physical Findings.—No xanthelasmata or other xanthomata were discovered in either the patient or control groups. No subject in either group was found to have any heart disease or any other incidental medical illness. One patient had developed a stroke at the age of 21 years. He had awoken one morning with paralysis of the right arm and his speech had been slurred. After 2 months' hospitalization he had improved and on physical examination at the time of the survey he had no residual signs (now aged 41 years).

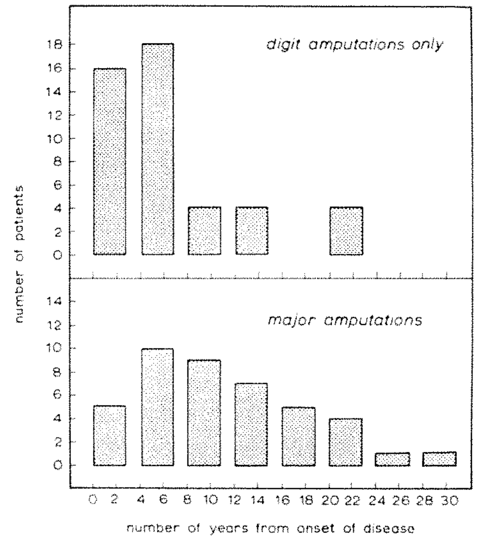

FIG. 4.—Patients with digital and major amputations compared with the length of history.

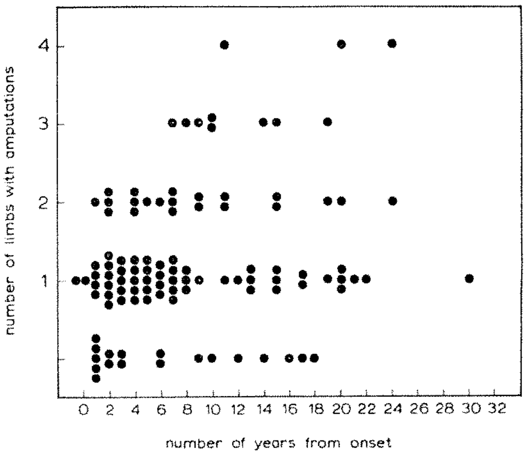

FIG. 5.—Number of limbs with an amputation compared with the length of history.

The Clinical Types.—Sixty patients presented a clinical picture of a slowly progressive peripheral arterial disease. In 59 patients the disease was periodic in nature, the slowly progressive pattern being interrupted by 'attacks' which in 16 patients were subacute in nature, resulting only in minor tissue loss such as ulceration or digital pulp atrophy. In the remaining 43 patients the 'attacks' were 'fulminant', commencing as an excruciatingly painful vesicle and progressing over a period of weeks to amputation. The degree of amputation was variable, most fulminant attacks resulting in the loss of several digits only, but in a minority of cases major amputation was the end-result of a single fulminant attack. When the intervals between attacks are averaged for the group as a whole attacks occurred every 29 months, but the range was wide, extending from 6 months to 10 years. Not only was this variation great from patient to patient, but for any individual there was no fixed pattern in the frequency or number of attacks.

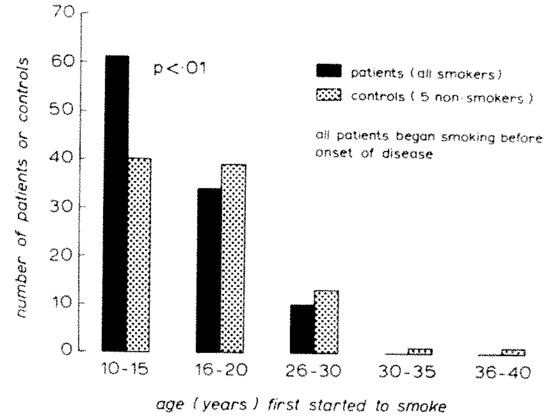

FIG. 6.—The age of commencement of smoking in the patients and their controls.

Fifteen patients developed an acute fulminant attack early in the course of their illness and after recovery from their amputation the disease has failed to progress. Six patients in this group have failed to show any progression of their disease for periods greater than 12 years.

Four patients, after commencing with an acute fulminant attack, developed circulatory compensation and have lost their symptoms.

Five patients presented a clinical picture which was not typical. Each of these patients developed their arterial disease after the age of 45 years, the eldest being 56 at the time of his first symptoms. All have their vascular disease confined to the lower limbs and 3 patients have one or both femoral pulses impalpable. One of this group is the only female patient in the series.

A summary of the 'clinical types' is shown in *Table V*. Only 84 patients could accurately be classified into clinical type as the remaining 22 had histories which were too short to judge the pattern of their disease adequately.

Aetiological Factors.—

1. *Tobacco.*—All of the 106 patients were smokers and all were smoking at the time of the survey. Ninety-five out of the 100 matched controls were smokers. Various types of cigarette were smoked, the commonest being Kawung, which is home-grown tobacco rolled in a tissue made from the leaves of a sugar palm. Another frequently smoked type was Kretek, which is a coarse form of tobacco mixed with cloves and spices and wrapped in normal tissue.

The type of cigarette smoked at the time of onset, and for the 3 years preceding the onset of the disease was evenly distributed between these two types and almost as large a group smoked the usual Western-type cigarette. Generally the type of cigarette smoked was the same in the patients and the controls.

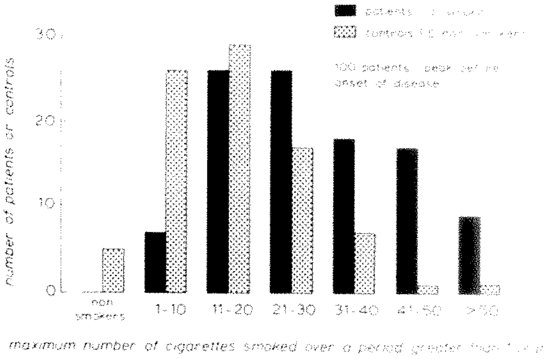

FIG. 7.—Peak smoking levels in the patients and their controls.

Table V.—SUMMARY OF CLINICAL TYPES

Clinical Type	*No. of Patients*
Slow progression with fulminant attacks	43
Slow progress with subacute attacks	16
Slow progress without attacks	1
Acute fulminant attack with failure of progression	15
Acute fulminant attack with circulatory compensation	4
Atypical	5
Unclassified	22
Total	106

All the patients had begun smoking before the onset of the disease.

If the patients are compared with the control group it is found that a significantly larger number of patients began smoking between the ages of 10 and 15 years ($P < 0{\cdot}01$) (*Fig.* 6).

Each respondent was asked about his peak smoking level, that is, the maximum daily number of cigarettes smoked consistently for a period of at least 1 year, and at what age was this peak smoking performed. One hundred patients smoked their peak before the onset of the disease, and at high levels of smoking (greater than 20 cigarettes per day) the patients consistently consumed more tobacco ($P < 0{\cdot}01$) than the controls (*Fig.* 7).

Thus, before the disease occurred the patients generally had begun smoking at an earlier age and were smoking more heavily than the controls. Nineteen patients had stopped smoking for periods of greater than 1 year, and 13 of these patients had noted an improvement in their condition, particularly in decreased rest pain and an increase in claudication distance. One patient related his attacks of migratory thrombophlebitis to commencing smoking after periods of cessation.

Sixteen patients had cut their smoking habits drastically (to less than 5 per day for a period greater than 3 years) and all but 1 claimed an improvement in the symptoms of rest pain and claudication. However, when compared with the patients who continued to smoke heavily there was no significant difference ($P > 0{\cdot}1$) in the mean period of time between attacks.

In the commonest clinical type of the disease, 25 patients related the periodicity of their attacks to times of increased smoking and the 2 patients whose disease did not progress over a long period of time had both cut their smoking over this period to less than 5 cigarettes per day.

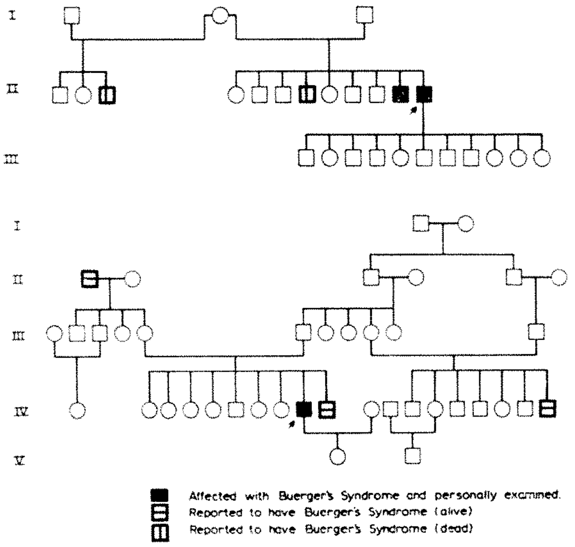
I
II
III
I
II
III
IV
V
■ Affected with Buerger's Syndrome and personally examined.
⊟ Reported to have Buerger's Syndrome (alive)
◫ Reported to have Buerger's Syndrome (dead)

FIG. 8.—Familial aggregation of the Buerger syndrome in two families.

2. *Racial Distribution.—Table II* shows the racial distribution in both the patient and control groups. This distribution does not show a predominance of any one grouping and closely parallels the ethnic structure of the population of West Java.

3. *Socio-economic Status.*—This was assessed by both interviewers, who took into account not only salary but also housing, family structure, mode of living, and food.

In general all the patients were from the poorer section of the community and there were no patients who could be judged middle class even by Indonesian standards. The wealthiest patient in the series earned about £15 per month and lived in a two-roomed concrete-floored cottage at the back of his market shop.

As further evidence that the disease predominates in the lowest socio-economic groups the four local Bandung hospitals were surveyed. The three public hospitals which catered almost exclusively for the poor had between 15 and 22 new patients admitted with a diagnosis of Buerger's disease per year. The remaining hospital, of comparable size, which was for rich patients had had no admissions with a diagnosis of Buerger's disease in the past 5 years.

4. *Occupation.*—The immediate 3-year period prior to the onset of the illness was considered. Twenty-nine patients were rice farmers who had spent up to 3 months of each year working with their feet immersed in water. Sixty-three patients were outdoor workers with various labouring jobs which involved working in bare feet or using only a primitive type of sandal. These people were vendors, market workers, outdoor labourers, and Betjak drivers. Only 14 patients in the group had indoor jobs during this period. When compared with their matched controls at the same stage of their lives the employment distribution was not significantly different.

At the time of the survey 56 patients have continued in the same employment but the remainder have been forced to stop work because of their illness.

5. *Diet.*—The usual diet of the respondents was made up of polished rice, vegetables (carrot, spinach, cabbage, potatoes in season, maize, roots such as yam, and cassava), dried or fermented fish, and soya-bean cake, all spiced with peppers, ginger, cinnamon, or onions and various local leaves and shoots.

Small portions of beef, mutton, or frog, plus lung, liver, kidney, or intestine were eaten once or twice weekly. This diet applies to times of plenty. In hard times it might contract to maize, cassava, and potatoes.

In 58 patients and 42 controls the diet was very poor in protein of any type (i.e., less than 2 oz. per week) and in more than half of these people the only source of protein was from soya bean.

There was no clear vitamin-deficiency syndrome seen in any of the respondents.

6. *Familial Aggregation.—Fig.* 8 shows familial aggregation of the disease in two families.

Two other families whose family history is incomplete had histories suggestive of other members having peripheral vascular disease. One patient had a brother who was 3 years younger and who was handicapped at work with hand claudication. He was not examined by the team. The remaining patient claimed that his grandfather died of gangrene of his feet whilst still quite young.

One patient had an identical twin brother who was also a smoker. This man was found and on physical examination was entirely normal.

7. *Geographical and Climatic Distribution.—Fig.* 9 shows the place where each patient lived in the 3-year period prior to the onset of his illness. This shows no particular clustering when it is remembered that an area sampling technique was not used. The grouping around Bandung is a reflection of the dense population in that region. Thus there are patients presenting from all climatic extremes in the area surveyed and no region or particular climatic factor appears to predominate. When compared with their matched controls, at the same stage of their lives, this geographical distribution is not significantly different.

8. *Past History of Illness.*—The patients had a scattered collection of past histories of trauma and infectious disease but the distribution was almost identical to that of the control group. Both the patients and the controls had a similar incidence of food and drug allergy and this was less than 10 per cent. Alcoholism was not seen in either the patient or the control group. There was no suggestion of ergot poisoning in any of these patients or their families.

9. *Cold Injury.*—Each respondent was read a story of an Indonesian farmer who had suffered from a classic episode of trench foot. The reaction of each respondent was noted. Twenty-three of the patients recognized the condition immediately and claimed that they had suffered a similar episode before the onset of their illness. In most of these 23 patients the first episode had been followed by temperature instability, inappropriate sweating, and sometimes repeated episodes of lesser severity. None of the controls had had trench foot.

Eight patients complained voluntarily of cold urticaria and in 4 this was of the immediate acquired type. The other 4 patients complained more of systemic symptoms, with a history suggestive of the familial form of cold sensitivity. Only 1 of this group of 8 patients had also suffered from trench foot. Two control subjects complained of the acquired form of cold sensitivity.

Thus, of the group of 106 patients, 30 patients had had some form of cold injury and this was in general associated with working with feet immersed in water over long periods of time.

10. *Mycotic Infection.*—Each respondent was shown a series of coloured photographs of various forms of dermatomycoses. Their response was noted. Forty-two patients claimed that they had had tinea pedis before the onset of their disease. Only 16 of the controls, when compared with the onset age of their matched patient, had had tinea pedis. The difference is highly significant ($\chi^2 = 13{\cdot}05$, $P < 0{\cdot}001$).

At the time of the survey 10 of the patients and 4 of the controls had clinical fungal infection.

11. *Laboratory Tests.*—In 28 patients the fasting blood-glucose, serum cholesterol, and serum-protein electrophoresis were measured, and a Wassermann reaction and Kahn test for syphilis were carried out.

No instance of hyperglycaemia was discovered. No patient had hypercholesterolaemia. In all the patients the electrophoretic pattern of the serum proteins was within normal limits.

In 2 patients the Wassermann reaction and Kahn test were positive.

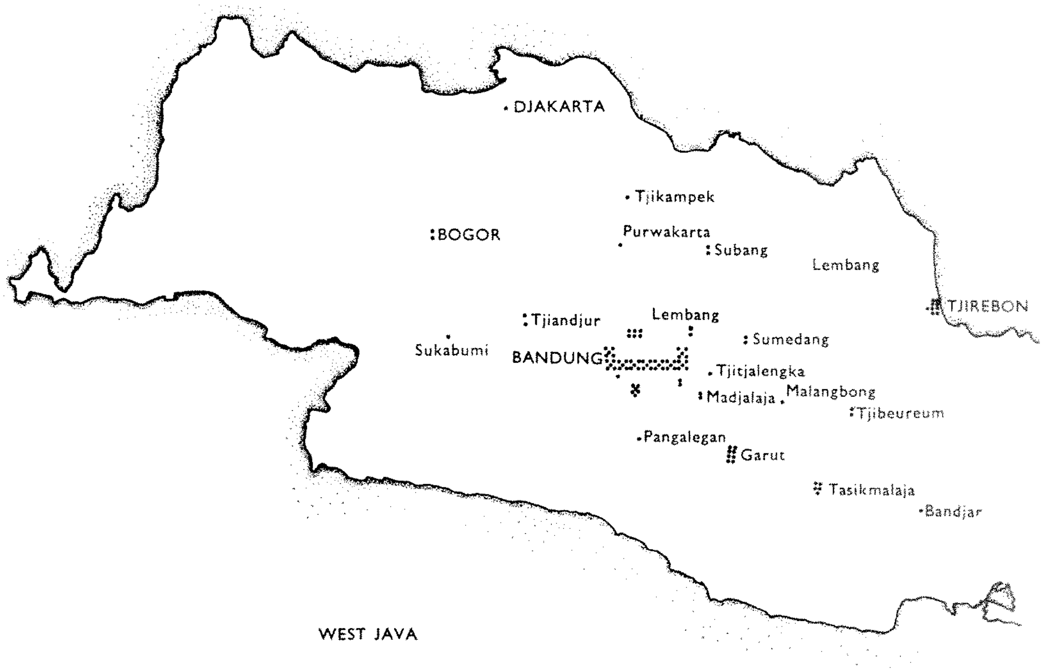

FIG. 9.—The province of West Java showing the place where each patient lived in the 3-year period prior to the onset of the disease.

DISCUSSION

The syndrome in the group of patients studied is a peripheral four-limb youthful type of arterial disease occurring in Indonesian males. Of the 106 patients who were studied by the survey team and who had been previously diagnosed as having 'Buerger's disease', 101 of them presented a picture consistent with the Buerger syndrome which has been described elsewhere (McKusick and Harris, 1961).

These 101 young Indonesian males had all developed their arterial disease before the age of 45 years and, of these, only 12 were over the age of 40 years at the time of onset of their disease. Thirty-five patients had four limbs involved and all the patients had one or both legs involved. Sixty-eight patients had one or both arms involved. The peripheral nature of the disease is suggested both by the amputation status of the group (*Figs.* 3–5) and also by the fact that nearly half the patients had normal femoral and popliteal pulses with distal pulses absent. Thirty-eight patients gave a history of migratory thrombophlebitis, and the conspicuous relationship of the disease to tobacco smoking has been established.

It may be wondered why 3 of the 22 patients with one or both femoral pulses impalpable are included in the group of 5 patients whose clinical picture is indistinguishable from juvenile atherosclerosis. The remaining 19 patients with one or both femoral pulses absent are evenly distributed throughout the series as regards the age of onset, length of history, number of limbs involved, and migratory thrombophlebitis, and no particular pattern emerges from a study of this group. A femoral arteriograph was available for 1 of these patients (*Fig.* 10). This shows a complete block of the superficial femoral artery and profunda system. There are abundant collaterals around the block. This patient developed his disease at the age of 27 years. He had a history of migratory thrombophlebitis and diminished pulsations in both radial arteries. The clinical picture and arteriographic appearances do not suggest juvenile atheroma in this patient.

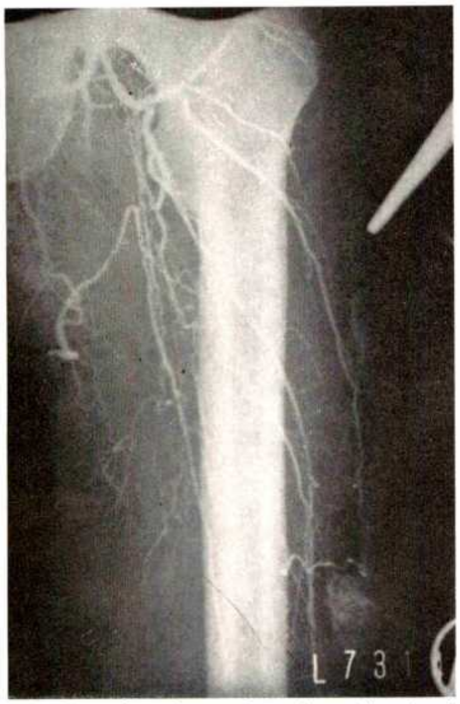

FIG. 10.—Femoral arteriogram of a patient with an impalpable femoral pulse.

The slowly progressive nature of the disease in this series, together with exacerbations producing increased arterial insufficiency resulting usually in digital amputation only, is similar to that described previously for Buerger's disease (Brown, Allen, and Mahorner, 1928; Juergens, 1972). This slowly progressive type of disease is different to the pattern seen in atherosclerosis, for although serious worsening nearly always occurs as a sudden event in patients with atherosclerosis this is usually a major deterioration, and spontaneous recovery from such an episode to a degree sufficient to provide a useful limb is most uncommon (Humphries, de Wolfe, Young, and Le Fevre, 1963).

It is interesting that the clinical types noted in the present series parallel the clinical types described in a large series from the Mayo Clinic over 40 years ago (Brown and others, 1928).

Being a field survey, histology was not available for any of the patients in the present series. Thorough documentation of the histological picture of 7 young Indonesian male smokers with spontaneous peripheral gangrene has been described previously (Lodder and Müller, 1937). Both acute and chronic lesions were described and the disease was identical to that described originally by Buerger (1908). It seems reasonable to conclude that the disease described by Lodder and Müller (1937) is the same as the one described in the present report.

Of the aetiological factors considered, age, sex, socio-economic status, occupation, familial aggregation, tobacco, cold injury, and past mycotic infection seem to be of some importance.

Other descriptions of the Buerger syndrome occurring in Asian countries (Whyte, 1917; McKusick and Harris, 1961; Yong, 1971) have all shown the disease occurring almost exclusively in the lower socio-economic groups although this is not a feature of the disease in Western countries (Goodman, Elian, Mozes, and Deutsch, 1965; Juergens, 1972).

Familial aggregation has been noted previously by other workers (Samuels, 1932; Weber, 1937; Martorell, 1952; Goodman and others, 1965), but of particular interest is the woman (*Fig.* 8) who has had 2 husbands and in both her sets of children the Buerger syndrome has appeared. A patient with a normal identical twin has not been described before.

Occupation probably reflects socio-economic status and both of these may be important only in so far as the increased susceptibility of the individual to cold injury which occurs in outdoor workers during the wet season. Patients with sensitivity to cold have been reported sporadically in the literature (Duke, 1925; Horton and Brown, 1929; Spittell, 1972), but not previously in association with vascular disease. Although minor degrees of feelings of abnormal coldness in an affected limb are well recognized in circulatory disease (Juergens, 1972) the cold urticaria described in the present series is a more specific entity.

Some investigators have reported a frequent history of frost-bite occurring prior to the onset of the Buerger syndrome (McKusick and Harris, 1961; Goodman and others, 1965), but others have not observed this (Juergens, 1972). Other studies have not noted the high incidence of trench foot. There is argument as to whether trench foot is basically the same process as frost-bite (Spittell, 1972), but it is interesting that the late vasospastic phase of trench-foot sensitivity to cold can be a marked feature (White, 1944). It may be that the patients with sensitivity to cold have actually suffered a minor degree of trench foot which they have since forgotten. It would be interesting to know the long-term follow-up of a large series of patients with previous trench foot. We have been unable to find any information about this in the literature.

Fungal infections are frequently present between the toes of patients with the Buerger syndrome (Eastcott, 1969), and some workers have suggested mycotic infection as an aetiological agent (Naide, 1941; Craven and Cotton, 1967). The problem that has never been clarified is whether the fungal infection occurs before or after the onset of the disease. The present study suggests that the fungal infection precedes the onset of the disease.

It is concluded that the clinical syndrome presented in this study is the same constellation of clinical symptoms and signs described as the Buerger syndrome in other studies. The environmental factors of significance in this syndrome as it presents in Java appear to be tobacco, cold injury, and a past history of mycotic infection.

Acknowledgements.—We wish to thank Professor P. A. Surjadi and Dr. J. E. Siregar and other members of the Board of Maranatha University for their financial help and also their support in all the phases of this study. We are grateful to Sdr. Adiwedjaja, Paryana, Hadiman, Soebiantoro, Surjadi, Budi, Tancar, and Bastion who all helped in various stages of the study. The Reverend D. E. Duncan and other members of the Overseas Missions Committee of the Presbyterian Church of New Zealand, Professor A. M. Clarke, Mr. G. F. S. Spears, Mrs. R. Molloy, Dr. Alan Smith of the University of Otago have all willingly and generously given their time at different periods during the project.

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METABOLIC CHANGES FOLLOWING VARYING DEGREES OF PARTIAL HEPATECTOMY IN THE RAT

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SUMMARY

1. The metabolic and functional changes that follow hepatectomy in the rat are related to the extent of liver resection.

2. Regenerating liver cells show an impaired ability to excrete bilirubin, bromsulphophthalein, and ^{125}I Rose Bengal during the early postoperative period.

THE liver remnant undergoes a rapid proliferative response after partial hepatectomy. The process has been extensively studied and in the experimental animal the rate and degree of this response have been related to the extent of hepatic resection (Bucher and Swaffield, 1964). Removal of large quantities of liver tissue in animals and in man results in alterations in liver function (Harkness, 1957; Aronsen, Ericsson, and Pihl, 1969; Blumgart and Vajrabukka, 1972). Attempts have been made to relate the metabolic changes following partial hepatectomy in man to the amount of tissue removed (Lin and Chen, 1965). However, it is difficult to interpret the results of such studies since partial hepatectomy in man involves the removal of liver tissue already damaged by the disease process and leaves a remnant often affected by prior compensatory hyperplastic change. In addition, liver resection in man is often accompanied by pre- or peroperative hypovolaemic hypotension. As a result the function of the liver remnant after operation may be compromised by the effects of tissue hypoperfusion.

In order to overcome these difficulties, different degrees of resection were performed in the previously normal rat liver and the changes that occurred in liver function after resection were studied.

MATERIALS AND METHODS

Animals.—Male Sprague-Dawley rats weighing between 250 and 320 g. were used. They received food and water *ad libitum* throughout the experiments.

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Operative Procedures.—Ether anaesthesia was used throughout.

1. Partial hepatectomy was performed using the method described by Higgins and Anderson (1931). This involved removal of the median and left lateral lobes of the liver. Studies on 30 animals in our laboratory have shown that this procedure removes 69 ± 2 per cent of liver tissue.

group II. Eight control animals, 4 having ether anaesthetic alone and 4 subjected to laparotomy and liver mobilization but without removal of any liver tissue, were added to each subgroup.

Blood samples were taken from all the animals before operation and then from alternate paired subgroups at 12 and 24 hours and 2, 3, 4, 7, 10, 13, 16, 19, 22, 25, and 28 days after operation.

Table I.—CHANGES IN TOTAL SERUM PROTEIN, SERUM ALBUMIN, SERUM ALANINE TRANSAMINASE, AND SERUM BILIRUBIN AFTER PARTIAL HEPATECTOMY (P.H.) and SUBTOTAL HEPATECTOMY (S. H.)

TIME	TOTAL PROTEIN		ALBUMIN		ALANINE TRANSAMINASE		BILIRUBIN	
	P.H.	S.H.	P.H.	S.H.	P.H.	S.H.	P.H.	S.H.
Preop.	6·87 ± 0·28	6·85 ± 0·31	2·99 ± 0·14	3·01 ± 0·14	24 ± 3·6	34·3 ± 5·83	0·20 ± 0·09	0·25 ± 0·00
Postop.								
12 hr.	5·65 ± 0·42	5·43 ± 0·17	2·96 ± 0·27	2·80 ± 0·00	181·33 ± 95·82	393·3 ± 261·1	0·43 ± 0·14	1·00 ± 0·28
24 hr.	5·73 ± 0·31	5·23 ± 0·44	2·92 ± 0·17	2·75 ± 0·00	160·0 ± 103·0	237·3 ± 61·5	0·37 ± 0·12	0·90 ± 0·20
2 d.	5·55 ± 0·26	4·75 ± 0·36	3·10 ± 0·29	2·61 ± 0·17	47·5 ± 12·9	96·2 ± 53·1	0·35 ± 0·05	0·95 ± 0·20
3 d.	5·45 ± 0·30	5·15 ± 0·60	2·67 ± 0·31	2·41 ± 0·36	31·8 ± 5·7	50·0 ± 8·9	0·43 ± 0·08	0·65 ± 0·17
4 d.	5·70 ± 0·13	5·91 ± 0·65	2·80 ± 0·06	2·66 ± 0·22	34·0 ± 9·9	41·8 ± 14·3	0·30 ± 0·14	0·46 ± 0·00
7 d.	5·90 ± 0·28	5·81 ± 0·17	2·87 ± 0·05	2·63 ± 0·17	28·3 ± 5·75	36·3 ± 7·8	0·35 ± 0·12	0·46 ± 0·10
10 d.	5·97 ± 0·27	6·42 ± 0·24	2·72 ± 0·12	2·92 ± 0·10	34·3 ± 9·0	43·3 ± 9·4	0·30 ± 0·11	0·52 ± 0·07
13 d.	6·25 ± 0·16	6·77 ± 0·19	2·85 ± 0·12	2·98 ± 0·07	33·5 ± 7·6	41·2 ± 8·3	0·32 ± 0·04	0·28 ± 0·10
16 d.	6·35 ± 0·21	6·52 ± 0·28	2·98 ± 0·07	2·87 ± 0·23	36·5 ± 7·1	40·7 ± 7·0	0·27 ± 0·05	0·35 ± 0·05
19 d.	6·58 ± 0·33	6·55 ± 0·18	2·88 ± 0·13	2·85 ± 0·14	32·3 ± 3·7	41·5 ± 4·0	0·28 ± 0·04	0·32 ± 0·07
22 d.	6·27 ± 0·15	7·02 ± 0·23	3·10 ± 0·13	2·00 ± 0·06	36·3 ± 9·4	39·8 ± 4·9	0·27 ± 0·05	0·28 ± 0·07
25 d.	6·80 ± 0·25	6·70 ± 0·30	3·30 ± 0·09	2·98 ± 0·12	32·3 ± 2·3	37·3 ± 4·1	0·25 ± 0·05	0·22 ± 0·10
28 d.	6·70 ± 0·27	6·95 ± 0·15	2·98 ± 0·26	2·97 ± 0·14	31·3 ± 1·6	36·2 ± 3·6	0·28 ± 0·13	0·27 ± 0·08

Table II.—CHANGES IN TOTAL SERUM PROTEIN, SERUM ALBUMIN, SERUM ALANINE TRANSAMINASE, AND SERUM BILIRUBIN AFTER LAPAROTOMY AND ETHER ANAESTHESIA

TIME	TOTAL PROTEIN (g. per 100 ml.)		ALBUMIN (g. per 100 ml.)		SERUM ALANINE TRANSAMINASE (i.u. per litre)		BILIRUBIN (mg. per 100 ml.)	
	Laparotomy	Anaesthetic	Laparotomy	Anaesthetic	Laparotomy	Anaesthetic	Laparotomy	Anaesthetic
Preop.	6·91 ± 0·31	6·70 ± 0·43	3·01 ± 0·10	3·04 ± 0·17	30·12 ± 8·8	29·13 ± 5·6	0·25 ± 0·10	0·29 ± 0·15
Postop.								
12 hr.	6·57 ± 0·14	6·63 ± 0·37	2·97 ± 0·20	3·10 ± 0·00	33·5 ± 6·4	26·3 ± 1·43	0·25 ± 0·00	0·22 ± 0·10
24 hr.	6·15 ± 0·60	6·65 ± 0·31	2·85 ± 0·10	3·08 ± 0·05	26·7 ± 7·6	33·5 ± 13·0	0·30 ± 0·00	0·30 ± 0·10
2 d.	5·95 ± 0·30	6·55 ± 0·37	2·82 ± 0·00	2·93 ± 0·09	33·5 ± 5·4	31·8 ± 5·4	0·30 ± 0·00	0·30 ± 0·00
3 d.	6·37 ± 0·50	6·38 ± 0·34	2·87 ± 0·26	3·00 ± 0·12	41·5 ± 11·5	34·8 ± 5·6	0·32 ± 0·00	0·32 ± 0·10
4 d.	6·25 ± 0·43	6·35 ± 0·37	2·77 ± 0·20	2·90 ± 0·14	35·2 ± 15·0	29·5 ± 7·2	0·32 ± 0·00	0·27 ± 0·10
7 d.	6·22 ± 0·42	6·50 ± 0·35	2·90 ± 0·14	2·90 ± 0·18	35·7 ± 13·4	33·0 ± 6·6	0·37 ± 0·00	0·27 ± 0·00
10 d.	6·50 ± 0·14	6·35 ± 0·20	3·00 ± 0·16	2·98 ± 0·26	29·5 ± 6·6	31·8 ± 5·1	0·15 ± 0·05	0·33 ± 0·10
13 d.	6·65 ± 0·52	6·80 ± 0·28	3·13 ± 0·05	3·03 ± 0·17	31·5 ± 7·2	29·3 ± 4·3	0·20 ± 0·08	0·23 ± 0·10
16 d.	6·63 ± 0·17	6·88 ± 0·19	2·98 ± 0·10	2·85 ± 0·10	36·3 ± 9·5	34·0 ± 5·5	0·28 ± 0·05	0·33 ± 0·19
19 d.	6·73 ± 0·15	7·03 ± 0·15	2·98 ± 0·17	2·73 ± 0·17	33·5 ± 6·6	35·3 ± 4·9	0·23 ± 0·05	0·28 ± 0·10
22 d.	6·85 ± 0·21	6·95 ± 0·17	3·13 ± 0·10	3·10 ± 0·12	32·0 ± 3·7	32·0 ± 2·8	0·25 ± 0·06	0·28 ± 0·05
25 d.	6·93 ± 0·34	7·00 ± 0·18	3·18 ± 0·17	2·85 ± 0·26	35·8 ± 6·7	34·2 ± 1·7	0·23 ± 0·05	0·30 ± 0·00
28 d.	6·58 ± 0·29	6·85 ± 0·24	2·98 ± 0·21	3·03 ± 0·17	33·8 ± 4·8	31·0 ± 5·5	0·30 ± 0·08	0·28 ± 0·05

2. Subtotal hepatectomy (Weinbren and Woodward, 1964). This involved resection of the median and left lateral lobes plus the caudate lobes and inferior division of the right lobe. Studies in our laboratory on 30 animals have shown that this procedure removes 80 ± 1·75 per cent of liver tissue.

All blood samples were taken from the jugular veins.

Arrangement of Experiments.—

1. *Liver-function Tests.*—Two groups of 18 animals each were used. All the animals in group I underwent partial hepatectomy, while the animals in group II underwent subtotal hepatectomy. Each of the main groups of animals were subdivided into three subgroups of 6 animals, each of the subgroups in group I being paired with a similar subgroup from

The total serum protein, serum albumin, serum alanine transaminase, and serum bilirubin were measured in each of these blood samples.

2. *Blood-glucose.*—Two groups of 6 animals each were used. The animals in group I were submitted to partial hepatectomy, while those in group II had a subtotal hepatectomy. Four control animals, treated as described above, were added to each group.

Blood samples were taken from all the animals before operation and then 6, 12, and 24 hours and 2, 3, 4, and 5 days after operation.

3. *Bromsulphophthalein Clearance.*—Two groups of 3 animals each were used. The animals in group I had partial hepatectomy and those in group II had subtotal hepatectomy. Four control animals were again added to each group, as described for the other experiments.

Five mg. of bromsulphophthalein (B.S.P.) were injected into the jugular vein of the animals and blood samples were taken from the opposite jugular vein at regular intervals up to 25 minutes after the initial injection. It was found that the highest value for serum B.S.P. was 1 minute after injection. This value was taken as 100 per cent and as the blood was cleared of B.S.P. the serum levels obtained were expressed as percentages of the value obtained at 1 minute. The blood-clearance studies were performed immediately after hepatectomy and at 24 hours, 7 days, and 10 days after operation.

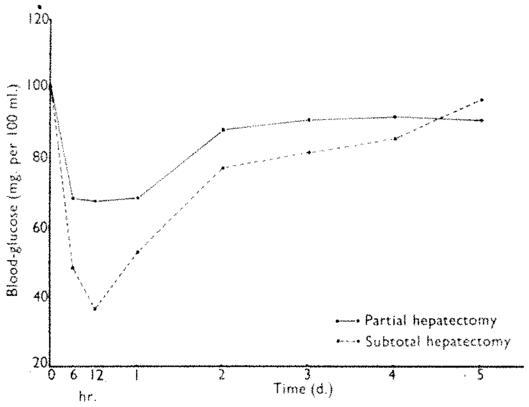

FIG. 1.—Changes in the blood-glucose levels after two-thirds partial hepatectomy and subtotal hepatectomy.

4. *Rose-Bengal Clearance.*—Similar groups of animals to those used to measure B.S.P. clearance were used to measure the clearance of radioactive Rose Bengal. Five μc. of ^{125}I Rose Bengal were injected into the jugular vein. The right leg of the anaesthetized rat was then isolated through a small hole in a thin lead screen and counts were made over the leg using a scintillation counter. The observations were made every minute up to the fortieth minute after the initial injection. Preliminary studies in our laboratory (Karran, Leach, and Blumgart, 1972) have shown this to be a reliable and reproducible method of assessing blood clearance of Rose Bengal.

Counts obtained were expressed as a percentage of the maximal value obtained 1 minute after injection. Rose-Bengal clearance studies were made immediately after operation and then 24 hours, 7 days, and 10 days after operation.

Biochemical Methods.—The total serum protein was measured using a micro-version of the standard method. Serum albumin was measured by a dye-binding method using brom-cresol green. The serum alanine transaminase was measured on an LKB reaction rate analyser using the method described by Wroblewski and Ladue (1956). The serum bilirubin was measured by a micro-version of the standard technique using diazotized sulphanilic acid.

To measure the blood-glucose 0·1 ml. of serum was added to 1 ml. of perchloric acid and centrifuged. Fifty μl. of the supernatant were added to 5 ml. of the colour reagent from a Boeringer sugar analysis kit. The solution was incubated at 37° C. for 15 minutes, and the colour reaction was read on a colorimeter using a 420-nm. filter.

To measure the serum B.S.P. 0·05 ml. of serum was added to 0·025 ml. of water and 0·3 ml. of $N/10$ NaOH. The test solution was read on a colorimeter at 540 nm. against a blank solution which used 0·3 ml. of $N/10$ HCl solution in place of $N/10$ NaOH. The serum B.S.P. level was then determined from a standard graph.

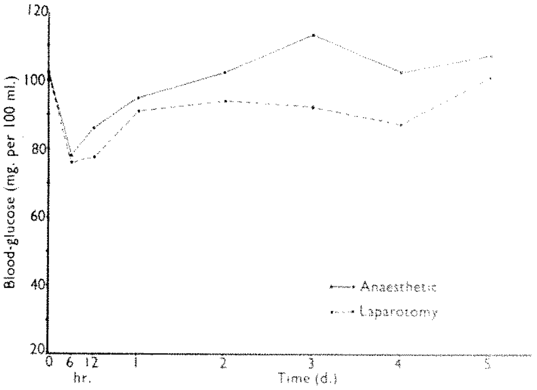

FIG. 2.—Changes in the blood-glucose levels after laparotomy and ether anaesthetic alone.

RESULTS

Our results show that metabolic changes following hepatectomy in the rat are related to the extent of liver resection.

1. Liver-function Tests.—*Table I* shows the changes in the total serum-protein levels in the two groups of hepatectomized animals. There was a fall in the total serum-protein levels after hepatectomy. This was significantly greater after subtotal hepatectomy at 24 hours ($P < 0·05$) and 48 hours ($P < 0·01$) postoperatively. The values had returned to within normal limits in both groups by the thirteenth postoperative day. A similar though less marked fall in the total serum protein was noticed in both control groups of animals during the early postoperative period (*Table II*).

There was no significant fall in the serum-albumin level following two-thirds partial hepatectomy. However, there was a marked fall in the serum-albumin level after subtotal hepatectomy. This fall in serum levels was maximal at 3 days after operation. Recovery to within normal limits had occurred by the thirteenth postoperative day.

There was a sharp rise in the serum alanine transaminase after hepatectomy. Despite wide variations around the mean values this rise in enzyme levels was much greater after subtotal hepatectomy. Enzyme levels had returned to within normal limits by the third postoperative day (*Table I*). There was no change in the serum alanine transaminase levels in the control groups (*Table II*).

There was a very slight rise in the serum-bilirubin levels during the first few days after two-thirds partial hepatectomy. However, there was a much greater rise in the serum bilirubin levels in the same period after subtotal hepatectomy. Serum-bilirubin levels had returned to within normal limits by the thirteenth postoperative day (*Table I*). *Table II* shows that there was no rise in the serum bilirubin in the control animals.

2. **Blood-glucose.**—There was a decrease in blood-glucose levels in both groups of hepatectomized animals during the first 48 hours after operation (*Fig.* 1). The changes were significantly greater after subtotal hepatectomy at 6 hours ($P < 0{\cdot}05$) and 12 hours ($P < 0{\cdot}001$) postoperatively. The blood-glucose levels had returned to normal within 48 hours after operation. There was a similar though less marked fall in blood-glucose in both groups of control animals (*Fig.* 2).

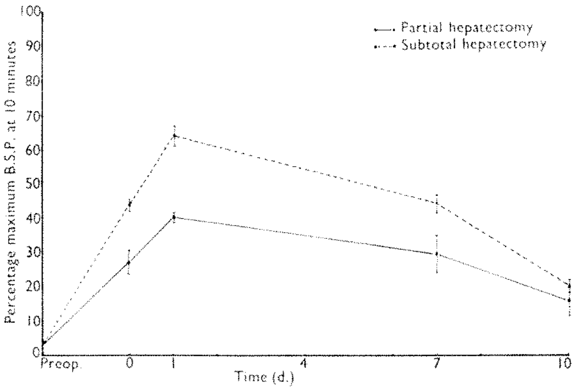

FIG. 3.—Percentage maximum serum levels 10 minutes after the injection of B.S.P. in the pre- and postoperative period after two-thirds partial hepatectomy and subtotal hepatectomy.

3. **B.S.P. Clearance.**—The mean values for the percentage maximal levels obtained at 10 minutes after the administration of B.S.P. in each of the clearance studies performed are shown in *Fig.* 3. There was quite a considerable delay in the clearance of B.S.P. immediately after hepatectomy. Twenty-four hours after operation there was even greater retention of B.S.P. and the changes were more marked in the subtotal hepatectomy group of animals. The rate of clearance of B.S.P. had almost returned to normal by the tenth postoperative day. Laparotomy did not produce a delay in B.S.P. clearance.

4. **Rose-Bengal Clearance.**—The mean values for the percentage maximal counts obtained at 10 minutes after the injection of ^{125}I Rose Bengal are shown in *Fig.* 4. There was a marked delay in the clearance of Rose Bengal immediately after operation, the changes being greater after subtotal hepatectomy. Twenty-four hours after operation there was an even greater delay in clearance but there was no significant difference between the clearance rates in the two groups of animals. The blood-clearance rates in both groups had returned almost to normal by the tenth postoperative day. Laparotomy did not produce a delay in the clearance of Rose Bengal.

DISCUSSION

It is difficult to relate the metabolic changes after hepatectomy in man to the degree of liver resection. The lobed liver of the rat allows easy partial hepatectomy of varying extent in a previously normal liver. The operative techniques do not leave large quantities of damaged or non-viable tissue attached to the liver remnant after partial hepatectomy. Furthermore, functional changes in the remnant are not influenced by the effects of previous disease, compensatory regenerative hyperplasia, and hypovolaemic hypotension.

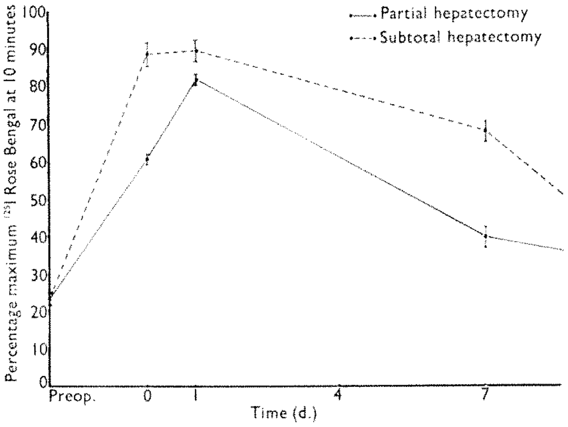

FIG. 4.—Percentage maximum counts 10 minutes after the injection of ^{125}I Rose Bengal in the pre- and postoperative period after two-thirds partial hepatectomy and subtotal hepatectomy.

Our experiments have shown that the metabolic changes after partial hepatectomy are related to the extent of liver resection. There is a well-recognized decrease in the serum levels of the total protein and albumin following partial hepatectomy in the rat (Chanutin, Hortenstine, Cole, and Ludwig, 1938; Bengmark, Olsson, and Rehnström, 1968). In our experiments the decrease in the serum levels of total protein and albumin was greater after subtotal hepatectomy than after two-thirds partial hepatectomy. A similar though less marked fall in the total serum-protein and serum-albumin levels occurred after laparotomy and ether anaesthesia alone. This latter finding suggests that the changes are at least in part related to the degree of stress to which the animal is submitted. However, it has been shown that there is a relative increase in the synthesis rate of albumin by the liver after partial hepatectomy but not following laparotomy (Chandler and Snider, 1970; Majumdar, Tsukada, and Lieberman, 1967). Other workers have demonstrated increases in protein synthesis 48 hours after partial hepatectomy (Schreiber, Urban, Zahringer, Reutter, and Frosch, 1971), and recent studies in our own laboratory have indicated an increase in protein synthesis within 12 hours of operation (Karran and others, 1972).

Elevation of the serum-alanine-transaminase level is thought to represent a reaction to acute cell injury (Wroblewski, 1959). We have shown that the rise in this enzyme is greater after subtotal hepatectomy. This may reflect the greater degree of cell injury in the remaining liver tissue after this operation as compared with the two-thirds partial hepatectomy. However, others have suggested that hypertransaminasaemia after liver resection may be related to increased pressure within the bile-ducts in the immediate postoperative period (Braun, Papp, and

Horvath, 1959; Almersjo, Bengmark, Hafstrom, and Olsson, 1969). We find this difficult to accept since T-tube drainage does not appear to affect the pressure within the biliary-duct system after experimental liver injury in dogs (Lucas, Lenaghan, and Walt, 1969). This observation does not, however, exclude a cholestatic effect at the canalicular level owing to hepatocyte engorgement or other factors.

Although McDermott, Greenberger, Isselbacher, and Weber (1963) reported a fall in the blood-sugar level after the resection of 70–90 per cent of the liver in man, neither Pack and Molander (1960) nor Lin and Chen (1965) found any significant change in the blood-sugar level of their patients. Similarly, Aronsen and others (1969) showed no change in the blood-sugar level after major hepatic resection. However, the latter authors administered large quantities of intravenous invertose during the postoperative period. Other workers have recently reported hypoglycaemia after liver resection for injury (Blumgart and Vajrabukka, 1972). In our experiments we noted a fall in the blood-glucose level during the first 24–48 hours after hepatectomy and this fall was significantly greater after subtotal hepatectomy. Similar findings have been reported by Weinbren and Dowling (1972). Although the low blood-sugar level found in the subtotally hepatectomized animals may reflect the effects of shock or liver hypoperfusion it is known that glycogen disappears from hepatocytes after partial hepatectomy (Harkness, 1957) and begins to reappear by about the twenty-fourth postoperative hour. Alterations in the energy metabolism in regenerating liver tissue have been reported (Simek, Chmelar, Melka, Pazderka, and Charvat, 1967) which may result in a decrease in liver-cell glycogen and a subsequent reduction in the reserve store for glucose. However, impaired gluconeogenesis may be equally responsible for the observed changes. We also noticed a slight fall in the blood-glucose level in the control animals. This may be the result of decreased food intake during the immediate postoperative period.

Weinbren and Billing (1956) have demonstrated a reduced capacity for the liver to clear a bilirubin load in the first 24 hours after two-thirds partial hepatectomy in the rat. They suggested that this was probably due to the loss of liver tissue and immaturity of the remaining liver cells during the early phases of the proliferative response. Despite this reduced capacity to clear bilirubin, we have shown no significant increase in the serum-bilirubin level after two-thirds partial hepatectomy. However, after subtotal hepatectomy there was a rise in the serum-bilirubin level which was maximal 24 hours postoperatively.

The delay in the blood clearance of B.S.P. and ^{125}I Rose Bengal immediately after operation is almost certainly related to the amount of liver tissue removed. It is of interest that there was an even greater delay in the blood clearance of both compounds 24 hours after operation and that the delay in the clearance of B.S.P. at this time was more marked in the subtotally hepatectomized animals. This delay, together with the reduced capacity of the partially hepatectomized liver to deal with bilirubin at this time, may reflect the inability of regenerating liver cells to excrete these substances. It is tempting to relate the delay in the proliferative response of the liver remnant after subtotal hepatectomy (Weinbren and Woodward, 1964) to similar causes.

The results of our investigations clearly show that the metabolic changes after liver resection in the rat are related to the amount of liver tissue removed. While the effects of liver resection in man may be influenced by pre-existing disease and by shock, due allowance should be made for the greater disturbance in metabolic function occasioned by the more extensive resections.

Acknowledgement.—This work was done with the aid of a grant from the Welsh Regional Hospital Board.

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THE LEUCOCYTE COUNT IN ACUTE APPENDICITIS

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SUMMARY

The leucocyte count was estimated in 100 consecutive cases of pathologically proved appendicitis. It is concluded that although a white-cell count below 10,000 per c.mm. does not exclude the diagnosis of acute appendicitis, such a result should prompt further review and consideration of the diagnosis.

IT has long been recognized that the white-cell count is elevated in acute appendicitis; however, little more precise information regarding the frequency and degree of elevation is available. This paper reviews the leucocyte count in 100 consecutive cases of pathologically proved acute appendicitis which were examined and operated upon by the author.

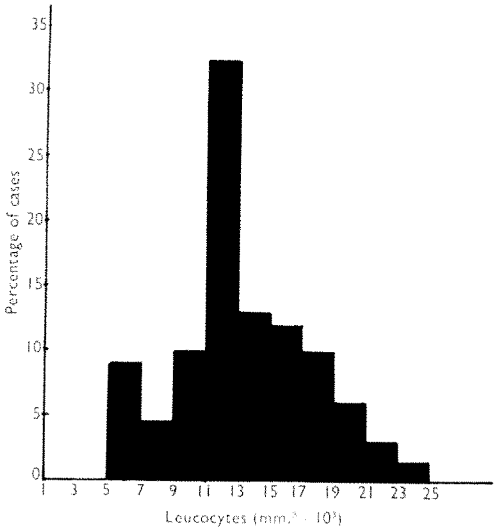

FIG. 1.—The leucocyte count in patients with acute appendicitis (100 patients).

MATERIAL AND METHODS

Over a period of 18 months, initially at the Royal South Hants Hospital, Southampton, and later at the General Infirmary, Leeds, a routine preoperative white-cell count was performed on each patient in whom the diagnosis of acute appendicitis was suspected. The leucocyte counts were performed by haematology technicians using a Coulter Cell Counter. The diagnosis of acute appendicitis was considered confirmed only when pathological examination of the removed appendix showed acute inflammatory changes. No attempt was made in this survey to correlate the level of the white-cell count with the degree of inflammation.

RESULTS

The ages of the patients ranged from 8 to 70 years and the white-cell count from 5500 to 23,500 per c.mm. Eighty-two of the patients (82 per cent) had a white-cell count of greater than 10,000. Of the remaining 18 per cent, 12 per cent had a count of between 9000 and 10,000. The distribution of the level of the white-cell count in the 100 patients is shown in *Fig.* 1.

DISCUSSION

Because of the wide variation in the range of the normal values of the white-cell count in healthy persons it is inevitable that some overlap will exist between the leucocyte counts of a group of healthy subjects and those of patients with acute appendicitis. However, 95 per cent of the population have a white-cell count of between 5000 and 10,000 (Hardison, 1968), and thus it is seen that the great majority of the patients with acute appendicitis in the present series had an appreciable rise in the leucocyte count.

The results of this series are comparable with those of the other reported series. Sasso, Hanna, and Moore (1970) showed a white-cell count of over 10,000 in 90 per cent of a series of 525 patients, whilst Lansden (1963) showed a significant leucocyte elevation in 84 per cent of 1000 cases of children with acute appendicitis. It is suggested that the routine white-cell count—a simple and non-time consuming investigation—is valuable in the assessment of a possible case of acute appendicitis.

Acknowledgements.—The author wishes to thank the Surgical Consultants at the Royal South Hants Hospital, Southampton, and at the General Infirmary, Leeds, for permission to study cases under their care.

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INTUSSUSCEPTION OF THE APPENDIX

BY R. H. L. DOWN AND T. BATES
LUTON AND DUNSTABLE HOSPITAL, BEDFORDSHIRE

SUMMARY

Two cases of intussusception of the appendix are reported. In both cases there was a palpable tumour within the caecum and a short thickened appendix. Both intussusceptions were predominantly mucosal and of a type not previously described.

INTUSSUSCEPTION of the appendix was first reported by McKidd in 1858 and since then about 130 cases have been recorded. The condition may mimic acute appendicitis or carcinoma of the caecum, but the diagnosis can only be made with certainty at operation.

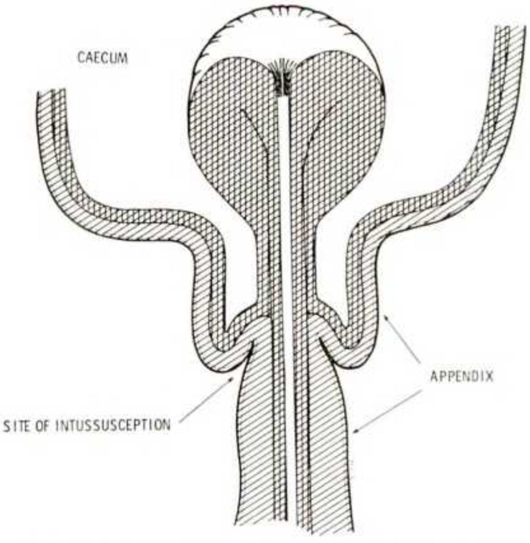

FIG. 1.—*Case* 1. Diagram of intussusception of the appendix. This shows that although there is a muscular intussusception the intracaecal tumour is oedematous intussuscepted appendicular mucosa.

McSwain (1941) described four types of intussusception of the appendix, but Paul and Ferraro (1967) modified this classification into five types. These may be simple or combined with intestinal intussusception. The great majority of cases are in fact inversion of the appendix (Jacobs, 1963) which may start at the tip of the appendix or at its base or may be complete. True intussusception, however, starts at a point between the tip and the base of the appendix, and the apex of the intussusceptum usually progresses proximally. The 2 cases reported here are of a type not previously described.

CASE REPORTS

Case 1.—A 23-year-old man presented in August, 1972, with a 10-hour history of vomiting and the sudden onset of severe pain in the right iliac fossa 2 hours before admission. There had been no previous abdominal pain or alteration in bowel habit. On examination there was marked localized tenderness in the right iliac fossa but no palpable mass.

At emergency operation through a gridiron incision a discrete polypoid tumour 2 cm. in diameter was palpable within the caecum. This arose from the base of the appendix which was thickened but not inflamed. It was subcaecal in position, 3·5 cm. in length, and had a thin mesentery. The tumour was recognized as an intussusception of the appendix and an attempt was made to reduce this by traction. A short segment of muscular intussusception was reduced 1 cm. distal to the base of the appendix. However, this did not appreciably change the size of the caecal tumour (*Fig.* 1). The greater part of the tumour was then expressed into the appendicular lumen where it was thought to be either excess mucosa or faeces. An attempt was made to carry out formal appendicectomy, but the muscle coat was so thick that the ligature slipped off and a tube of appendicular mucosa 1·5 cm. in length extruded from the stump. After excision of the redundant mucosa no residual tumour could be felt within the caecum and the appendix stump was ligated and inverted. The patient was discharged well on the fifth postoperative day.

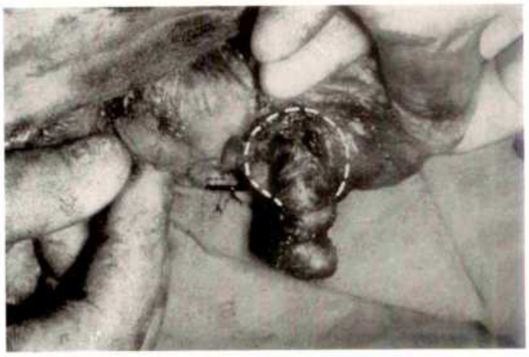

FIG. 2.—*Case* 2. Photograph of the short thickened appendix. The caecal tumour is outlined.

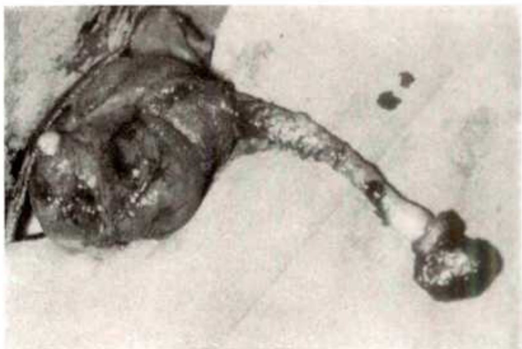

FIG. 3.—*Case* 2. Photograph showing the tube of appendicular mucosa that was reduced after division of the muscle coat of the appendix.

Histology of the appendix showed fibrous obliteration of the distal third of the appendix but a good lumen in the proximal portion, with marked muscular hypertrophy. The cuff of excised mucosa was oedematous.

Case 2.—A 27-year-old woman presented as an out-patient in May, 1969, with a recent history of severe cramping pain in the right iliac fossa lasting several hours. Physical examination was normal apart from some tenderness in the right iliac fossa. Interval appendicectomy was advised, but the patient became pregnant and the operation was postponed. She was seen again in August, 1971, having had six similar attacks of pain. On examination there was tenderness in the right iliac fossa but no palpable mass.

In October, 1971, an elective operation through a grid-iron incision was performed. There were adhesions surrounding the appendix which was not acutely inflamed but was only 2 cm. in length (*Fig.* 2). It was broad at the base and its mesentery was free of fat. There was a smooth firm mass 1·5 cm. in diameter palpable within the caecum adjacent to the base of the appendix which was thought to be a carcinoma. The incision was extended and the caecum was mobilized. It was then recognized that the tumour might be an intussusception of the appendix although the muscle coat did not appear to be intussuscepted. The muscle was circumcised near the base of the appendix and, by traction on the distal part, a tube of mucosa about 8 cm. in length was withdrawn (*Fig.* 3). As the mucosal intussusception was reduced the tumour within the lumen of the caecum became smaller and finally disappeared. Routine appendicectomy with inversion of the stump was then carried out. Postoperatively the patient made a good recovery and was discharged on the fifth postoperative day.

Histology of the appendix showed evidence of past inflammation with muscular hypertrophy. The tube of reduced mucosa was oedematous.

DISCUSSION

The diagnosis of simple intussusception of the appendix is rarely made preoperatively. Cases that present as an emergency are usually explored for acute appendicitis. Barium-enema examination may occasionally be diagnostic in those cases with recurrent attacks of pain (Skarby, 1941), but in the majority of cases the caecal filling defect is thought to be a carcinoma (Howard, Ellis, and Delaney, 1970).

The caecal tumour in both the present cases was oedematous intussuscepted appendicular mucosa. In *Case* 1 a true intussusception of the appendix was demonstrated, but in spite of fully reducing the muscular intussusception the mucosal intussusception remained palpable within the caecum. In *Case* 2 an extensive mucosal intussusception of the appendix was reduced. Although no muscular intussusception could be shown at operation this is suggested by the history of recurrent attacks of pain and the finding of a short thick appendix with a thin mesentery (Forshall, 1953). This type of predominantly mucosal intussusception has not previously been reported.

Various pathological factors have been suggested as the cause of appendicular intussusception, including roundworms (McKidd, 1858), mucocele (Morgan, 1937; Welch, Hellwig, and Foeneke, 1962; Mann, Wolf, and Greenblatt, 1964), endometriosis (Fink, Santos, and Goldberg, 1964; Howard and others, 1970), carcinoid (Hickinbotham, 1951) and lymphoid hyperplasia (Wakeley, 1939). However, Rolleston (1898) suggested that prolapse of the mucosa and subsequent intussusception may result from the appendix expelling a faecalith by peristalsis. This theory was based on the incidental finding at autopsy of a faecalith impacted within the appendicular mucosa which had prolapsed into the caecum. Although no faecalith was found in the present cases, Rolleston's suggestion that a faecalith initiated the intussusception is attractive. It is suggested that the attempt to extrude a faecalith produces mucosal oedema, which then acts as the apex of the intussusceptum once the faecalith has been expelled into the caecum.

Failure to recognize intussusception of the appendix at operation may result in caecotomy (Day, 1963; Howard and others, 1970) or right hemicolectomy (Campbell and McCormick, 1959; Weiner and Sala, 1962). Right hemicolectomy for this condition has been reported as a result of the use of a 'no-touch' technique, following a radiological diagnosis of carcinoma of the caecum (Howard and others, 1970). When a tumour is present within the caecum it is important to exclude intussusception of the appendix, since the correct management of this condition is reduction and appendicectomy.

Acknowledgements.—We wish to thank Mr. R. V. Fiddian for his encouragement and permission to publish details of patients under his care, and also Miss S. Dandre who drew the diagram, Mr. J. Harrison who produced the photographs, and Mrs. M. Parker for typing the manuscript.

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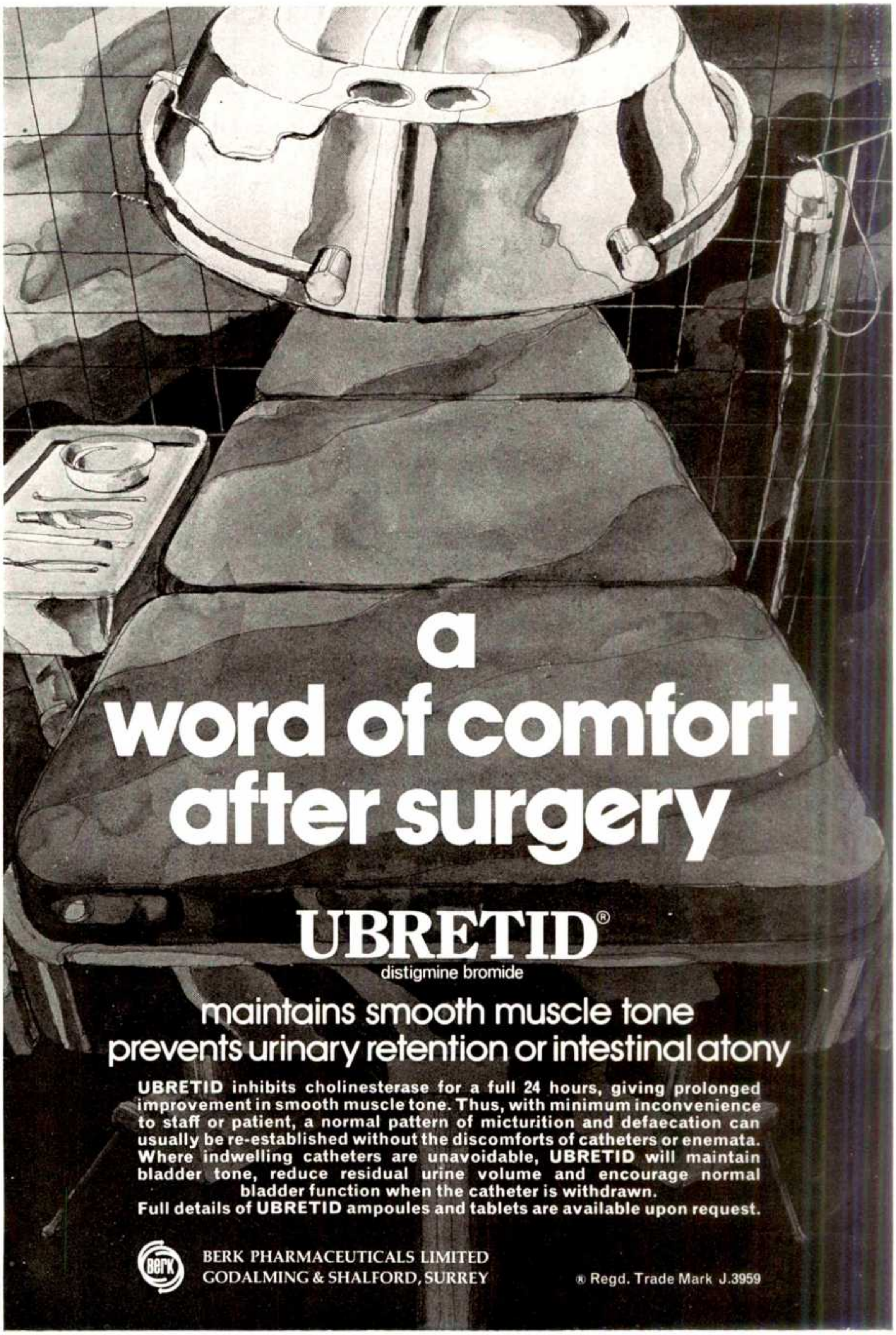

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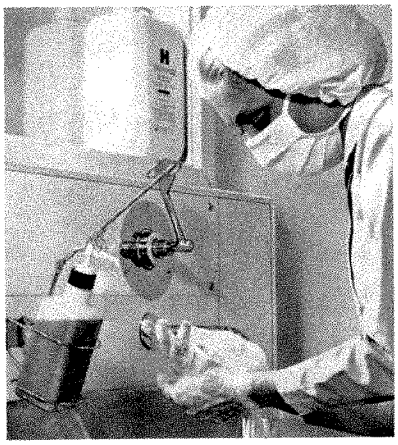

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AN UNUSUAL PRESENTATION OF GAS GANGRENE

By ALISTAIR FRASER-MOODIE*

ST. HELIER HOSPITAL, CARSHALTON, SURREY

SUMMARY

Gas gangrene is now uncommon in this country, particularly as a postoperative complication of elective abdominal surgery. A case of a patient who developed gas gangrene of the scrotum after a sigmoid colectomy for diverticulitis is described. A search through the relevant literature failed to reveal any similar cases.

CASE REPORT

A. M., a 69-year-old retired chauffeur, was admitted to St. Helier Hospital, Carshalton, on 11 Aug., 1970, for investigation.

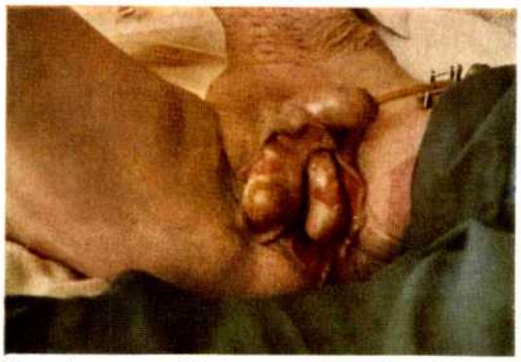

FIG. 1.—Appearance of the scrotum after extensive débridement and hyperbaric oxygen treatment.

He complained of a persistent ache in the lower left quadrant of his abdomen for several months which was relieved by passing wind or a motion. Previously he had opened his bowels daily, but now he strained a lot and only passed motions twice a week. Over a year he had lost 10 kg. in weight. He had been a mild diabetic for 20 years, but was well controlled on a low-carbohydrate diet.

On examination the patient had a palpable tender sigmoid colon. Sigmoidoscopy to 15 cm. showed no abnormality. A barium-enema examination demonstrated gross diverticular disease of the large bowel. The possibility of a carcinoma could not be excluded, and on 13 Sept. a laparotomy was performed after the bowel had been prepared with neomycin and phthalylsulphathiazole. Gross diverticulitis involving mainly the sigmoid colon with adhesions to the pelvic wall and bladder was found. Sigmoid colectomy was performed and a drain to the anastomosis was brought out through the abdominal wall. A right transverse colostomy was fashioned to protect the anastomosis.

Histological examination of the specimen confirmed the diagnosis of diverticulitis, and there was no evidence of malignancy.

The patient's postoperative course was uneventful for 10 days, apart from a mild chest infection which was treated with physiotherapy and ampicillin. However, on the tenth postoperative day he suddenly developed a pyrexia of 39·5 °C. He then experienced pain in his scrotum, which swelled up rapidly to the size of a cricket ball in the next 6 hours. By that time the soft tissues of his perineum were crepitant to touch, and finally two gangrenous areas appeared on his distended scrotum. The patient became confused and his general condition deteriorated rapidly.

A clinical diagnosis of gas gangrene of the scrotum and perineum was made and the patient was immediately transferred to Heatherwood Hospital, Ascot, for hyperbaric oxygen therapy. After 2 hours of hyperbaric oxygen treatment an extensive débridement was carried out under a general anaesthetic. All the offensive necrotic tissues of his scrotum and perineum were excised until healthy tissues were exposed, and the raw areas were left to granulate. From the excised tissues *Clostridium welchii* and *C. septicum* were cultivated anaerobically, and *Proteus vulgaris* with *Escherichia coli* aerobically.

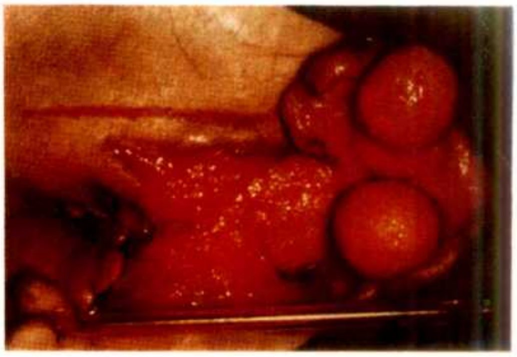

FIG. 2.—The scrotum and perineum after exploration of the wound. The catheter shown could be inserted 20 cm. into the abscess cavity.

He was treated four times a day with 2 MU. of benzyl penicillin for the anaerobic infection and 500 mg. of ampicillin for the aerobic infection.

The patient's general condition slowly improved with intensive nursing care and regular medical attention. Two-hourly hyperbaric oxygen treatments at 3 atmospheres pressure were continued twice a day for a week. Supportive measures included frequent hydrogen peroxide dressings, saline baths twice a day, and a blood transfusion of 4 pints. After 3 days cultures no longer grew anaerobic organisms and after 2 weeks the patient was transferred back to St. Helier Hospital (*Fig.* 1).

Here his nursing care was continued for a further 7 weeks as he was unable to look after himself. He became depressed by his long illness and regularly complained of pain in his perineum. Wound cultures only grew the same aerobic organisms, *E. coli* and *P. vulgaris*, both of which were sensitive to ampicillin, on which he continued throughout his illness. The edges of the wound healed slowly by granulation but there was a persistent offensive discharge, presumably from an intrapelvic source. Therefore on 8 and 22 Oct. the wound was explored under a general anaesthetic. On each occasion a huge pelvic abscess anterior to the rectum was laid open and drained. *Fig.* 2 shows a catheter which could be inserted 20 cm. into the cavity.

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After the last anaesthetic the patient's condition gradually deteriorated again. He became disorientated with a high swinging temperature. The pain was now severe in his right thigh, and radiographs showed small gas bubbles which were not evident clinically (*Fig.* 3).

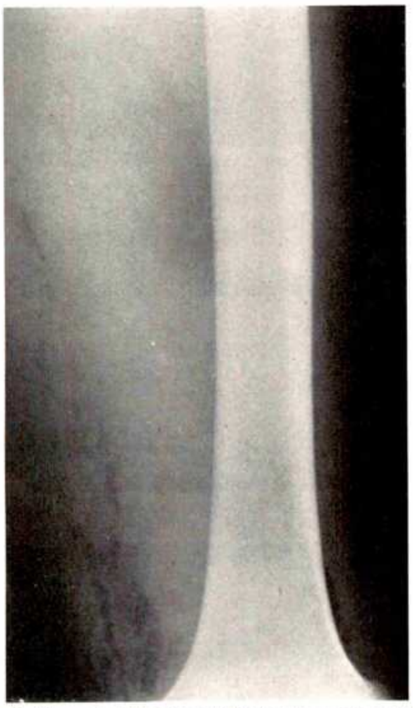

FIG. 3.—Radiograph of the right thigh showing small gas bubbles.

On 2 Nov. the patient was transferred back to Heatherwood Hospital. On admission the whole of his right thigh was crepitant to touch, with gangrenous areas below the knee. Massive doses of benzyl penicillin and frequent hyperbaric oxygen treatments were recommenced but he died within 48 hours.

No post-mortem was carried out.

DISCUSSION

The clostridial organisms probably originated from the patient's own bacterial flora—an auto-infection. This elderly diabetic was particularly susceptible to gas gangrene after a bowel resection for several reasons. There may well have been a poor circulation to the anastomosis, with areas of necrotic tissue and a weakened inflammatory response systemically. The large-bowel anastomosis leaked, giving rise to the huge pelvic abscess that was drained twice.

Clostridial organisms frequently inhabit the alimentary tract and are readily recoverable from the faeces (Sterne and Von Huyningen, 1958). The antibiotic bowel preparation offered little resistance to clostridia and so these organisms could reach the perineum and scrotum directly from the bowel. The air of operating theatres has in the past been shown to contain the spores of these organisms, indicating another possible source of infection (Lowbury and Lilly, 1958).

The patient died 2 months after the original operation for diverticulitis from gas gangrene of the right leg as a result of the spread of residual organisms inside the pelvis through the thigh muscles. These organisms can remain dormant in a wound for many years before a patient develops gas gangrene (Hendry, 1930). Once established, the infection can spread quickly through healthy muscle, but always in the direction of the fibres (Anderson, 1967).

In the present case *E. coli* and *P. vulgaris* were cultivated from the wound throughout the patient's illness. Aerobes and anaerobes act together to digest protein most effectively—an example of bacterial synergism (Meleney, 1931).

A review of 7 cases of gas gangrene of the scrotum and perineum showed this condition to be 'a distinct complication of perianal abscesses and fistulae' (Himal and Duff, 1967).

Gas gangrene of the thigh owing to the spread of infection from an intra-abdominal source has rarely been reported. The sources in cases recorded in the literature were: from an appendix abscess (Gordon, 1936); from diverticulitis (Dawson and Fiardy, 1948; Nichols, 1961); from a carcinoma of the colon (Wyman, 1949).

Few bacterial infections are so virulent and in the present case prompt recognition and treatment were not enough. Perhaps intramuscular penicillin cover throughout the operation would have prevented gas gangrene. There was, however, no indication for this preoperatively.

This case serves as a reminder of this terrifying condition, as gas gangrene remains a constant threat to the safety of surgical patients, striking unexpectedly, even after elective surgery.

Acknowledgement.—I should like to thank Mr. B. P. Flannery, F.R.C.S., Consultant Surgeon, St. Helier Hospital, Carshalton, for allowing me to publish this case.

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THE SURGICAL MANAGEMENT OF AMOEBIASIS IN CHILDREN

BY LEWIS SPITZ

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SUMMARY

Five children with severe complications of acute amoebic dysentery are described. The results of a simple defunctioning proximal ileostomy are encouraging. Prior administration of anti-amoebic therapy and postoperative intensive medical care are mandatory for a successful outcome.

CONSERVATIVE medical measures are usually sufficient for the successful management of patients suffering from severe amoebiasis. However, complications such as acute intestinal perforation, which is a relatively common occurrence in children (MacDougall, 1960), complete intestinal obstruction, and rupture of an hepatic or pulmonary abscess develop in an estimated 0·5 per cent of dysenteric cases (Wray, Stark, Brackney, and Moretz, 1964). In such cases the clinician is confronted with the choice between continued medical therapy and surgical intervention in a severely debilitated child. Both these courses are accompanied by an extremely high mortality-rate (Wijesundera and de Silva, 1962; Grigsby, 1969).

Table I.—DETAILS OF THE CASES IN THE PRESENT SERIES

CASE	AGE AND SEX	DIAGNOSIS	INDICATION FOR SURGERY	OPERATIVE PROCEDURE	SUBSEQUENT COURSE	RESULT
1. J. R.	5 yr. M.	*E. histolytica* in stool	Acute intestinal perforation	Terminal defunctioning ileostomy	1. Intractable post-amoebic ulcerative colitis with strictures 2. Colectomy and ileorectal anastomosis	Alive and well
2. F. M.	3 yr. 7 mth. F.	Stools negative Latex C.F.T. positive	Rupture of liver abscess Acute toxic megacolon	1. Drainage of liver abscess 2. Terminal defunctioning ileostomy	1. Complete resolution 2. Closure of ileostomy	Alive and well
3. P. M.	2 yr. 3 mth. F.	Stools negative Latex C.F.T. positive	External intestinal fistula with distal obstruction	1. Subtotal colectomy 2. Ileostomy	Ileosigmoid anastomosis	Alive and well
4. A. M.	2 yr. 6 mth. M.	Stools positive Latex C.F.T. positive	Intestinal obstruction	Terminal defunctioning ileostomy	1. Intractable post-amoebic ulcerative colitis with strictures 2. Colectomy and ileorectal anastomosis	Alive and well
5. D. M.	1 yr. 3 mth. M.	Stools negative Latex C.F.T. positive	Intestinal obstruction	Right transverse colostomy	1. Intractable post-amoebic ulcerative colitis with strictures 2. Colectomy and ileorectal anastomosis	Alive and well

This report documents the successful surgical management of 5 young children with life-threatening complications of amoebiasis at Baragwanath Hospital in the period from April, 1971, to November, 1972.

CLINICAL CASES

The 5 children varied in age from 15 months to 5 years.

All 5 patients were severely toxic and dehydrated on admission. Anti-amoebic and antibiotic therapy was commenced from the outset on the clinical diagnosis of amoebiasis, which was subsequently confirmed by laboratory investigations (*Table I*). *Cases* 1 and 2 developed complications early in the course of the disease. The first case developed an acute perforation of the transverse colon, for which a simple defunctioning ileostomy was performed. Rupture of an extensive right hepatic abscess and toxic megacolon occurred in the second child. A defunctioning ileostomy was created and the liver abscess was evacuated of 800 ml. of purulent material by means of an indwelling catheter (*Fig.* 1). Three months later, following complete resolution of the pathological process, the ileostomy was closed. *Case* 3 developed an external intestinal fistula at the umbilicus after 2 months of intensive medical therapy. Owing to the persistence of distal obstruction it failed to close on conservative treatment. Laparotomy revealed a perforation of the caecum with a fistulous tract to the umbilicus. The transverse colon was extensively strictured. A subtotal colectomy and defunctioning ileostomy were performed. In *Cases* 4 and 5 extensive stricture formation of the colon resulted in complete intestinal obstruction after many weeks of medical therapy. Because of severe debility in both cases, simple defunctioning proximal enterostomies were performed.

The early postoperative course was extremely stormy in all the cases. Aggressive antibiotic therapy, intravenous alimentation, and general intensive care were required.

Severe intractable post-amoebic ulcerative colitis, necessitating subtotal colectomy and ileorectal anastomosis, developed in 3 of the 4 cases in which the colon was left in situ (*Cases* 1, 4, and 5; *Figs.* 2 and 3). All the children are now alive and free of the disease.

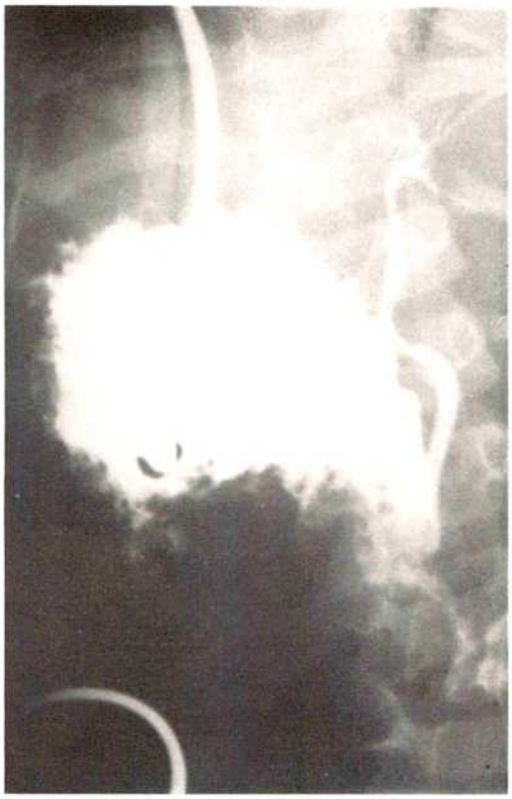

FIG. 1.—*Case* 2. Sinogram showing a large right hepatic abscess cavity with free drainage into the biliary system.

DISCUSSION

Pathology and Pathogenesis.—*Entamoeba histolytica* produces lesions of the colonic mucosa by a process of active locomotion and by the secretion of a cytolytic substance. The pathological process is usually confined to the mucosa and submucosa. Penetration of ulcers into the muscular wall of the intestine is rare and usually slow, with serosal inflammation encouraging adhesions to adjacent viscera and omentum. Perforation occurs most frequently in the caecum, ascending colon, and rectosigmoid (Keen, Gilmore, and von Stone, 1956) and is commonly extraperitoneal or into an area sealed by adhesions. Amoebic abscesses may follow retroperitoneal colonic perforations, and occasionally internal or external fistulas develop (Dinner and Bader, 1961). Intraperitoneal perforation with generalized peritonitis carries a high mortality-rate, especially in children (Wijesundera and de Silva, 1962; Powell and Wilmot, 1966b; Raffensperger, Szanto, Saunders, and Woodward, 1967).

Strictures result from ulceration of the intestinal wall with subsequent scarring. The stenotic area may be narrow or broad and most frequently involves the ascending colon and rectosigmoid regions.

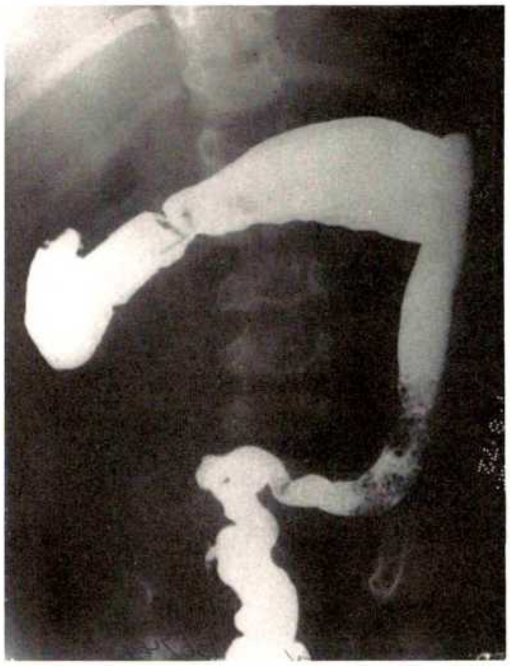

FIG. 2.—*Case* 4. Barium-enema film showing a blind fistulous tract in the mid-rectum, loss of haustral pattern, and stricture formation.

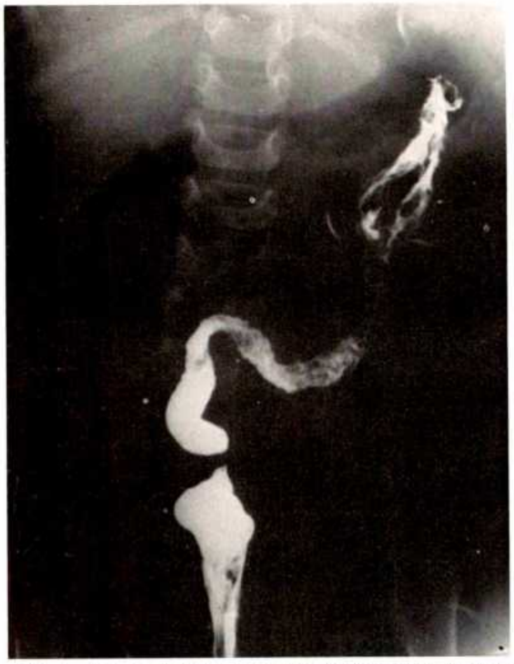

FIG. 3.—*Case* 5. Barium-enema film showing a stricture in the lower rectum and extensive pseudopolypi formation in the distal colon.

Multiple strictures are occasionally encountered in chronically infected patients. The majority of stenoses resolve on amoebicides and antibiotics (Turner, Lewis, Hayes, and Ziment, 1971).

The development of post-amoebic ulcerative colitis is almost entirely confined to patients with severe amoebic dysentery (Bank, Burns, Marks, and Stein, 1971). The severity is related to the degree and extent of the initial damage to the bowel wall (Powell and Wilmot, 1966a). Strictures are common. The course of most cases is that of slow progressive improvement. A few cases experience a steady downhill course, and for them colectomy may be indicated on the basis of intractability (Stein and Bank, 1970).

Diagnosis.—The most common presenting feature in children with severe amoebiasis is bloody mucous diarrhoea, accompanied by oedema and corrugation of the rectal mucosa. Sigmoidoscopically, the colonic mucosa is ulcerated and friable. Confirmation of the clinical diagnosis requires the demonstration of *E. histolytica* by microscopic examination of the stools, rectal scrapings, or rectal biopsies. Failing this, the latex complement-fixation test should be carried out.

Treatment.—In acute amoebic infection the need for initial intensive anti-amoebic and antibiotic chemotherapy cannot be emphasized too strongly. These drugs should be commenced immediately the clinical diagnosis is made (Rives, Heibner, and Powell, 1955; Pelàez, Villazòn, and Zaraboso, 1966). The worst therapeutic failures occur in patients in whom the amoebic cause remains unrecognized and in whom surgical treatment is undertaken without the prior administration of amoebicidal drugs (Chen, Chen, and Lin, 1971). Continued conservative medical management in the presence of life-threatening complications such as intestinal perforation with generalized peritonitis, intestinal obstruction, or fulminating amoebic colitis with toxic megacolon carries a high mortality. Only 5 of Barker's (1958) 19 patients with colonic perforation survived therapy. In the series of Powell and Wilmot (1966b) of 75 patients with generalized peritonitis complicating severe amoebic colitis who were treated conservatively only 44 patients survived when the onset of peritonitis was slow and insidious. In patients with established peritonitis on admission or with the rapid onset of peritonitis the outcome was almost invariably fatal, especially in childhood. Emergency surgical intervention should be strongly considered when general and abdominal signs deteriorate markedly after 24–48 hours of intensive anti-amoebic therapy or in the presence of an acute episode such as an acute intestinal perforation or sudden increase in abdominal distension (Stein and Bank, 1970). The poor general condition of these patients is not conducive to extensive surgical procedures, such as colectomy. A proximal defunctioning ileostomy (Theron, 1947; Rives and others, 1955; Stein and Bank, 1970) is a life-saving procedure in children when combined with aggressive anti-amoebic and antibiotic chemotherapy, prolonged intravenous alimentation, and general intensive care.

The development of intractable post-amoebic ulcerative colitis with severe stricture formation necessitated subsequent subtotal colectomy in 3 of the 4 cases in whom the colon was left in situ, indicating the extreme degree of the initial pathological process.

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CHOLEDOCHOSCOPY IN CHOLEDOCHOLITHIASIS

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SUMMARY

Stones are overlooked in the bile-ducts during operations for gall-stones sufficiently often to pose a continuing problem. The choledochoscope, first described 50 years ago, has recently been developed to a degree which makes it valuable in locating common-duct stones, besides permitting observation of changes in the ducts which are not otherwise demonstrable.

At 37 duct explorations, among a total of 135 gall-stone operations, endoscopy was found valuable in clarifying equivocal pre-exploratory cholangiograms, or on occasion taking their place, and in detecting stones not removed using the usual methods of detection. It is suggested that endoscopy is quicker and more readily repeatable than post-lithotomy cholangiography, is unaffected by bubbles entering the duct system, and avoids exposure of staff and patient to X-rays. However, it should be used in conjunction with pre-exploratory cholangiography.

THIS communication is based on the findings at operations for gall-stones at which a flexible fibre-optic choledochoscope was used to examine the interior of the extrahepatic bile-ducts.

CHOLEDOCHOSCOPES

There has never been a widespread demand for a choledochoscope, probably because unlike other endoscopes its use must be confined to peroperative endoscopy.

The first choledochoscope, virtually a speculum, was described by Bakes of Brno in 1923. The next instrument, a modified angled cystoscope, appeared in 1942 (McIver, 1942). The most widely employed rigid instrument was that of Wildegans of Berlin; this choledochoscope underwent considerable development allowing the use of instruments for biopsy and diathermy (Wildegans, 1958). Reports from a number of countries in Europe and America describe some hundreds of endoscopies with this instrument almost without incident; the reports are generally favourable to its use and suggest that it should take over part of the role of the cholangiogram (Wildegans, 1958; Griesmann, 1959; Jelink, 1959; Brocks, 1960; Shore and Lippman, 1962; Schein, 1969.)

The first flexible fibre-optic instrument appeared from the American Cystoscope Manufacturers Inc. in 1965 and is the instrument used in this series. It has a length of 50 cm. and a diameter of 6 mm. The eye-piece is adjustable for the individual eye, and a focusing device allows sharp definition of objects up to contact with the objective lens. The instrument is sterilized in ethylene oxide gas, and for use is attached to a light source and a supply of sterile saline which passes through an irrigation channel to wash out and fill the ducts. A teaching attachment allows a second viewer to watch the field under view, but there is no channel for instruments.

It is a straightforward matter to insert the illuminated endoscope upwards through the usual choledochostomy to and beyond the confluence of the left and right hepatic ducts which is marked as a rule by a carina-like eminence; beyond it secondary branchings may be seen. To enter the lower duct the instrument must be bent into a U-shape, and insertion is sometimes impeded by the overhanging ribs. The bend through 180° has the effect of reversing the direction of apparent movement of the object in the vertical axis which has to be allowed for in manipulating the viewing tip to scan the interior of the lower duct. The sphincter can usually be brought into view and the whole common duct thus examined. Thorough irrigation and a clear viewing medium are as essential as in cystoscopy.

THE PRESENT SERIES

In this series of gall-stone cases there were two main indications for choledochoscopy: to look for residual stones after choledocholithotomy before concluding the operation, and to explore ducts which have been opened for possible stones on indirect evidence without any having been demonstrated by palpation or radiography.

No complications were met and sepsis has not increased as a result of choledochoscopy; no special precautions were observed. The patients ranged in age from 19 to 74 years, with a mean of 55 years; there was no mortality.

Choledochoscopy was carried out at 37 operations on 35 patients among a total of 135 operations for gall-stones (27 per cent of operations). Stones were found in the ducts on 26 occasions in 24 patients; no stones were present in the remaining 11 ducts.

At 24 of the operations when stones were present as many of the stones as possible were first removed by the customary blind techniques; only afterwards was the choledochoscope inserted to search for more stones. Endoscopy used in this way has been classified as 'post-lithotomy' choledochoscopy. At the other 13 operations the uses made of endoscopy varied and have been classified as 'exploratory' choledochoscopy. This group includes the 2 remaining duct-stone cases; in both these cases post-lithotomy choledochoscopy was not employed because sphincterotomy was required to extract the stones and this was adequate to allow the passage of any stones which might have been missed.

POST-LITHOTOMY CHOLEDOCHOSCOPY

At the 24 operations in this group choledochoscopy was carried out after stones had been removed from the ducts. Signs of residual stone were seen in 11 instances (46 per cent), and the ducts appeared clear of stones in the other 13. In the latter cases the operation was terminated and a T-tube was inserted on 12 occasions; in 1 case a choledochoduodenostomy was substituted because of gross dilatation of the duct.

When residual stones were seen efforts were made to remove them with the help of repeated choledochoscopy, until either the duct seemed clear of stones or any in view could not be retrieved, as was the case in 2 patients with stones lodged in hepatic ducts. Though more have been needed, one or two reinsertions of the choledochoscope usually sufficed in the search for and the removal of residual stones, after which the operation was terminated with the insertion of a T-tube in 8 cases. In 3 cases, when stones could not be removed or permanent drainage was needed, a choledochoduodenostomy replaced the T-tube.

Thus, there were 20 patients with T-tubes available for postoperative cholangiograms, and in *Table I* the choledochoscopy findings for these patients are compared with the cholangiograms. The 4 patients with choledochoduodenostomies are excluded.

Table I.—CHOLEDOCHOSCOPY FINDINGS COMPARED WITH THE POSTOPERATIVE CHOLANGIOGRAM IN 20 PATIENTS IN THE POST-LITHOTOMY GROUP

CHOLEDOCHOSCOPY FINDINGS		POSTOPERATIVE CHOLANGIOGRAM	
		No Stone	Missed Stone
Ducts clear	12	11	1
Residual stones seen and removed	5	4	1
Residual stones suspected —not removed	3	0	3
Total 20	20	15	5

Table I shows that at 12 endoscopies the ducts appeared clear after the initial removal of stones, but the subsequent cholangiograms indicated that stones had been missed in 1 patient. Reoperation was required, when the missed stones were easily seen with the endoscope; they were removed and a choledochoduodenostomy was constructed. At 5 endoscopies residual stones were seen after the initial removal; following further removals and repeat choledochoscopies the ducts appeared clear. However, the postoperative cholangiograms showed that yet more stones had been missed in 1 patient. Again, stones were visualized by endoscopy at reoperation in this patient, but one of the stones could not be extracted and a choledochoduodenostomy was performed. At the remaining 3 operations residual stones were thought to have been seen by choledochoscopy after the initial removal. Two of these were the first 2 endoscopies of the series, and in both cases further exploration failed to retrieve any more stones; accepting this, the endoscopic appearances were ascribed to debris and not to compact stone. The operations were consequently terminated, only to have the endoscopic impression confirmed by the postoperative T-tube cholangiograms. Similar appearances suggestive of stone were encountered at a third and later operation; therefore before closing the abdomen a T-tube cholangiogram was performed which, however, did not confirm the presence of a residual stone; nevertheless, the postoperative cholangiogram a week later revealed a missed stone. In each of these 3 patients the missed stones were small and single and were later passed spontaneously without secondary operations; they were partly concealed from the view of the endoscope in the lower duct by webs of fibrin.

EXPLORATORY ENDOSCOPY

Pre-exploratory cholangiography was employed in most of the 13 patients in this group. Endoscopy was performed to clarify, or in a few instances to replace, cholangiography.

In 3 patients the cholangiograms were normal, but because of preceding jaundice or pancreatitis the ducts were opened. However, endoscopy showed no signs of stone. In 2 patients stones were demonstrated by the cholangiograms and endoscopy followed. One of these patients had previously undergone choledocholithotomy without endoscopy; it was of interest that the stones missed at the previous operation were readily seen with the endoscope and duly removed through a transduodenal sphincterotomy. In the other patient a stone thought to have been shown in the ampulla on the cholangiogram could not be confirmed visually, the lower duct being poorly seen. However, the ampulla was approached transduodenally and after division a stone was found and removed.

In the remaining 8 patients pre-exploratory cholangiograms were either of dubious significance because contrast material did not enter the duodenum or were of poor quality or were not available. There were indications for opening the ducts in each case. No stones were seen. Postoperative T-tube cholangiograms were available for all 13 patients and confirmed the absence of stones in each.

Among the 4 patients with sphincters impermeable to contrast medium, 1 was seen to have a mild cholangitis probably associated with recent pancreatitis, and another, shortly after an attack of severe colic, showed haemorrhages at the sphincter, the damage presumably being due to the passage of a stone.

Endoscopy before removing stones did not provide additional diagnostic information in the 5 patients in whom the cholangiograms were normal or showed stones. However, in the remaining 8 cases, when cholangiography alone was inconclusive or not available, endoscopy not only resolved the question of the presence or absence of stone but also showed inflammatory and traumatic consequences of preceding events which were otherwise not demonstrable.

DISCUSSION

Though choledochoscopy is not limited to searching for duct stones this is its major function. Pre-exploratory cholangiography provides the best means of ascertaining whether there are stones in the intact duct system, but it can by no means always indicate their number. Indeed, how to ensure that ducts are completely cleared of multiple stones remains a major problem in gall-stone surgery; to achieve it can tax technique to the limit.

In the present series choledochoscopy undoubtedly reduced the number of duct stones which were missed. In the group of 11 ducts in which residual stones were seen by post-lithotomy choledochoscopy, the remaining stones were removed in 4 cases and choledochoduodenostomies were provided to facilitate the escape of stones in 3 other cases. Of the remaining 4 cases in which mainly small stones were left in the ducts, it can safely be said that with greater experience of endoscopy there would have been fewer errors, bearing in mind that the first 2 endoscopies of the series contributed 2 of the missed stone cases and that signs of stone were seen in 3 of the 4 cases.

Two secondary operations were required among 24 patients with duct stones who had endoscopy at the primary operation (8 per cent). They are equivalent to 1·5 per cent of the 135 operations for gall-stones carried out during the period reviewed. This compares with 3 per cent of secondary operations for missed stones found by Glen (1972) among all operations for benign biliary disease.

Table II summarizes the findings for the whole series of 37 endoscopies in relation to locating stones. There were no false-positive findings in ducts shown to be free of stones by subsequent cholangiography.

Table II.—RESULTS OF ENDOSCOPY IN 37 OPERATIONS

Presence of Stones in Duct	*No. of Operations*	
Present	26	False negatives 6
Not present	11	False positives 0

False-negative findings, i.e., stones missed, are known to be 5 from the post-lithotomy group and 1 from the exploratory group of choledochoscopies, making a total of 6 in 26 endoscopies, which is a rather high figure. If the first 2 endoscopies are excluded because of lack of experience, the number of false negatives becomes 4 of 24 examinations of ducts in which stones were certainly present, an incidence of 17 per cent. In fact, a poor view was obtained in 1 of these 4 cases, and a stone consequently not seen by endoscopy but shown by the preliminary cholangiogram was successfully removed. The two investigations are complementary and neither should be considered entirely in isolation; however, good visualization steadily becomes easier to achieve and in consequence the number of false negatives should decrease.

Operative cholangiography after stone removal and before closure of the abdomen offers a means of assessing clearance of the ducts. Compared with radiography choledochoscopy is quicker, much more readily repeatable, and introduces no radiation hazard to the patient or the staff. Furthermore, after removing stones and dilating the sphincter, bubbles entering from the duodenum or through the T-tube may cause real difficulty in interpreting the radiographs but they do not affect the endoscopic interpretation.

It is well recognized that practice is necessary to interpret appearances and to obtain useful information by endoscopy of any kind. The problem for choledochoscopy in this respect is a real one because individual surgeons are likely to use it sporadically (in this series it was used in about 1 in 4 operations for gall-stones). Undoubtedly simulation could be employed to remedy this failing, using suitable tubes as ducts and photography to portray normal and abnormal appearances. Important points in relation to stone are the inflammatory changes which are often present, including fibrin strands and veils sometimes tinged here and there with yellow. They may readily conceal small stones. Again a small free-floating stone may only be glimpsed as it moves along a wide duct in the stream of irrigating fluid. The cholesterol stone appears bright yellow in the strong illumination and anything with this colouring needs close scrutiny; a well-defined edge marks it as a stone which if only seen briefly warrants a careful continuing search.

The fibre-optic flexible choledochoscope is undergoing further development, and a model incorporating useful advances and excellent vision is already available from Japan. The endoscope seems likely to find a specific place in the armamentarium of biliary surgery, for though expensive and requiring care in handling and maintenance its use can contribute much to the difficult problem of avoiding secondary operations for duct stones.

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DIAGNOSTIC YIELD OF FIBRE-OPTIC ENDOSCOPY IN THE OPERATED STOMACH

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SUMMARY

Fibre-optic instruments have been used on 212 occasions to examine 177 patients who were symptomatic after peptic ulcer surgery. A diagnosis other than gastritis was reached in 83 patients, including 46 ulcers. Five ulcers were not seen—4 as a result of using inadequate equipment early in the series. Radiology detected only 60 per cent of the ulcers and raised many false-positive diagnoses. Expert review of the radiographs corrected many originally mistaken interpretations. Retained suture materials were seen by endoscopy and removed using biopsy forceps. Gastric mucosal congestion and gastritis were common in the operated stomach, but the clinical significance of these changes remains obscure in the absence of a control series. Fibre-optic endoscopy is now an essential part of the investigation of patients who are symptomatic following ulcer surgery.

WHILST most operations for peptic ulcer are successful, up to 20 per cent of patients remain symptomatic and about 5 per cent develop recurrent or anastomotic ulceration (Goligher, Pulvertaft, Irvine, and others, 1972). The diagnosis and management of these patients can prove difficult. The patient whose symptoms return unchanged shortly after a vagotomy and drainage operation for a duodenal ulcer is very likely to harbour a recurrence. However, all too often the symptoms are atypical and the history is distorted by previous surgery and experience. Acid studies may be helpful but in themselves cannot prove the presence or absence of ulceration. Properly performed insulin testing is a reliable guide to the completeness of vagotomy, but the collection of acid in patients who have undergone partial gastric resection may be difficult and the results unreliable (Baron, 1970; Scobie and Rovelstad, 1965). Radiology of the operated stomach can be equally difficult (Fawcett, Johnston, and Duthie, 1969; Kim and Evans, 1959). Although a stomal or recurrent ulcer can sometimes be shown unequivocally, surgical distortion frequently reduces the confidence of the radiologist in diagnosing or excluding an ulcer. The large folds of a pyloroplasty or around a gastrectomy stoma produce confusing radiological appearances.

Fibre-optic endoscopes have come into routine use for examination of the oesophagus, stomach, and duodenal bulb. The latest instruments are well suited to the difficulties encountered in the distorted stomach, providing extreme flexibility and manœuvrability, with good suction, biopsy, and washing facilities (Cotton and Williams, 1972). In a total experience of over 2000 endoscopies we have been impressed by the diagnostic yield obtained in many patients with symptoms following ulcer surgery. The results of a small series are presented here.

PATIENTS AND METHODS

Two hundred and twelve examinations have been performed in 177 patients who were symptomatic following a variety of operations for peptic ulceration (*Table I*). The time intervals from the original operation to endoscopy were: partial gastrectomy, 2–42 years (mean, 11 years); vagotomy and pyloroplasty, 2 months to 12 years (mean, 4 years); vagotomy and gastro-enterostomy, 1–23 years (mean, 10 years).

Table I.—PREVIOUS OPERATIONS PERFORMED IN THE PATIENTS EXAMINED

PREVIOUS OPERATION	NO. OF EXAMINATIONS	NO. OF PATIENTS
Partial gastrectomy		
Polya	83	72
Billroth-I	16	14
Vagotomy and pyloroplasty	69	61
Vagotomy and gastro-enterostomy	28	17
Other	16	13
Total	212	177

Five symptom groups were distinguished: 48 patients had 'typical' dyspepsia (discomfort with a definite relation to food with relief being obtained from alkalis); 75 patients had less well-defined abdominal discomfort, including atypical pains and vomiting; 18 patients complained mainly of heartburn, 17 patients presented with acute gastro-intestinal bleeding; 19 patients had iron-deficiency anaemia.

Examinations were mainly performed on out-patients using a local anaesthetic throat spray and intravenously administered atropine, 0·6 mg., and diazepam, 5–30 mg. The aim was to examine the entire oesophagus and stomach and the proximal duodenum and/or jejunal loops in every patient. The oesophagus could not be examined early in the series when only a lateral-viewing gastroscope was available. Olympus models GFB and GFBK were used alone on 26 occasions. Forward-viewing oesophagogastroduodenoscopes were used 166 times (American Cystoscope Makers Models 7089, 7089A, 7089J, 7089P on 111 occasions, and Olympus Model GIFD on 45 occasions), supplemented at the same examination of 31 patients by the use of the lateral-viewing Olympus JFB duodenoscope. This instrument was used alone on a further 20 patients. Follow-up information at 6–36 months was obtained by examination of the patients' records.

RESULTS

Examinations were satisfactorily completed in all the patients without complications. Twenty patients underwent repeat examinations (1 case on 9 separate occasions). *Table II* lists the diagnosis reached by endoscopy in 83 patients. No diagnosis (apart from gastritis, discussed below) was made at the time of endoscopy in the remaining 94 patients; for 84 of the latter group, adequate follow-up information was available. Seven lesions which were missed by endoscopy have subsequently been discovered: 3 recurrent duodenal ulcers after pyloroplasty (while no duodenoscope was available), 2 gastric cancers (1 beyond a mid-gastric stenosis, and 1 diagnosed visually and on biopsy as a benign gastric ulcer), 1 anastomotic ulcer (bleeding profusely), and 1 gastric ulcer in a deep pit near a gastrectomy stoma. In another 11 patients symptoms have been explained by a lesion outside the oesophagus, stomach, and duodenum: pancreatic cancer (1), gall-stones (2), jejunal adhesions (5), colonic cancer (3). Of the remaining 66 patients, 49 are apparently well or much improved, 7 are receiving psychiatric treatment, and 10 continue to complain of disabling but often atypical symptoms (3 having undergone negative laparotomies).

Table II.—ENDOSCOPIC DIAGNOSES (EXCLUDING GASTRITIS) IN 177 PATIENTS

Diagnosis	*No. of Cases*
Oesophagus	
Oesophagitis	12
Varices	1
Web	1
Cancer	1
Stomach	
Cancer	5
Ulcer	7
Erosions	4
Metaplastic polyp	3
Bezoar	1
Anastomosis	
Ulcer	12
Ulcer and suture	7
Suture	4
Stenosis	4
Duodenum	
Ulcer	19
Ulcer and suture	1
Suture	1
Total	83

Comparison with Radiology.—Forty-six out of the known total of 51 ulcers were visualized by endoscopy. *Table III* provides a comparison with radiology in ulcer diagnosis. Thirty-nine of the known ulcer patients underwent barium-meal examination within 3 weeks of endoscopy; ulcers were diagnosed in only 23 cases (i.e., 40 per cent were missed). In 18 other patients from the whole series ulcers were suspected radiologically (with varying degrees of confidence) which were not confirmed by endoscopy or subsequent follow-up. Six out of 7 gastric cancers were diagnosed from the barium-meal examination but the 1 small oesophageal cancer was missed. In 8 other patients radiology incorrectly raised the possibility of malignancy, usually near a gastrectomy stoma.

A total of 109 barium-meal examinations was reviewed without knowledge of the clinical status by two radiologists with particular interest in gastro-intestinal diagnosis. Ten out of 22 previously false-positive or false-negative reports of ulcer or tumour were corrected. Hiatus hernia and/or oesophageal reflux was seen radiologically in 10 of the 12 patients shown endoscopically to have oesophagitis; by contrast oesophagitis was not apparent endoscopically in 4 other patients with radiological evidence of hiatus hernia. Barium-meal examinations did not detect erosions, small metaplastic polyps, or retained suture material.

Retained Suture Material.—Twenty-eight sutures were seen endoscopically in 13 patients, in 8 of whom the sutures were closely associated with ulcers at the suture line. Retained sutures were discovered at 1, 2, 12, and 16 years after gastro-enterostomy, 3 months, 1, 2, 2, 2, and 3 years after pyloroplasty, and 1, 4, and 5 years after partial gastrectomy. Attempts were made to remove the sutures in 8 patients, using the endoscopy biopsy forceps, with success in 6 cases. Of the latter cases, 3 patients appear to be definitely improved at 3, 7, and 9 months, and 1 is unchanged at 1 year. In 2 patients symptoms returned at 3 and 4 months, further sutures were removed, and the patients are well at 1 and 2 years respectively. Two ulcers healed when associated sutures were removed.

Table III.—COMPARISON OF ENDOSCOPY AND RADIOLOGY IN ULCER DIAGNOSIS

TYPE OF ULCER	KNOWN ULCERS	ENDOSCOPY		RADIOLOGY			
		Positive	Negative	Positive	Negative	Not done	False Positive ?
Gastric	8	7	1	5	2	1	3
Anastomotic	20	19	1	6	7	7	4
Duodenal	23	20	3	12	7	4	11
Total	51	46	5	23	16	12	18

Of the other 7 patients with sutures, 3 have undergone suture-line resection and further ulcer surgery, with the apparent cure of symptoms. One patient was found at operation to have a large carcinoma of the pancreas, another patient awaits further operation, and 1 patient has been lost to follow-up. In the final patient the suture material disappeared spontaneously before repeat endoscopy.

Mucosal Congestion and Gastritis.—After a partial gastrectomy or drainage operation, bile reflux into the stomach was often profuse, requiring endoscopic suction and the instillation of silicone materials to ensure a complete mucosal view. Mucosal congestion (and easy bleeding) of the gastric mucosa was a common finding, particularly near the stoma. The significance of this often dramatic appearance is obscure and further information has been sought by multiple endoscopic mucosal biopsies. *Table IV* gives the figures for the visual and histological changes in a total of 54 patients who were not found to have recurrent ulcer following gastric resection. Histological abnormalities were present in more than half of the patients biopsied, but showed only poor correlation with visual abnormalities.

Table IV.—Comparison of the Visual and Histological Changes in 54 Patients without Recurrent Ulcer after Gastric Resection

Histology	Visual Appearances of Gastric Mucosa*			
	Body		*Stoma*	
	Normal	Congested	Normal	Congested
Normal	19	6	1	10
Superficial gastritis	6	14	2	28
Atrophic gastritis	1	2	—	3
Acute gastritis	3	3	—	1
Total	29	25	3	42

* Stomal biopsies were taken (in all but 9 patients) within 2 cm. of the stomal margin, and body biopsies from the mid-portion of the gastric body.

Histological changes of the gastric body mucosa (mid-greater curvature) were also common in patients who had undergone vagotomy and pyloroplasty. In 9 patients with recurrent duodenal or pyloric canal ulcer the body mucosa showed normal histology in 5 cases and superficial gastritis in 4 cases. In 31 other patients with no evidence of an ulcer histological findings were: normal, 7; superficial gastritis, 20; atrophic gastritis, 3; acute gastritis, 1.

Diagnostic Significance of Symptomatology and Insulin Testing.—Of the 51 patients known to have recurrent gastric, duodenal, or anastomotic ulceration, 29 had typical dyspeptic symptoms, 14 had vague and atypical distress or predominant vomiting, and 8 had no dyspepsia at all (4 presented with acute bleeding and 4 with anaemia). Looked at in reverse, there was a total of 48 patients in the whole series who were classified as having typical dyspepsia. Twenty-eight of these patients were found to have ulcers, 2 had cancers, 2 had retained sutures, 2 had anastomotic stenosis, and no lesion (apart from gastritis) was discovered in 14 cases.

Insulin tests were carried out on 37 of the patients who had previously undergone vagotomy (none was done within 6 months). Twenty patients showed an early positive response to the test. Of these, 9 were found to have an ulcer. No ulcers were found in 4 patients with a late positive response, but of 13 patients with a negative response, 3 harboured ulcers.

DISCUSSION

When a patient returns with symptoms after peptic ulcer surgery it is essential to know whether or not a recurrent ulcer is present. Many authors have stressed the difficulties in radiological diagnosis following gastric resection (Samuel, 1954). In a randomly selected series of 60 radiographs of patients who had undergone Billroth-I operations, Kim and Evans (1959) found that more than half showed some irregularity of the lesser curvature, with 5 pseudo-ulcers and 3 pseudo-tumours, in addition to confusing folds around the stoma. Such folds may obscure stomal ulcers (Gabrielsson, 1972) or falsely simulate them. Ulcers were seen radiologically in only 52·3 per cent of a series of 325 patients with proved recurrent gastrojejunal ulceration at the Mayo Clinic (Wychulis, Priestly, and Foulk, 1966) and in 50 per cent of a series of 125 patients reported by Hirschowitz (1970). Barium-meal examination showed ulcers in only 4 out of 14 patients with suture-line ulcers (Small, Smith, Faulkner, Sircus, and Bruce, 1968). Block and Wolf (1965) and Gleeson and Ellis (1968) stressed the difficulties in diagnosing recurrent ulceration in the presence of a pyloroplasty. Reporting a series of 74 patients with recurrent duodenal or gastrojejunal ulceration following vagotomy and drainage, Fawcett and others (1969) stated that radiology was 'seldom helpful', ulcers being detected in only 47 per cent of cases. By contrast, Williams and Toye (1970) said that radiological studies have great value in this situation. The original assessment of radiographs from their 24 symptomatic patients provided 4 false-negative and 2 probable false-positive results; only on expert review were these reports corrected.

In our series radiography detected 60 per cent of the ulcers while endoscopy showed 90 per cent of them. Of 126 other patients, radiography raised a possible diagnosis of ulceration in 18 cases and of tumour in 8, which could not subsequently be substantiated. Expert review corrected 10 out of the 22 false-negative or false-positive reports. Results from our own series do not reflect the overall accuracy of radiology in the operated stomach, since patients were often selected for endoscopy because of equivocal or negative radiographic findings.

The overall accuracy of endoscopy in the operated stomach is equally relevant and difficult to ascertain. Gastroscopy and gastrophotography have been advocated (Gear and Dowling, 1970; Kasugai, Kato, Takase, and others, 1966; Gabrielsson, 1972) and dismissed (Wychulis and others, 1966; Goligher and others, 1972). Hirschowitz (1970) claims to have detected 90 per cent of 125 recurrent ulcers by gastroscopy. However, these facts and references are now less relevant, since gastroscopy alone is obsolete and oesophagogastroduodenoscopy should be performed. Four of the 5 ulcers were missed in the present series while using only a lateral-viewing gastroscope, which cannot enter a pyloroplasty and often gives an incomplete survey beyond a gastro-enterostomy stoma. It is clear that patients should be examined with a modern, fully manœuvrable forward-viewing instrument with good suction and biopsy facilities (ACMI Model 7089P or Olympus GIFD). In most cases this will provide a complete survey of the oesophagus, stomach, pyloroplasty, and duodenal bulb, or stoma and jejunal loops. Sometimes, the pouches of a pyloroplasty, or the areas of jejunum just beyond a stoma, may be difficult to visualize with a forward-viewing instrument. In such circumstances there should be no hesitation in also using a lateral-viewing fibrescope at the same examination; the highly flexible Olympus JFB duodenoscope is particularly well suited to this task.

Considerable reliance is usually placed upon the results of insulin testing in patients who are symptomatic after vagotomy. In this series less than half of the patients with positive insulin tests were found to have ulcers, and there were 3 patients with recurrent ulceration in the presence of negative insulin tests. One of these ulcers was associated with retained suture material. This has been recognized as the cause of anastomotic ulceration for many years (Tanner, 1951), but some surgeons continue to use non-absorbable material, which can ulcerate through from the seromuscular layer. In the present series 7 out of the 20 anastomotic ulcers were associated with suture material. Sutures have previously been removed endoscopically with clinical benefit (Tanner, 1951; Kasugai and others, 1966; Gear and Dowling, 1970) but the significance of suture material in the absence of ulceration is open to question (Hirschowitz, 1970). Endoscopic removal of sutures appears to have alleviated dyspeptic symptoms in several of our patients. We have seen small anastomotic ulcers and erosions heal and recur in association with suture material, but have also seen sutures disappear entirely between examinations.

The mucosa of the operated stomach frequently appears congested or atrophic with easy contact bleeding. These appearances are particularly marked around a gastro-enterostomy stoma ('stomatitis'; *Table IV*) and are attributed to the reflux of duodenal or jejunal juice, which may be profuse at endoscopy.

It is easy to assume that these changes are an important cause of dyspeptic symptoms, particularly since biopsies usually show evidence of gastritis (*Table IV*), and when definitive lesions provide a diagnostic label for only half of the patients investigated (*Table II*). Such an assumption is quite invalid in the absence of a control series. We are unaware of any systematic endoscopic study of asymptomatic patients following ulcer surgery, but there is abundant evidence that gastritis is very common. Mucosal biopsies taken by capsule from healthy individuals following partial gastrectomy have shown some degree of gastritis in 44–66 per cent (Coghill and Wynne-Williams, 1958; Lees and Grandjean, 1958; Johnson, 1966; Camarinos, Brus, Jacob, and others, 1970), our own figure for symptomatic patients being 56 per cent (*Table IV*). In 86 patients 10–18 years after vagotomy and pyloroplasty Stempien (1971) found superficial and atrophic gastritis in 86 per cent. Patients with postoperative gastritis are less likely to have recurrent duodenal ulceration (Johnson, 1966). Thus, one should not assume that mucosal congestion or chronic gastritis is a cause of symptoms. Acute gastritis may be associated with treatable super-infection of the upper gut.

The incidence of chronic gastritis increases with the length of time after operation (Price and Cotton, 1973). Endoscopy has a useful role to play in monitoring the development of gastric atrophy and intestinal metaplasia, which may well be important in regard to the increased risk of malignancy in the resected stomach (Kobayashi, Proka, and Kirsner, 1970). Endoscopy and biopsy are also useful in following the course of gastric ulcers left in situ following non-resective surgery (i.e., vagotomy and drainage procedure).

The present series refers only to patients who are symptomatic after leaving hospital. Endoscopy may occasionally be useful in the early postoperative period. While radiology is usually adequate in detecting hold-up at an anastomosis, endoscopy can often distinguish between its different causes (ulceration, oedema, sutures) and we have relieved the obstruction in 1 patient by passing an instrument through an oedematous stoma. Demaret, Hirschowitz, and Luketic (1971) have pointed out that the relationships of the efferent and afferent loops to the stoma of a gastro-enterostomy are more easily assessed by endoscopy than radiology and stressed the complications of the 'double-barrelled' stoma.

Attention to detail can improve the diagnostic yield of barium-meal examinations in the operated stomach. However, it is clear that the investigation of symptomatic patients is incomplete, and may be inadequate, without properly performed endoscopy.

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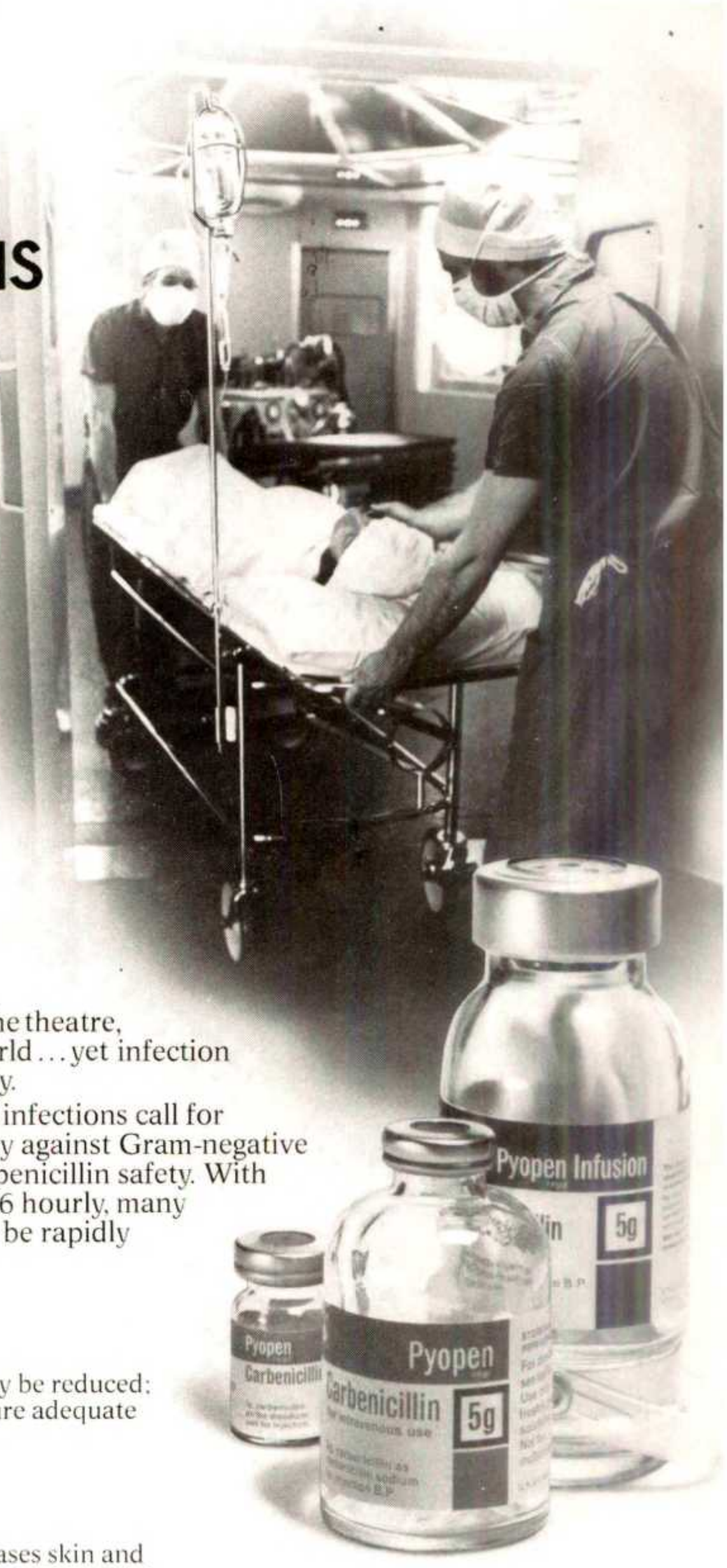

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COLONOSCOPY IN THE DIFFERENTIAL DIAGNOSIS OF CARCINOMA FROM DIVERTICULITIS OF THE SIGMOID COLON

By ALAN C. B. DEAN and J. P. NEWELL

DEPARTMENT OF SURGERY, UNIVERSITY OF EDINBURGH, AND THE ROYAL INFIRMARY, EDINBURGH

SUMMARY

1. Thirty-six patients in whom barium-enema examination had suggested the possibility of carcinoma in a segment of diverticular disease were examined by colonoscopy.

2. Colonoscopy is particularly difficult in such patients and it failed to examine the diseased segment in 17 cases.

3. Colonoscopy gave a firm diagnosis of carcinoma in 4 cases, excluded it in 5, and was helpful in another 9. There was 1 false negative.

COLONOSCOPY is becoming increasingly recognized as a valuable diagnostic procedure in patients with disease of the colon. Its advantages over sigmoidoscopy with a rigid instrument are that it allows examination of a much greater extent of the bowel with less discomfort to the patient (Dean and Shearman, 1970). The extent of the bowel examined is dependent on careful cleansing of the bowel and on its configuration. Sharp bends cannot always be negotiated and in practice it may be difficult or impossible to advance the instrument right through the sigmoid colon. The sigmoid colon offers difficulties to the radiologist too, particularly in distinguishing carcinoma from areas of narrowing in diverticulitis. This paper describes the use of the colonoscope in patients presenting this diagnostic problem.

PATIENTS

Thirty-seven patients have been studied: 22 females and 15 males, the average age being 69 years (range, 59–84 years). All the patients had had one or more barium-enema examinations which had shown diverticular disease in the sigmoid colon with a narrowed segment raising the suspicion of a coexisting carcinoma. The barium-enema films of 2 of these patients are shown in *Figs.* 1 and 2. In some cases this doubt persisted after repeating the barium-enema examination with an intravenous injection of an anticholinergic drug.

All the patients were examined at least 6 weeks after any acute exacerbation of diverticulitis. They were prepared by taking a laxative, usually Senokot, the night before the examination, followed by a thorough bowel wash-out on the morning of the examination. This was not always easy in older patients with disease in the sigmoid colon. The patients were examined without any premedication unless they were unduly apprehensive, when an intravenous injection of up to 2 mg. of phenoperidine and 10 mg. of droperidol, depending on the patient's weight, was given. Intravenous Pro-banthine (15 mg.) was given to some patients in an attempt to facilitate the passage of the instrument through acutely angulated or narrowed segments. The patients were examined in the left lateral position.

THE INSTRUMENT

The short colonoscope (Olympus CFSB) was used on the first 19 patients. It has an effective length of 75 cm. and the tip can be moved through 180° (110 up and 70° down) in one plane. In 6 of these patients the examination was repeated using the long colonoscope (Olympus CFLB), not because of its greater length but because its tip can be moved through 180 in two planes at right angles to each other and it is thus easier to manœuvre it around acute bends. This instrument alone was used in the last 17 patients.

RESULTS

The results are summarized in *Table I.*

In 17 of the 36 patients the examination was a failure, usually because the instrument could not be passed into the diseased segment owing to sharp angulation of the bowel. In 3 cases inadequate bowel preparation was also responsible. Of the 19 patients in whom the examination was successful, 4 were shown to have carcinoma and in 5 the whole of the suspicious segment was examined without any sign of carcinoma being seen. In 9 cases the full length or the whole circumference of the suspicious segment could not be inspected, but sufficient was seen for carcinoma to be excluded with reasonable confidence. These 14 patients in whom no carcinoma was seen have now been followed up for periods of from 6 months to 2 years, 2 having had sigmoid colectomy, and so far in no case has the subsequent course shown that carcinoma was present. In the 1 false negative the narrowed segment was examined and found to be rigid but the mucosa was intact. Laparotomy 2 weeks later showed that the bowel was invaded by transperitoneal spread from carcinoma of the stomach.

Table I.—RESULTS OF EXAMINATION BY COLONOSCOPY IN 36 PATIENTS WITH A NARROWED AREA IN THE SIGMOID COLON SHOWN BY BARIUM-ENEMA EXAMINATION

NO. OF PATIENTS	MEAN DISTANCE AND RANGE EXAMINED (cm.)	CARCINOMA DIAGNOSED	CARCINOMA EXCLUDED	CARCINOMA NOT SEEN	FALSE NEGATIVE	FAILURE
19	37 29–60	4	5	9	1	—
17	28 17–36	—	—	—	—	17

In 6 patients in whom difficulty was encountered with the short colonoscope the examination was repeated using the long colonoscope in the hope that the increased manœuvrability would enable further advance. In 2 cases this instrument allowed a successful examination, but in the other 4 patients only a few more centimetres of bowel could be examined and the examination was still unsuccessful. In the latter part of the study the long colonoscope seemed to achieve better results, but increasing experience may also have been responsible.

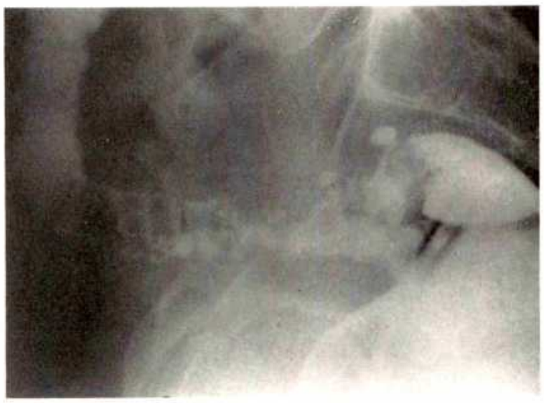

FIG. 1.—Diverticular disease in the sigmoid colon of a 74-year-old man. Persistent narrowing and irregularity are suggestive of carcinoma, but colonoscopy showed no evidence of tumour. A repeat barium-enema examination 1 year later showed diverticular disease with no evidence of carcinoma and the patient remains symptom-free.

DISCUSSION

The sigmoid colon is probably the most difficult part of the colon for the radiologist to examine. This is due to the configuration of the bowel, with tortuous segments of colon overlying each other in many views, and to the nature of the diseases occurring there. In patients with radiological appearances of diverticular disease it may be very difficult to determine whether an area of persistent narrowing is due to diverticulitis or to a carcinoma (Shanks and Young, 1969), and often laparotomy is undertaken in case a carcinoma is lurking undiagnosed in the abnormal segment. Even at laparotomy the distinction between carcinoma and diverticulitis can be extremely difficult. The present study was undertaken to assess the value of colonoscopy in this situation.

The narrowing, sharp angulation and fixation so often present make this a particularly difficult group of patients to examine, and in 17 patients the instrument could not be passed into or through the diseased segment. This was due not only to acute angulation of the bowel and inability to distend it with air but also in some cases to continuous soiling with liquid faeces coming through the narrow segment. The instrument must be advanced under visual control in the direction of the lumen and if the bowel cannot be distended this may be impossible. Because of the risk of damage to the inflamed bowel analgesic drugs were not given and sedation was avoided whenever possible. No patient was examined less than 6 weeks after an acute episode of diverticulitis. Pro-banthine was not found to be helpful in facilitating a difficult examination.

In 19 patients colonoscopy was successful in viewing all or most of the suspicious segment. The cases where the whole segment was viewed satisfactorily tended to be those with more localized disease. In 4 patients a carcinoma was diagnosed and in 5 cases no evidence of carcinoma was seen. In these 9 patients the examination was obviously of value, and their subsequent course has confirmed the accuracy of the diagnosis in each case.

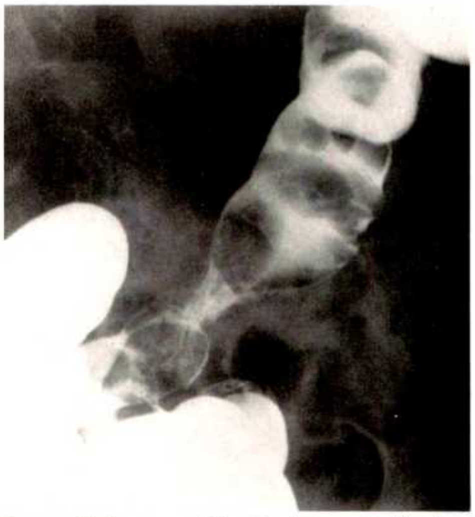

FIG. 2.—Barium-enema film after intravenous Pro-banthine in an 84-year-old woman. Stenosis of the sigmoid colon was diagnosed radiologically as either carcinoma or localized diverticular disease. Colonoscopy was negative. A repeat barium-enema examination 14 months later showed minimal narrowing only. The diagnosis was, therefore, uncertain but laparotomy was avoided on the evidence of colonoscopy.

The false negative was due to infiltration of the colon from the peritoneal surface by a gastric carcinoma. Fortunately the misleading impression at colonoscopy did not adversely affect the outcome in this case since laparotomy was undertaken, but it emphasizes that the greatest caution is needed before claiming to exclude carcinoma because no evidence of it has been seen at endoscopy.

In the remaining 9 patients the whole sigmoid colon could not be examined satisfactorily because of failure to pass an acute bend at or above the apex of the sigmoid loop, or because the upper part of the sigmoid colon had not been adequately cleared of faeces, or because the whole circumference of the bowel could not be seen throughout the examination. In these cases enough of the narrowed segment was seen for it to be judged very unlikely that a carcinoma was present. No case of carcinoma has since occurred in this group. The technique is thus a useful addition to radiology in patients presenting this difficult diagnostic problem, and may avoid an unnecessary laparotomy when the lesion is benign and expedite it when the lesion is malignant.

Acknowledgements.—We wish to thank the surgeons and physicians in the Royal Infirmary, Edinburgh, who have referred some of these patients for examination, and the nursing staff for undertaking the careful preparation of the patients. We are grateful to the Ernest and Minnie Dawson Cancer Trust for a generous grant for the purchase of the Olympus CFLB colonoscope.

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EMERGENCY OESOPHAGEAL TRANSECTION IN UNCONTROLLED VARICEAL HAEMORRHAGE

BY P. GEORGE, C. BROWN, G. RIDGWAY, B. CROFTS, AND S. SHERLOCK

ROYAL FREE HOSPITAL, LONDON

SUMMARY

The results of emergency oesophageal transection are described. The overall operative mortality-rate was 45 per cent. There were no operative deaths in the patients with extrahepatic obstruction and normal liver function. The operative mortality-rate for the patients with cirrhosis was 53 per cent, or a salvage rate of 47 per cent if one considers that this is a highly selected group of patients (albeit negatively)—patients with impaired liver function who had not responded to intensive medical treatment and who were still bleeding at the time of surgery.

SINCE 1964 at the Royal Free Hospital, London, oesophageal transection has been performed as an emergency procedure for uncontrollable haemorrhage in 35 patients with oesophageal varices.

Bleeding from oesophageal varices accounts for only 0·01 per cent of hospital admissions in Britain and for approximately 3·0 per cent of patients admitted with haematemesis and melaena (Desmond and Reynolds, 1972).

The management of patients with bleeding oesophageal varices poses a difficult problem. Irrespective of the method of management the results have been depressing, with mortality-rates ranging from 30 to 80 per cent (Sherlock, 1964; Orloff, Halasz, Lipman, Schwabe, Thompson, and Weidner, 1967).

MEDICAL MANAGEMENT

The blood-loss is replaced, ideally 50 per cent of the loss with fresh blood. Vitamin K is given parenterally.

Measures are taken to prevent hepatic pre-coma. Enemas or colonic wash-outs are given. Neomycin and lactulose are administered orally.

If the bleeding does not stop spontaneously vasopressin (20 units in 200 ml. of 5 per cent dextrose) is given intravenously. More than one dose may be necessary. If the bleeding continues a Sengstaken-Blakemore tube is passed through the mouth and the balloons are inflated to compress the varices. The tube must not be left in position for more than 24 hours, and if at the end of that time there is further bleeding a direct surgical approach is necessary.

At this hospital the operation of choice has been an oesophageal transection.

OPERATIVE TECHNIQUE

The anaesthetized patient is placed in the right lateral position and the chest is opened through the bed of the left eighth rib. The oesophagus is isolated immediately above the gastro-oesophageal junction.

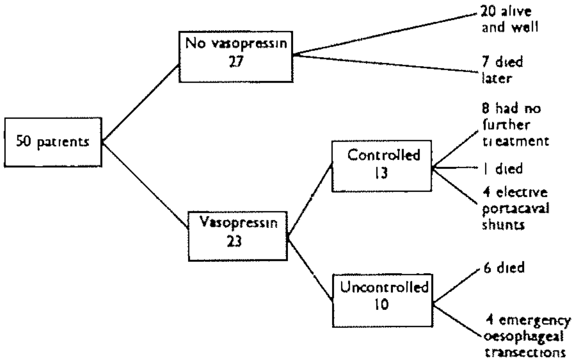

FIG. 1.—Summary of the progress of the last 50 patients admitted to the Royal Free Hospital, London, with bleeding oesophageal varices secondary to cirrhosis.

Table I.—AETIOLOGY OF BLEEDING OESOPHAGEAL VARICES IN 30 PATIENTS UNDERGOING OESOPHAGEAL TRANSECTION

AETIOLOGY	NO. OF CASES	AGE (yr.)		OPERATIVE MORTALITY
		Average	Range	
Alcoholic cirrhosis	7	40	42–66	4
Primary biliary cirrhosis	2	56	50–62	1
Active chronic hepatitis	2	30	21–39	1
Secondary biliary cirrhosis	1	60	—	0
Partial nodular transformation	1	60	—	1
Granulomatous	1	52	—	0
Postnecrotic	1	52	—	1
Cryptogenic cirrhosis	15	55	40–68	8

Any varices on the surface of the oesophagus are ligated and divided. The vagus nerves are identified and avoided. The longitudinal muscle is opened for 4–5 cm. and the inner circular muscle and mucosa are cored out by blunt dissection. The inner core is transected and resutured with two continuous chromic catgut sutures. Bleeding from the cut varices is controlled by holding the distal part of the 'cored-out'

Table II.—PREOPERATIVE INVESTIGATIONS AND POSTOPERATIVE PROGRESS IN 30 PATIENTS UNDERGOING OESOPHAGEAL TRANSECTION

CASE	AGE AND SEX	AETIOLOGY	COMA	JAUNDICE	ASCITES	ALBUMIN (g. per cent)	BILIRUBIN (mg. per cent)	A.S.T. (I.U./l.)	Alk PO$_4$ (K.A U./100 ml)	BLOOD-LOSS (pints)	COMPLICATIONS	PROGRESS AND SURVIVAL
1	59 M.	Alc.	+	–	++	3·3	0·8	32	18	11	Pneumothorax	Died at 9 wk. from hepatic failure and myocarditis
2	46 F	Alc.	–	++	++	3·4	5·3	36	12	25	Haemorrhage→laparotomy	Died at 32 d. from acute gastric ulcer and cirrhosis
3	66 M.	Alc	–	–	+++	4·4	0·5	16	19	4	None	Alive and well at 4 yr. + ascites
4	49 M.	Alc.	–	–	++	3·2	0·8	55	18	10	Coma	Alive and well at 2 yr +
5	44 M	Alc.	–	+++	++	2·8	10	56	28	10	Hepatic failure	Died at 3 d.
6	49 F.	Alc	–	+	++	3·4	1·2	29	20	10	Hepatic failure	Died at 4 d.
7	42 M	Alc.	+	+	+	2·4	1·8	20	15	22	Leak/empyema	Died at 8 d
8	62 F	P B.C.	–	++	+	3·2	8·5	16	10	23	None	Died at 2 yr. from bleeding duodenal ulcer and adrenal adenoma
9	50 F	P.B C.	–	+	–	3·9	1·2	24	65	15	Left effusion and respiratory failure	Died at 3 d
10	21 M.	A.C.H.	–	++	–	4·3	5	11	13	50	None	Shunt performed 3 mth later. Died 4 yr. later from hepatic failure
11	39 M.	A.C.H.	+	+	++	3·4	4·5	150	33	32	Hepatic failure	Died at 5 d.
12	60 F.	2B.C	–	+	+	4	4	38	34	22	Left haemothorax. Coma	Alive and well at 3 mth
13	60 F.	P.N T.	+	+++	+++	2·5	11	25	5	32	Hepatic failure	Died at 8 d.
14	52 M	Gran.	–	+	–	4	1·2	27	72	17	None	Shunt performed 1 mth. later. Alive and well 1 mth later
15	52 M	P.N.C.	+	+	+++	2·6	1·9	228	9	19	Hepatic failure	Died at 6 d Post-mortem examination showed a hepatoma
16	62 M	Crypt.	+	+	+++	2·2	1·6	7	16	11	None	Alive and well at 18 mth + ascites and pre-coma
17	51 M.	Crypt.	–	+	+++	3·8	4	44	58	10	Wound infection	Alive and well at 3 yr.+
18	46 F.	Crypt.	?	?	?	?	?	?	?	36	None	Bled at 15 mth →shunt. Alive at 4 yr.+ P.S.E +
19	62 F.	Crypt.	–	+++	–	3·5	10·4	65	13	?	Empyema	Died at 2 yr from bleeding
20	58 M	Crypt.	–	+	+	3	1·6	15	41	4	None	Died at 18 mth from bleeding
21	57 M.	Crypt.	+	++	+	3·3	5	950	12	18	Hepatic failure	Died at 7 d.
22	60 F	Crypt	–	+	+	3·3	1·9	85	12	24	Respiratory failure	Died at 2 d
23	54 M	Crypt.	–	+	–	3·1	1·2	38	6	19	Leak (hepatic failure)	Died at 15 d.
24	56 F.	Crypt.	–	–	++	3·5	0·7	13	46	28	Cardiac arrest	Died at 5 hr. Post-mortem examination showed a cardiac aneurysm
25	61 M.	Crypt.	–	++	+	3·2	6·0	16	9	7	Hepatic failure. Bleed from gastric varices. Duodenal ulcer	Died at 9 d.
26	68 F.	Crypt.	–	+	–	4·8	2	10	8	34	Hepatic failure	Died at 15 d. Post-mortem examination showed cirrhosis and neoplasm of stomach
27	40 M.	Crypt.	+	++	++	2·8	8·5	57	17	22	Hepatic failure	Died at 6 d.
28	53 M.	Crypt.	–	+	++	3·1	2·2	120	10	32	Leak (and hepatic failure)	Died at 14 d.
29	40 M	Crypt.	–	+	–	3·1	3·3	46	4	10	None	Shunt performed 6 mth. later. Died 7 yr. later from a fractured femur
30	51 M.	Crypt.	+	+	+	3·4	3·5	15	12	9	None	Alive and well at 1 mth +

Alc., Alcoholic cirrhosis. P.B.C., Primary biliary cirrhosis. A.C.H., Active chronic hepatitis. 2B.C., Secondary biliary cirrhosis. P.N.T., Partial nodular transformation. Gran., Granulomatous cirrhosis. P.N.C., Post-necrotic cirrhosis. Crypt., Cryptogenic cirrhosis. A.S.T., Aspartate transaminase. Alk. PO$_4$, Alkaline phosphatase. P.S.E., Portasystemic encephalopathy.

mucosa between the fingers and thumb of the left hand. Just before the suturing is completed a radio-opaque nasogastric tube is passed into the stomach. The longitudinal muscle is repaired with interrupted chromic catgut sutures.

The chest is closed in the usual manner using an underwater drain.

POSTOPERATIVE MANAGEMENT

Nothing is given orally until the fifth day, when a Gastrografin swallow is performed. If this shows no leak from the anastomotic site then oral feeding is commenced. The chest drain is removed if the chest radiograph is satisfactory after the Gastrografin swallow.

Protein is restricted initially and graduated amounts are given later on, dependent upon the liver function and satisfactory electro-encephalogram recordings.

If the general condition of the patient and hepatic function permit, then an elective portacaval shunt is performed approximately 6 weeks later.

RESULTS

Two groups of patients are considered separately: first, those with portal hypertension secondary to cirrhosis (*Cases* 1–30), and secondly those in whom the hypertension is secondary to an extrahepatic block (*Cases* 31–35).

1. **Intrahepatic Obstruction.**—In the majority of patients with haemorrhage from oesophageal varices control can be gained by medical means.

Fig. 1 summarizes the progress of the last 50 patients admitted to this hospital with bleeding varices secondary to cirrhosis (Parbhoo, Owens, and Sherlock, 1972).

In 10 cases the haemorrhage was not controlled medically and in 4 of these an emergency oesophageal transection was performed. The other 6 patients had terminal hepatic failure.

The aetiology of the disease in 30 patients undergoing oesophageal transection is shown in *Table I*, and the preoperative investigations and postoperative progress of these patients are summarized in *Table II*.

There were 16 postoperative deaths (death within 32 days of operation)—an operative mortality-rate of 53 per cent (*Table III*). Hepatic failure was the commonest cause of death.

Table III.—Cause of Postoperative Death

Cause of Death	*No. of Cases*
Hepatic failure	9
Oesophageal leak	3
Acute gastric ulcer and hepatic failure	1
Cardiac aneurysm	1
Respiratory failure	2

Two patients bled again during the postoperative period. *Case* 2 died of hepatic failure following a partial gastrectomy for an acute gastric ulcer. *Case* 25 bled terminally from a large gastric varix on the ninth postoperative day. Following transection his liver function rapidly deteriorated; his bilirubin had risen to 34 mg. per cent and his blood-urea to 190 mg. per cent.

Subsequent Progress.—Three patients (*Cases* 10, 14, and 29) had elective portacaval shunts performed 3 months, 1 month, and 6 months respectively after transection. *Case* 10 survived for 4 years and then died of hepatic failure. *Case* 29 survived for a further 6 years and died of complications following a fractured neck of the femur.

There was 1 other death in the first postoperative year (*Case* 1). This was a man who died 9 weeks postoperatively of hepatic failure and myocarditis. Post-mortem examination showed that he also had a hepatoma.

There are 9 patients on whom elective shunts have not been performed and to date 5 have re-bled. The haemorrhage was the cause of death in 3 of these 5 patients.

One patient (*Case* 18) bled 15 months following her transection. An emergency portacaval anastomosis was performed and she is alive 4 years later.

These results are summarized in *Table IV*.

Liver Function.—An attempt has been made to try to correlate liver function with survival or postoperative mortality. The preoperative measurements of serum albumin, bilirubin, and aspartate transaminase have not always been an accurate reflection of hepatic function since many patients had been transfused large volumes of blood prior to their transfer to this hospital.

There was no significant difference between the preoperative bilirubin and albumin levels in the two groups. However, there was only 1 survivor with a serum-albumin level of less than 3·0 g. per cent (*Case* 16).

Estimation of the aspartate transaminase level gave a slightly better correlation. The values for those surviving ranged from 7 to 65 units and for those dying postoperatively from 10 to 950 units.

The presence or absence of ascites did not vary significantly between the two groups.

A history of pre-coma or coma during the haemorrhage leading to the transection indicated a poor prognosis. Five out of 9 such patients died within a few days postoperatively of hepatic failure, 1 died 9 weeks later of hepatic failure and myocarditis (*Case* 1), and 1 case (*Case* 7) developed a leak at the line of transection. Of the 2 survivors, *Case* 16 is still alive 18 months later but has ascites and repeated episodes of portasystemic encephalopathy. *Case* 30 is alive and well 1 month postoperatively.

The average blood replacement prior to surgery in the patients who survived was 15 pints as compared with 22 pints in those who died in the postoperative period. Whether this difference is significant in itself is hard to judge because in the latter group liver function was worse and not unnaturally there was less desire to operate and medical treatment was more prolonged.

Oesophageal Complications.—All 3 patients (*Cases* 7, 23, and 28) who developed leaks at the site of the transection died. Two of these patients had pulled out their nasogastric tube and an attempt, wrongly, had been made to replace it!

One patient (*Case* 8) developed a stricture at the site of the transection which required dilatations. She also had a chronic duodenal ulcer with oesophageal reflux and she eventually died 2 years after transection from haemorrhage from her duodenal ulcer.

2. **Extrahepatic Obstructions.**—There were 5 patients in this group (*Table V*). In 2 cases there was a history of neonatal sepsis.

Case 32 had had osteomyelitis of her femur and spine complicated by hepatic abscesses. These had been drained at the age of 3 weeks and had grown *Staphylococcus aureus*. She was the only patient in this group to suffer any postoperative complication. She developed a left-sided empyema and lung abscess which required drainage—the causative organism was again *Staph. aureus*. She was also the only patient in this group to have further haemorrhages (two small bleeds almost 4 years after transection).

Table IV.—SUBSEQUENT PROGRESS OF THE OPERATIVE SURVIVORS

CASE	AGE (at the time of transection)	TIME OF HAEMORRHAGE AFTER TRANSECTION (mth.)	BLOOD-LOSS (pints)	CAUSE	OUTCOME
8	62	21 and 24	3 and 22	Duodenal ulcer	Died after second haemorrhage
16	62	10	10	Varices and healed duodenal ulcer	Alive and well at 14 mth.+. No further haemorrhage.
17	51	25	2	Varices	Alive and well at 7 yr.+. No further haemorrhage.
19	62	24	26	Varices	Died
20	58	18	29	Varices and duodenal ulcer	Died
3	66	No further haemorrhage			Alive and well at 4 yr.+
4	49				Alive and well at 2 yr.+
12	60				Alive and well at 3 mth.+
30	51				Alive and well at 1 mth.+

1 patient (*Case* 1) died 9 weeks postoperatively of liver failure and myocardial infarction Post-mortem examination showed a hepatoma

3 patients (*Cases* 10, 14, and 29) had an elective portacaval anastomosis.

1 patient (*Case* 18) had an emergency portacaval anastomosis following a haemorrhage 15 months after transection.

Table V.—DETAILS OF 5 PATIENTS WITH EXTRAHEPATIC OBSTRUCTION

CASE	AGE AND SEX	PREVIOUS HAEMORRHAGES		BLOOD-LOSS PRIOR TO OPERATION (pints)	POSTOPERATIVE PROGRESS	FURTHER HAEMORRHAGES
		No.	Blood-loss (pints)			
31	10 M.	2	6	19	No complications	None. Alive and well at 6 years
32*	9 F.	?	?	14	Empyema of left chest and lung abscess	2 at 45 and 48 mth. Blood-loss 3 and 4 pints respectively
33	20 M.	3	67	26	No complications	None. Alive and well at 3 years
34*	11 M.	5	19	30	No complications	None. Alive and well at 9 mth
35	15 M.	3	32	28	No complications	None Alive and well at 2 mth.

* History of neonatal sepsis.

Case 34 had required an exchange transfusion at birth for jaundice. This had been complicated by umbilical sepsis.

All 5 patients had normal pre- and postoperative liver-function tests. There was no operative mortality.

DISCUSSION

Ideally an attempt is made to control the haemorrhage by conservative means and then to proceed to an elective definitive operation, e.g., portacaval or splenorenal shunt. The 1-year survival of patients treated this way is 85 per cent (Hourigan, Sherlock, George, and Mindel, 1971; Rothwell-Jackson and Hunt, 1971).

The length of time that patients are treated conservatively varies markedly from hospital to hospital.

There have been few prospective studies, but Orloff (1967) attempted to compare medical and surgical therapy in the United States. The results of medical treatment were so bad, the survival rate being only 17 per cent, that this form of treatment was abandoned. The survival rates of patients submitted to early surgery were 54 per cent for varix ligation and 53 per cent for emergency portacaval shunt. In this country the survival figures with conservative management are considerably different, which in part reflects the difference in the aetiology of the cirrhosis.

In the period 1953–65 there were 245 admissions for bleeding oesophageal varices to one hospital (Rothwell-Jackson and Hunt, 1971). In 171 patients (70 per cent) the bleeding was controlled medically and an elective shunt was later performed.

The most useful drug in the medical management is vasopressin, which decreases splanchnic blood-flow and portal venous pressure (Schwartz, 1970). More than one dose may be necessary. Temporary (no blood-loss for 24 hours) or more permanent cessation of the haemorrhage will be obtained in the majority of cases (Shaldon and Sherlock, 1960; Merrigan, Plotkin, and Davidson, 1962).

If the bleeding is not controlled with intravenous Pitressin then a Sengstaken-Blakemore triple-lumen tube is passed orally (not through the nose) to compress the oesophageal varices. Conn (1970) described his results of using the tube in 90 patients. The bleeding was controlled in only 65 per cent of cases and furthermore in 20 per cent of the cases the death of the patient could be attributed directly to its use, the commonest complications being regurgitation and aspiration pneumonia. This is not our experience. Provided that the tube is correctly placed the haemorrhage is controlled, and the incidence of regurgitation and aspiration pneumonia can be reduced by using a quadruple-lumen tube, the extra lumen being used to aspirate saliva, etc., from the oesophagus.

Extrahepatic Obstruction.—In approximately 50 per cent of these patients the portal vein thrombosis is secondary to sepsis, umbilical sepsis and osteomyelitis being the commonest foci (Thompson and Sherlock, 1964).

The treatment is primarily medical in the hope that more portasystemic anastomoses will develop spontaneously (Stathers, Ma, and Blackburn, 1968). Cirrhosis is not a sequela (Hsia and Gellis, 1955). Certainly as the child becomes older the haemorrhages tend to become less frequent and severe. If definitive surgery has to be performed then a splenorenal anastomosis is the operation of choice, but for the procedure to stand a reasonable chance of success the diameter of the splenic vein should be at least 1 cm. (Hallenback and Adson, 1961). Alternatively, the superior mesenteric vein can be anastomosed to the inferior vena cava (Foster, Holcomb, and Kirtley, 1963).

Walker (1964) discussed the results of 24 patients with extrahepatic obstruction undergoing elective oesophageal transection. Eight re-bled seriously (33 per cent), the cases having been followed for periods of up to 11 years. Britton and Crile (1963) found that 4 of their 14 cases (29 per cent) had re-bled after 3–14 years.

One of our patients has so far re-bled (*Table V*) but longer follow-up is necessary, for it is not uncommon for these patients to have intervals of 5 years or more between bleeds.

There was no operative mortality in this group—a reflection of their normal liver function.

Intrahepatic Obstruction.—A variety of operative procedures has been described to control the haemorrhage when medical treatment has failed. The least traumatic of these is injection of the veins with sclerosants via an oesophagoscope (Macbeth, 1955; Hunt, Johnstone, and Rodgers, 1969). More extensive procedures include transoesophageal ligation of the varices via a thoracic approach (Boerema, 1949; Linton and Ellis, 1956; Crile, 1957; Rothwell-Jackson and Hunt, 1971). Welch (1956) described a similar operation through an abdominal approach. Walker (1960, 1964) reported an oesophageal transection which may be either mucosal or complete, while Tanner (1950, 1961) described a gastric transection (porta-azygos disconnexion).

Other surgeons have tried oesophagogastric resection either with an oesophagogastric anastomosis or using a loop of jejunum or colon to complete the anastomosis (Cooley and DeBakey, 1954; Koop and Roddy, 1958; Habif, 1959; Hallenback and Adson, 1961; Self, 1969). The latter operations are formidable and extensive procedures and certainly should not be used as emergency procedures.

At present in this country either an emergency portacaval shunt is performed or a direct approach is made to the bleeding varices by oesophageal transection or by the Boerema-Crile operation.

The operative mortality-rate for elective portacaval shunts is between 6 and 12 per cent (McDermott, Palazzi, Nardi, and Mondet, 1961; Brown and Walker, 1967; Panke, Rousselot, and Burchell, 1968; Hourigan and others, 1971). The mortality for emergency shunts, even when only 'good-risk' patients are operated upon, is higher at 20–50 per cent (Shaldon and Walker, 1962; Ekman and Sandblom, 1964; Rothwell-Jackson and Hunt, 1971).

The advantages of a transection operation are:—

1. It is relatively simple, and control of haemorrhage is obtained near the beginning of the operation.

2. Portal blood is not diverted away from the liver. Except in so far as any surgical procedure may adversely affect liver function, the effect on liver function of this operation is the beneficial one of stopping haemorrhage.

The disadvantages are:—

1. It involves doing a thoracotomy and oesophagotomy. As most of the patients have severe impairment of liver function it is perhaps not surprising that some patients have postoperative breakdown of the oesophageal anastomosis. This complication is a real disadvantage of the operation though the incidence in the present series (9 per cent) is less than in other reports, for example 17 per cent in the series of Rothwell-Jackson and Hunt (1971), and is due to the poor healing power of these patients which may in part be due to their hypo-albuminaemia. By doing a mucosal transection as opposed to a full-thickness transection one aims to minimize this complication.

2. It is not definitive. It does nothing to lower portal venous pressure, although it does not increase it, and thus unless further surgery is undertaken these patients are likely to have further haemorrhages (*Table IV*) as a result of the re-formation of varices across the suture line.

3. It does nothing to stop bleeding from gastric varices, though Walker (1964) stated that bleeding from submucous varices below the hiatus was rare.

Rothwell-Jackson and Hunt (1971) presented a series of 58 cases of patients with cirrhosis and uncontrollable haemorrhage. They were treated by the Boerema-Crile operation. Over a period of 5 years 31 patients were operated on with an operative mortality of 50 per cent, and only 3 patients who survived were considered subsequently for portacaval shunts. These figures for a similar group of patients are almost identical to our own.

The patients with cirrhosis and haemorrhage who do not respond to conservative measures may be divided into two main groups: (*a*) those who would have been considered for elective shunts had the bleeding been controlled medically; (*b*) those in whom a shunt would not be considered.

As regards the former group only a controlled prospective study will show whether an emergency portacaval shunt or a two-stage procedure (transection followed by a shunt) is the better treatment.

In the latter group the mortality-rate would be 100 per cent without surgical intervention.

Acknowledgement.—We should like to thank Mrs. Last for her secretarial assistance.

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LONG-TERM RESULTS OF SURGICAL TREATMENT FOR BLEEDING OESOPHAGEAL VARICES IN CHILDREN WITH PORTAL HYPERTENSION

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SUMMARY

The long-term results of surgical treatment for bleeding oesophageal varices in children with portal hypertension are reviewed. Twenty-four children below the age of 13 years who presented with gastro-intestinal bleeding over a 20-year period form the basis of this study. The importance of the aetiology of portal hypertension on the long-term follow-up has been studied. The results of surgical treatment in controlling haemorrhage are assessed.

Though extrahepatic obstruction is considered to be associated with a better long-term prognosis than intrahepatic disease the results of treatment in both groups were similar, with a 7-year survival rate of 75 per cent. Shunt surgery as a definitive procedure is advised in both groups, though the type of shunt used will depend on the age of the child and the site of obstruction.

PORTAL hypertension though uncommon in children is still one of the most important causes of major gastro-intestinal haemorrhage in this age-group. Most authors consider that surgical treatment for portal hypertension is justified only for the arrest of severe bleeding which cannot be controlled by other means or for the prevention of further haemorrhage in a patient who is at risk (Walker, Shaldon, and Vowles, 1961).

The long-term results of surgical treatment in the adult population leave much to be desired (Voorhees, Price, and Britton, 1970). The frequency of recurrent bleeding after direct ligation of the varices within the stomach and oesophagus is very high (Mikkelson and Pattison, 1959; Walker, 1960; Tanner, 1961), and the majority of surgeons consider that these procedures are justified solely in an attempt to control acute bleeding in a patient who is unfit for shunt surgery (Tanner, 1961; Rothwell-Jackson and Hunt, 1971). The hazards of shunt surgery, however, are not to be underestimated even when this is undertaken as an elective procedure (Riddell and Wilkinson, 1964; Hunt, 1965). Although the risk of encephalopathy may be reduced by side-to-side portacaval anastomosis or by a peripheral shunt (Burchell, Rousselott, and Panke, 1968; Lord, Rossi, Daliana, and Rosati, 1970), the danger of thrombosis in small-vessel anastomoses makes some of these procedures frequently unreliable (Hunt, 1965).

The results of surgical treatment in children, in terms of survival, appear to be more encouraging (Foster, Holcomb, and Kirtley, 1963). On the other hand, recurrent bleeding after surgery is a frequent event (Trusler, Morris, and Mustard, 1962). The principal factor in the more favourable natural history of these patients is a higher incidence of extrahepatic obstruction associated with normal liver function (Voorhees, Harris, Britton, Price, and Santulli, 1965). Although bleeding is better tolerated in these subjects, shunt surgery in early life involves the anastomosis of small-calibre vessels and the failure rate is higher (Foster and others, 1963). Some surgeons also consider that bleeding has a natural tendency to spontaneous remission (Hsia and Gellis, 1955), so that devascularizing procedures might therefore be justified. There are few reports in which the long-term results of surgery in children with cirrhosis have been studied (Trusler and others, 1962; Voorhees and others, 1965).

The present analysis is concerned with the long-term results of surgery for bleeding gastro-oesophageal varices in children. In over half of the children in this series cirrhosis was the prime cause of portal hypertension.

CLINICAL MATERIAL

During the 20-year period 1947–67, 142 patients have received surgical treatment for severe gastro-intestinal bleeding complicating portal hypertension in the Department of Cardio-thoracic Surgery, the General Infirmary, Leeds. Twenty-four of these patients (17 per cent) were under the age of 13 years and form the basis of this report.

For the purpose of this retrospective review the hospital records of all the patients have been examined and all the known survivors were interviewed. The details of the patients who have died or have been lost to follow-up were compiled by means of a questionnaire which was sent to the close relatives of these patients. Relevant radiographic and histological findings were reviewed. In all but one of the survivors (operated upon in 1964) the follow-up exceeds 10 years.

Age and Sex Distribution.—There was an even distribution from neonatal to the age of 13 years, with 50 per cent of the cases occurring before the age of 6 years. Four patients (17 per cent) presented within the first year of life and in 3 of these cases the obstruction was extrahepatic in origin. There was an equal number of male and female patients.

Clinical Features.—The initial presentation in 19 patients was the onset of severe unheralded gastro-intestinal bleeding. In all the cases bleeding occurred prior to surgery (*Table I*) and was therefore the principal indication for operation. In addition, 4 children presented with hepatosplenomegaly, 1 with ascites, and 2 with jaundice.

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The principal clinical findings are shown in *Table II*. Splenomegaly was found in all but 4 children; hepatomegaly and chronic anaemia were also frequent findings. It is interesting to note the occurrence of haemorrhoids in 3 children. Pancytopenia (W.B.C. 2000 and platelets 50,000) was found in 6 patients, although stigmata of liver disease were noted in only 5 cases.

Table I.—PRESENTING SYMPTOMS

Symptom		*No. of Cases*
Severe gastro-intestinal bleeding		24
Haematemesis and melaena	15	
Haematemesis alone	5	
Melaena alone	4	
Hepatosplenomegaly		4
Jaundice		2
Ascites		1

Table II.—CLINICAL FEATURES AT THE TIME OF SURGERY

Clinical Feature	*No. of Cases*
Splenomegaly	20
Hepatomegaly	15
Chronic anaemia*	11
Pancytopenia†	6
Features of liver failure:—	
Jaundice	2
Liver palms	2
Spider naevae	3
Ascites	4
Caput Medusae	3
Haemorrhoids	3

* Haemoglobin, 7 g.
† W.B.C., 2000, platelets, 50,000.

Diagnosis.—Gastro-oesophageal varices were demonstrated by barium-swallow examination in all the subjects and the varices were invariably confirmed by oesophagoscopy when this was performed (15 cases). Although splenoportography was undertaken in only 7 cases this was of considerable value in distinguishing between prehepatic and intrahepatic obstruction.

Aetiology.—The aetiology of portal hypertension in this series is shown in *Table III*. Extrahepatic obstruction was present in 10 children (42 per cent). Of these cases, the obstruction was confined to the portal vein in 9. One patient had a splenic vein thrombosis and normal liver histology. Bleeding occurred in this case from gastric varices. Thrombus occlusion of the portal vein occurred in 6 children; 2 had had exchange transfusions performed within a week of birth for Rhesus incompatibility and 2 had neonatal staphylococcal infections, one in the umbilical stump and the other in the buttock. Congenital absence of the portal vein was found in 3 children. This was associated with a cavernous transformation in 1 of them.

Table III.—AETIOLOGY OF PORTAL HYPERTENSION

AETIOLOGY	NO OF CASES	CLINICAL FINDINGS*				
		Splenomegaly	Pancytopenia	Ascites	Haemorrhoids	Liver Failure
Cirrhosis	12	9	5	0	1	5
Portal cirrhosis (non-specific)	5	4	2	—	—	3
Congenital hepatic fibrosis	5	5	1	—	1	—
Post-necrotic scarring	2	—	2	—	—	2
Extrahepatic obstruction	10	9	1	4	2	0
Splenic vein thrombosis	1					
Portal vein thrombosis (exchange transfusion, 2; umbilical sepsis, 1; buttock abscess, 1; unknown aetiology, 2)	6					
Absent portal vein (congenital atresia, 2; cavernoma, 1)	3	3	1	3	1	—
Idiopathic	2	2	—	—	—	0
Total	24	20	6	4	3	5

* Clinical findings apart from bleeding.

Histological evidence of liver disease was demonstrated in half of the patients. In 5 children features of congenital hepatic fibrosis, with dense bands of collagen surrounding relatively normal hepatic lobules, were found. In 2 of these patients their siblings were also known to have had the same pathology. Liver biopsy revealed a disordered architecture with centrilobular necrosis, periportal inflammation and sinusoidal hyperplasia in 2 patients where previous hepatitis had been present. There were 5 cases in whom patchy areas of fibrosis with a non-specific infiltrate of lymphocytes and eosinophils amongst islands of regeneration were seen. These cases were classified as idiopathic juvenile portal cirrhosis. There remain 2 children in whom the cause of portal hypertension was never established; in both cases liver histology was unremarkable and no evidence of extrahepatic obstruction was found.

The clinical features were studied in each group and a high incidence of pancytopenia with signs of liver failure was found in the children with cirrhosis It was interesting to note the absence of features of hepatocellular failure in the children with congenital hepatic fibrosis, and the frequency of pancytopenia in the patients with post-necrotic scarring. In contrast, liver failure and pancytopenia were rarely found in the children with extrahepatic obstruction On the other hand, 3 of our cases had haemorrhoids before the age of 13 years.

Associated Pathology.—In addition to the stigmata of portal hypertension, 2 patients with congenital absence of the portal vein were found to have an atrial septal defect, 1 of which was associated with anomalous pulmonary venous drainage. Bronchiectasis occurred in 1 patient with cirrhosis, and polycystic disease of both kidneys was found in a child with congenital hepatic fibrosis.

Surgical Treatment.—Surgical treatment consisted of gastro-oesophageal devascularization in 7 patients, splenectomy in 9 patients, and shunt surgery in a further 8 cases. The frequent use of direct surgical measures and splenectomy reflects the incidence of extrahepatic obstruction. Because of this, recurrent bleeding frequently occurred, requiring a total of 15 further operations on 11 patients.

Table IV.—TOTAL SURVIVAL RATE

LENGTH OF FOLLOW-UP (yr.)	NO. OF PATIENTS OPERATED UPON	NO. LOST TO FOLLOW-UP	KNOWN SURVIVORS	
			No.	Per cent
5	24	—	19	80
7	24	—	18	75
10	23	3	13	57
15	15	4	7	47
20	8	4	3	38

Table V.—RESULTS OF SURGICAL TREATMENT

TREATMENT	NO. OF CASES	FURTHER OPERATIONS			DEFINITIVE PROCEDURES	MORTALITY		SURVIVAL (yr.)					ALIVE	DEAD	LOST TO FOLLOW-UP
		1	2	3		Hospital	Early*	1	3	5	7	10			
Devascularizing procedures	7	5	1	–	2	1	1	2	–	–	1†	2	2	4	1
Splenectomy alone	9	6	2	1	3‡	1	—	–	–	–	2†	5§	5	1	3
Shunts	8	—	–	–	8	—	—	–	1	–	3	4	5	3	—
S.R.A.	1	—	–	–	1	—	—	–	–	–	1	–	1	–	—
Side-to-side P.C.A.	5	—	–	–	5	—	—	–	1	–	1	3	3	2	—
End-to-side P.C.A.	2	—	–	–	2	—	—	–	–	–	1	1	1	1	—
Total	24	11	3	1	13	2	1	2	1	–	3	11	12	8	4

* Within 6 months of surgery.
† Lost to follow-up.
‡ Patients treated for pancytopenia by splenectomy.
§ One patient lost to follow-up.
P.C.A., Portacaval anastomosis; S.R.A., Splenorenal anastomosis.

Table VI.—COMPLICATIONS FOLLOWING SURGERY

INITIAL OPERATION	COMPLICATION	NO. OF CASES	SUBSEQUENT OPERATIONS FOR BLEEDING
8 shunts (7 P.C.A. + 1 S.R.A.)			2 further shunts with thrombectomy
	Encephalopathy	3	
	Re-bleeding (thrombosis of shunt)	1	2 from recurrent thrombosis of shunt
	Diabetes	1	
8 splenectomies			
	Postoperative thrombosis (mesenteric portal vein thromboses)	2	
	Re-bleeding	6	
	Duodenal ulcer	1	
7 devascularizations			11 further devascularizations
	Re-bleeding	6	11
	Atonic stomach	1	1
	Dysphagia	1	1

The remainder of this report is concerned with the results of surgical treatment with particular reference to the aetiology and clinical presentation of the patients under review.

RESULTS

Of the 24 children treated for severe gastrointestinal bleeding complicating portal hypertension, 12 (50 per cent) are known to be alive at the present time. In 11 of these at least 10 years have elapsed since surgery was first performed. Eight (33 per cent) patients have died and 4 are now lost to follow-up, though all of the latter group were alive at least 8 years after surgical treatment. The overall survival figures are shown in *Table IV*.

Analysis of Initial Surgical Treatment.—The results of the initial surgical treatment for bleeding are shown in *Tables V* and *VI*. Gastro-oesophageal devascularization by meticulously dividing all the veins draining the lower oesophagus and cardia was performed in 7 children. In all but 2 cases further devascularizing procedures were required for recurrent bleeding, either upon the oesophagus alone (3 cases) or on the stomach as well (2 cases) using a modified Tanner's transection with extensive porta-azygous disconnexion. The results were uniformly disappointing, with 4 deaths within a year of the operation and only 2 known survivors. These procedures were followed by gastric stasis in 2 patients, requiring subsequent pyloroplasty, and by temporary dysphagia, requiring dilatation only, in 2 other cases.

Splenectomy alone was performed in 9 cases. There was 1 hospital death, 3 patients are now lost to follow-up, and 5 patients are alive. Further surgery (9 devascularizing procedures) for recurrent bleeding was required in all except 3 children in whom splenectomy was performed for pancytopenia. In the latter cases the blood-count returned to normal in the weeks following surgery, re-bleeding did not occur, and all are alive and symptom-free. Two patients developed thrombotic episodes after splenectomy; a superior mesenteric thrombus occurred, requiring extensive bowel resection in 1 child in the early postoperative period; in the other case thrombus formation in the portal vein occurred associated with massive ascites and severe haemorrhage requiring three devascularizing procedures. Both these patients are alive, despite considerable morbidity, 8 and 19 years respectively after surgery.

Table VII.—RESULTS OF SURGERY IN RELATION TO AETIOLOGY

AETIOLOGY	NO. OF CASES	SHUNTS	DEVASCULARIZATION	SPLENECTOMY	MORTALITY		ALIVE	DEAD	LOST TO FOLLOW-UP
					Hospital	Early			
Cirrhosis	12	7 (+1*)	1 (+3)	4 (+1)	–	–	5	4	3
Portal cirrhosis	5	1	– (+3)	4	–	–	2	–	3
Post-necrotic scarring	2	2	–	–	–	–	–	2	–
Congenital hepatic fibrosis	5	4 (+1*)	1	– (+1)	–	–	3	2	–
Extrahepatic obstruction	10	1 (+1*)	5 (+9)	4	2	1	5	4	1
Portal vein thrombosis	6	1 (+1*)	3 (+4)	2	1	1	3	2	1
Absent portal vein	3	–	2 (+5)	1	1	–	1	2	–
Splenic vein thrombosis	1	–	–	1	–	–	1	–	–
Idiopathic	2	–	1	1	–	–	2	–	–

* Thrombectomy of portal vein prior to portacaval anastomosis.
Figures in parentheses refer to subsequent operations.

Shunt procedures were undertaken in 8 children. Splenorenal anastomosis was used in only 1 child, aged 8 years, with a thrombus occlusion of the portal vein. In the remainder of the cases portacaval anastomosis was performed using a side-to-side anastomosis in 5 patients and an end-to-side shunt in 2 cases. None of these patients required further surgery, and although re-bleeding did occur in 1 patient this was shown to be due to late thrombosis of the shunt associated with ascites and liver failure from which she died. The overall known survival following shunt surgery was 63 per cent, though with only 1 exception all were alive 7 years after surgical treatment. Transient encephalopathy occurred in 3 cases. Both patients with an end-to-side anastomosis developed episodic stupor. In each case symptoms were adequately controlled on dietary measures and oral neomycin alone. Portacaval anastomosis was performed after initial thrombectomy in 2 other patients with a portal vein thrombosis. Bleeding and thrombosis recurred within 3 months of both procedures, however, and interruption of the varices at the oesophagus was thereafter required.

Surgical Treatment in relation to Clinical Presentation.—The only long-term survivors among the patients with pancytopenia were those treated by splenectomy alone. Of the patients with ascites prior to surgery, none left hospital after the initial surgical treatment. The operative stigmata of liver failure were not invariably associated with a poor long-term survival since 60 per cent of the patients with these remain well at follow-up and all survived for at least 5 years.

Results with reference to the Aetiology of Portal Hypertension.—In 12 children with cirrhosis 7 were treated by portacaval anastomosis, 4 by splenectomy, and 1 by direct ligation of the varices (*Table VII*). Although the 7-year survival was 75 per cent, less than half of the patients in this group are now known to be alive. It is said that the prognosis of patients with congenital hepatic fibrosis is much better than for those with infantile portal cirrhosis. However, our figures do not substantiate this view. There were no major complications following operation in patients with portal cirrhosis. In contrast, hepatocellular failure and encephalopathy occurred frequently after operation in the children with congenital hepatic fibrosis.

Table VIII.—RESULTS OF EMERGENCY AND ELECTIVE SURGERY

OPERATION	NO.	ALIVE	DEAD	LOST TO FOLLOW-UP
Initial operation				
Category:—				
A (1 shunt)	4	2	1	1
B	5	2	2	1
C (7 shunts)	15	8	5	2
Total	24	12	8	4
Further operations				
Category:—				
A (1 shunt)	8	1	6	1
B	0	—	—	—
C (1 shunt)	7	5	0	2
Total	15	6	6	3

A, Emergency operation within 24 hours of uncontrollable haemorrhage. B, Operation within a week of severe bleeding. C, Elective operation.

The results of surgical treatment in the children with extrahepatic obstruction were disappointing. The majority of these patients required repeated devascularizing procedures and the high mortality was directly attributable to massive uncontrollable haemorrhage.

Results in relation to the Timing of Operation.—Despite the small number of patients in this study there was no evidence that emergency operations carried a higher mortality when performed as an initial procedure (*Table VIII*). On the other hand, when surgical treatment for recurrent bleeding was performed, a far higher mortality-rate was found when this was undertaken as an emergency measure.

Morbidity in the Long-term Survivors.—By reviewing the 16 survivors in the first 8-year period following surgery 9 were found to be asymptomatic and fully employed. Five patients have had recurrent bleeding which has required further hospital admissions, but nearly all have been back at work between these attacks. There are 2 patients with controlled encephalopathy, neither of whom has been regularly employed.

Cause of Death.—Eight patients died following surgery; in 5 this occurred as a direct result of uncontrollable gastro-intestinal haemorrhage and in the remaining 3 from hepatocellular failure. The high mortality in the children with extrahepatic obstruction was entirely due to massive haemorrhage which theoretically should have been avoidable. It is not surprising, however, that most of the deaths in the cirrhotic group were the direct result of hepatic failure.

DISCUSSION

The clinical features of the children with portal hypertension in this study are similar to those described elsewhere (Trusler and others, 1962; Foster and others, 1963). Other authors also point out the importance of excluding portal hypertension in the differential diagnosis of splenomegaly in this age-group. Although it is said that bleeding is uncommon in the first year of life (Voorhees and others, 1965), 4 of the patients in this review bled during this time. It has been suggested that transient ascites often precedes the onset of varices in patients with extrahepatic obstruction (Mikkelson, 1966). We found that bleeding and ascites often coexisted in these cases. Many authors are of the opinion that the incidence of haemorrhoids is no higher in patients with portal hypertension than in the rest of the population (Goligher, 1967). Nevertheless, 3 cases in this series of 24 patients represent a significant incidence, particularly in the infant population. We should also like to stress the frequent occurrence of pancytopenia associated with hypersplenism in children with cirrhosis.

Much discussion has centred on the importance of omphalitis and exchange transfusion in the aetiology of extrahepatic obstruction (Shaldon and Sherlock, 1962; Thompson and Sherlock, 1964; Mikkelson, 1966). Although portal hypertension is a rare complication of these incidents, 50 per cent of the cases in this series had a history of one of these occurrences. In at least 2 cases extrahepatic obstruction was considered to be due to congenital atresia of the portal vein and in both cases this was associated with an atrial septal defect. This association had not previously been recorded. On the other hand, the coexistence of portal hypertension and polycystic disease, which occurred in 1 of our patients, has recently been described (Gailsford and Bloor, 1968).

Congenital hepatic fibrosis is an uncommon cause of infantile portal hypertension (Sherlock, 1968b). These patients usually present with bleeding varices, and hepatocellular damage is considered uncommon. For this reason, therefore, shunt operations have been advocated. There were 5 children with this condition in the present series. However, the results of portacaval anastomosis were disappointing, with 2 deaths, 1 of which was due to hepatic failure. The majority of reports include a small number of patients in whom the aetiology of portal hypertension has never been explained (Hsia and Gellis, 1955; Sherlock, 1968a). Two patients in this study are considered to be in a similar category. These cases may be due to presinusoidal fibrosis associated with normal liver architecture (Mikkelson, Edmondson, Peters, Redeker, and Reynolds, 1965).

It is unrewarding to compare the long-term results from other centres, particularly because of the variation in the aetiology and the duration of follow-up. However, in series with a similar length of follow-up and incidence of cirrhosis, the results of surgery compare favourably with those of the present series (Trusler and others, 1962; Foster and others, 1963; Voorhees and others, 1965; Foukalstrud and Longmire, 1969).

All attempts to control bleeding by gastro-oesophageal surgery directed to the varices themselves can only be considered to be of temporary benefit (Mikkelson, 1966; Rothwell-Jackson and Hunt, 1970). Splenectomy is regarded as being inadequate and also jeopardizing the construction of splenorenal shunts in extrahepatic obstruction (Trusler and others, 1962; Foster and others, 1963). In addition, however, there is an increased risk of thrombosis following splenectomy which was a major cause of morbidity in 2 of our patients. On the other hand, splenectomy for pancytopenia with hypersplenism in 3 patients with cirrhosis was associated with excellent results.

The results of surgery in patients presenting with ascites was uniformly disappointing. When emergency devascularization was undertaken after a previous operation for bleeding a high mortality was noted, even though many of these patients had an extrahepatic obstruction, in which bleeding is said to be well tolerated (Voorhees and others, 1965).

The benefit obtained from portacaval anastomosis was encouraging, particularly as all these operations were performed in children with cirrhosis. However, most of the patients were at least 7 years of age at the time of operation. Shaldon and Sherlock (1962) point out that portacaval anastomosis for patients with liver disease should not be undertaken under the age of 8 years because of the dangers of thrombosis at the site of the shunt. A splenorenal anastomosis was only performed in 1 patient with prehepatic obstruction, largely because the ages of the remaining subjects precluded such a procedure. Attempts to clear the portal vein of thrombus prior to portacaval anastomosis for extrahepatic obstruction were so disappointing that this procedure has virtually been abandoned. Since patients with extrahepatic obstruction usually present at an early age where for reasons of vessel size splenorenal shunts may be complicated by thrombosis, the procedure is now usually reserved for children over the age of 8 years (King and Shumacker, 1958; Trusler and others, 1962). For this reason the mesenteric caval shunt is considered to be the treatment of choice in patients under 5 years of age with prehepatic obstruction (Lord and others, 1970; Rothwell-Jackson and Hunt, 1970).

CONCLUSIONS

Portal hypertension in children may be due to intra- or extrahepatic obstruction. Congenital hepatic fibrosis may account for a small number of patients in the former group in whom hepatocellular damage is clinically unrecognizable. Prehepatic obstruction may be either congenital, in which case other anomalies of development may coexist, or acquired following exchange transfusion or neonatal sepsis.

The majority of these patients present with major gastro-intestinal haemorrhage. Bleeding oesophageal varices must be considered to be an absolute indication for surgery since recurrent bleeding will invariably occur and the hazards of emergency surgery in such a situation are considerable.

Extrahepatic obstruction is best treated by splenorenal anastomosis in patients over the age of 8 years or by mesenteric-caval shunt before this age. Children with cirrhosis deserve definitive shunt surgery if further bleeding is to be prevented. Direct gastro-oesophageal surgery is of temporary benefit only, but is justified after failed protosystemic shunts or in patients where for reasons of age these procedures would be technically inadvisable.

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TRANSECTION OF THE OESOPHAGUS FOR BLEEDING OESOPHAGEAL VARICES

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SUMMARY

Emergency ligation of bleeding oesophageal varices using the Milnes Walker technique was performed in 38 patients. Haemorrhage continued or recurred in hospital in 11 patients, all of whom subsequently died. A further 10 patients died in hospital following operation from hepatic failure and a variety of other causes. Five patients were finally considered suitable for elective shunt surgery, but of 12 patients who were discharged without a further operation, only 2 have re-bled. Although the overall 6-month survival was 32 per cent, in patients with good preoperative liver function this rose to 71 per cent, and the simple scoring system for grading the severity of disturbance of liver function was found to be of value in predicting the outcome of surgery.

Since the results of emergency ligation of bleeding oesophageal varices in our hands have been so disappointing we are currently using it less and are trying the mesenteric caval jump graft as an emergency operation for the control of bleeding varices.

ABOUT half of the patients admitted to hospital with bleeding oesophageal varices die during their admission (Ratnoff and Patek, 1942; Hislop, Waters, Kellock, and Swynnerton, 1966; Orloff, 1966), and the first aim of treatment must be to stop the haemorrhage by the fastest and simplest means available. Although treatment with the Sengstaken-Blakemore tube and intravenous vasopressin is usually effective initially, the former can be used for only 24–48 hours and the latter may have serious cardiac side-effects (Beller, Trevino, and Urban, 1971). In many patients haemorrhage recurs after initial control (Shaldon and Sherlock, 1960; Hermann and Traul, 1970), and in those in whom there are features of terminal liver failure no further treatment is indicated, but in others some form of surgery is required. Our policy (Williams and Dawson, 1968) has been to carry out ligation of the oesophageal varices via the transthoracic approach (Walker, 1964) after controlling the haemorrhage for 24 hours by other means, as this is a simpler and more rapid procedure than emergency portacaval anastomosis and has a lower immediate postoperative mortality. The aim was to assess these patients during the ensuing 6–8 weeks for definitive portacaval anastomosis after the bleeding had been controlled.

In this paper we report the results of such an approach in the management of 38 patients admitted as an emergency with bleeding oesophageal varices, the results being considered in relation to the severity of liver failure present as assessed by a simple grading system.

PATIENTS, PREOPERATIVE ASSESSMENT, AND THERAPEUTIC RÉGIME

The series comprises 38 patients seen between January, 1966, and July, 1972. It is a consecutive series except for 18 patients who formed part of an evaluation of prolonged infusion of the superior mesenteric artery with vasopressin (Murray-Lyon, Pugh, Nunnerley, Laws, Dawson, and Williams, 1973) in the control of oesophageal bleeding. Four of these patients who later had ligation of their varices are included in this series. No patient had undergone previous surgery for variceal haemorrhage. The causes of portal hypertension were alcoholic cirrhosis (13), cryptogenic (13), active chronic hepatitis (6), primary biliary cirrhosis (3), Wilson's disease (1), partial nodular transformation of the liver (1), and extrahepatic portal vein block (1). Varices were demonstrated in every patient by barium-meal studies or endoscopy, and no other potential bleeding site was shown prior to operation.

Nineteen patients had hepatic encephalopathy, 19 had jaundice, and ascites was clinically detectable in 17 patients. The combination of jaundice, ascites, and encephalopathy was present in 13 patients. These clinical features formed part of our grading of the severity of liver disease which was based on that originally described by Child (1964), but in addition included prolongation of the prothrombin time and omitted the assessment of body nutrition (*Table I*).

Table I.—GRADING OF SEVERITY OF LIVER DISEASE

CLINICAL AND BIOCHEMICAL MEASUREMENTS	POINTS SCORED FOR INCREASING ABNORMALITY		
	1	2	3
Encephalopathy (grade)*	None	1 and 2	3 and 4
Ascites	Absent	Slight	Moderate
Bilirubin (mg. per 100 ml.)	1–2	2–3	>3
Albumin (g. per 100 ml.)	3·5	2·8–3·5	<2·8
Prothrombin time (sec. prolonged)	1–4	4–6	>6
For primary biliary cirrhosis:—			
Bilirubin (mg. per 100 ml.)	1–4	4–10	>10

* According to grading of Trey, Burns, and Saunders (1966).

This system makes use of weighting whereby 1, 2, or 3 points are scored for increasing abnormality of each of the five parameters measured. Thus, in patients with good hepatic function the total score is 5 points whereas patients with poorer hepatic reserve have scores of up to 15 points. Those patients whose score totalled 5 or 6 were considered to be good operative risks (grade A), 7, 8, or 9 moderate (grade B), and patients with 10–15 poor operative risks (grade C). Allowance is made in the grading for patients with primary biliary cirrhosis in whom the level of serum bilirubin is usually out of proportion to other evidence of hepatic failure. Of the complete series, 7 patients were placed in grade A, 13 in grade B, and 18 in grade C categories.

Details of Therapy.—All the patients were placed on an anti-hepatic coma régime and parenteral vitamin K was given routinely. Blood transfusion was required in each patient and in most patients an attempt was made to control the haemorrhage for 24–36 hours prior to carrying out the transection. For this, systemic vasopressin was used in 6 patients and in 3 of these a Sengstaken-Blakemore tube was also passed. The latter was used alone in 18 patients and in 4 other patients who had initially received vasopressin by selective infusion of the superior mesenteric artery.

The oesophagus was transected by the Milnes Walker technique via a left thoracotomy approach. Large peri-oesophageal veins were ligated, the lower oesophagus was exposed and mobilized, and an atrial clamp was placed across the oesophagogastric junction. The lower oesophageal muscle was split longitudinally, the mucosal tube containing the submucosal varices was dissected free, and the clamp was opened. The mucosal tube was then pulled up and the clamp was reapplied, thus allowing a lower mucosal transection. The mucosal tube was resutured with continuous catgut, the subsequent healing process occluding the varices. Oral fluids were avoided for the first 5 postoperative days and a Gastrografin swallow was then performed to confirm that there was no leakage from the oesophagus.

RESULTS

Following operation the bleeding continued or recurred in 11 patients (*Table II*), all of whom subsequently died in hospital from the bleeding (9) or following an emergency portacaval anastomosis (2) carried out in an attempt to control the bleeding. The sources of haemorrhage were shown to be a separated oesophageal anastomosis (1), the suture line (2), an oesophageal varix above the suture line (1), a tear in the stomach mucosa (1), and a large acute gastric ulcer (1). No certain bleeding site could be found in 4 cases and in the remaining case no autopsy was performed.

Table II.—RESULTS OF TRANSECTION OF THE OESOPHAGUS COMPARED WITH THE PREOPERATIVE CLINICAL GRADING

GRADE	NO OF PATIENTS	RE-BLED	DIED		SURVIVED FOR 1 YEAR
			In Hospital	Within 6 Months	
A	7	1	2	0	5
B	13	4	5	2	4*
C	18	6	14	3	0†

* Plus 2 patients who survived for less than 6 months

† Plus 1 patient who survived for less than 6 months.

Of the remaining 27 patients in whom bleeding was controlled, 10 died in hospital within 30 days of transection of the oesophagus from liver failure (4), chest complications (3), unexpected cardiac arrest (1), disseminated hepatoma (1), and meningitis (1). Thus 21 (55 per cent) of the total series of 38 patients did not survive to leave hospital.

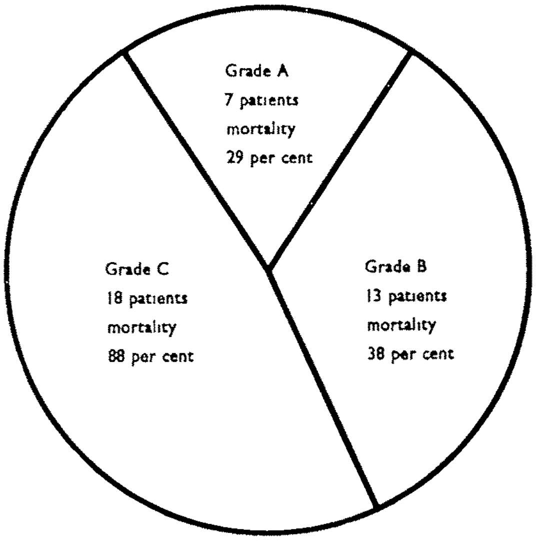

FIG 1.—Operative mortality in each grade of liver disease.

Of the 17 patients who were discharged from hospital, 5 had an elective portasystemic shunt and 3 of these are alive after 2 years and 2 have died of liver failure. The remaining 12 patients had no further treatment as their liver function was not considered adequate for a shunt procedure, and of these, 4 are alive at 2 years including the 2 patients without cirrhosis, and 3 are alive at less than 6 months after operation. Two other patients have died of liver failure and 1 of anorexia nervosa. Only 2 patients so far have re-bled, one dying at 6 months and the other at 1½ years.

For the complete series of 38 patients the overall 6-month survival was 32 per cent and the 2-year survival 20 per cent. When the results are considered in relation to the grading of severity of liver disease significant differences between the groups are observed (*Table II* and *Fig.* 1). Thus, of the grade A patients, 5 (71 per cent) left hospital and survived for at least 6 months, and 3 (43 per cent) survived for 2 years. Eight patients (62 per cent) of the grade B group left hospital and 4 (36 per cent) were alive at 6 months and also at 2 years. Only 4 (22 per cent) of the grade C patients left hospital, and none survived for 6 months.

DISCUSSION

The 55 per cent mortality in hospital in this series is similar to that reported by others for oesophageal variceal ligation. In Walker's (1964) series, 6 of the 16 cirrhotic patients died postoperatively. However, in most of the other reported series the Boerema-Crile operation has been employed (Orloff, 1966, 1967). In this procedure a longitudinal incision is made through both the muscular and mucosal layers and oesophageal closure is potentially less safe. Indeed, in the series of 58 patients reported by Rothwell-Jackson and Hunt (1971) there were 10 patients in whom the anastomosis leaked and all of these died. There was only one anastomotic leak in our series. It is difficult to compare the results of the various series because of differences in type and severity of liver disease, but comparison would be facilitated by the adoption of a grading system such as we have used. Both types of operation seem to control variceal haemorrhage in most patients and the high operative mortality is to a large extent a reflection of the severity of the underlying liver disease.

The outcome of operation in our series did not seem to be influenced by the age or sex of the patient, the presence of jaundice or encephalopathy, or individual liver-function tests considered separately. However, with one exception no patient with moderate or gross ascites or a combination of jaundice, ascites, and encephalopathy survived to leave hospital. Our method of grading the severity of liver disease is more flexible than that originally described by Child (1964), in which a low serum albumin alone was sufficient to place a patient who otherwise had good liver function into grade C. In the present series the operative mortality and long-term survival were closely related to the preoperative grade, and in grade C the results were so poor that operation on such patients does not seem justified unless there is a clear additional and reversible factor which may partially account for the poor liver function. For instance, in 1 patient the C grading on admission was partly due to a period of heavy drinking and her score improved by 5 points postoperatively whereas no other patient improved by more than 2 points. If all grade C patients are omitted from analysis the operative mortality in our series is reduced to 35 per cent.

It was disappointing that bleeding continued or recurred in hospital after operation in 11 of the 38 cases. Although the source of the haemorrhage was not always obvious, in most cases it seems likely to have been due to varices at or above the suture line, and a more extensive portasystemic disconnexion (Tanner's operation; Tanner, 1961) might have been more effective although this is a more major operation. Only 5 patients were considered suitable to follow the planned course and to undergo elective portacaval anastomosis, and this is an indication that most patients admitted as emergencies with bleeding varices have severe underlying liver disease. However, it is interesting that only 2 of the 12 patients who were discharged without a further procedure have re-bled and 7 of these patients are still alive.

Acknowledgements.—We are grateful to Sister Gladys and the nurses of Todd Ward for their expert care of the patients reported here.

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INTERPOSITION TEFLON MESENTERIC CAVAL SHUNT FOR BLEEDING OESOPHAGEAL VARICES

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SUMMARY

A modified mesenteric caval shunt using a Teflon 'H' prosthesis has been performed in 4 poor-risk patients with cirrhosis and exsanguinating haemorrhage from oesophageal varices and a fifth patient with portal vein thrombosis. Although 2 patients ultimately died, the procedure was effective in arresting the haemorrhage and is technically simple to perform.

SIDE-TO-END mesenteric caval shunt is technically difficult to perform and the division of the inferior vena cava results in undesirable sequelae. Thus, this type of operation has hitherto been largely confined to patients with extrahepatic portal obstruction in whom neither the portal nor the splenic vein is available for anastomosis. However, the recent report of Lord, Rossi, Daliana, and Rosati (1970) suggests that a satisfactory mesenteric caval shunt can be readily constructed by using a Teflon prosthesis between the two veins in the form of an 'H'.

We have used this technique in 5 patients in whom bleeding from oesophageal varices continued despite protracted conservative therapy. Four of the 5 patients were considered to be poor risks because of age or liver failure and it was felt that this operation might prove to have a lower mortality than other types of shunt surgery in such subjects. In the fifth patient a mesenteric caval shunt seemed to be the only appropriate procedure available.

SURGICAL TECHNIQUE

Under general anaesthesia and with adequate means for rapid intravenous infusion, the abdomen is opened through a long midline incision. After a thorough inspection of the intra-abdominal viscera, the transverse colon is lifted upwards and forwards by an assistant and dissection is begun at the root of the mesocolon, having first palpated the position of the superior mesenteric artery. The superior mesenteric vein lies to the right of its companion artery, crossing the third part of the duodenum to pass behind the pancreas (*Fig.* 1). It was necessary on each occasion to carry the dissection over the duodenum to the lower edge of the pancreas in order to mobilize a sufficient length of vein of wide calibre for anastomosis. It has also proved necessary to sacrifice one or two jejunal, colonic, and duodenal branches of the vein in order to provide access.

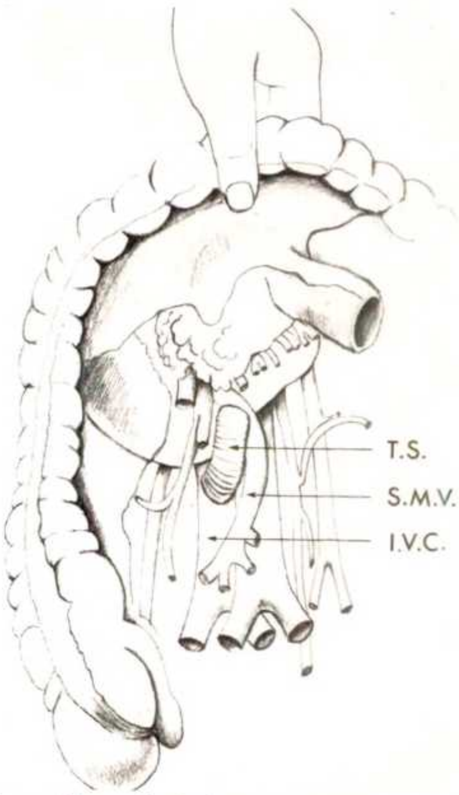

FIG. 1.—Diagram showing the position of the Teflon prosthesis (T.S.) between the superior mesenteric vein (S.M.V.) and the inferior vena cava (I.V.C.).

Having ensured that the superior mesenteric vein is patent and of sufficient calibre to accept the Teflon graft, the inferior vena cava is exposed by mobilizing the right colon and caecum towards the midline. The anterior and lateral surfaces of the vena cava are cleaned for about 5 cm. but it has not been necessary to complete the dissection around the vena cava.

The superior mesenteric vein is clamped and by rotating the clamps to expose its posterior surface a Teflon graft between 16 and 18 mm. in diameter is anastomosed to a suitably placed venotomy with a 00000 continuous Dacron suture. The graft is then passed through a hole in the right mesocolon so as to lie in a natural curve around the duodenum. The prosthesis is cut to a suitable length and the other end is anastomosed to the inferior vena cava which has been side-clamped with a large hexagonal clamp. Before completing this anastomosis the graft is first flushed by releasing the clamp on the superior mesenteric vein which is temporarily reclamped while placing the last one or two stitches (*Fig.* 1).

The right colon is replaced without fixation and the peritoneum over the superior mesenteric vessels is repaired with a continuous catgut suture. The abdomen is closed in layers with non-absorbable sutures.

CASE REPORTS

Case 1.—A female, aged 66 years, was admitted to another hospital in a coma, following a massive haematemesis. There was no previous history of liver disease, but jaundice, peripheral stigmata of liver disease, hepatomegaly, and ascites were present. Eighteen pints of blood were transfused, the coma was treated with neomycin and colonic wash-outs, and the patient underwent surgery 12 days later.

Immediately prior to operation the serum bilirubin was 3·6 mg. per cent, serum albumin 3·0 g. per cent, serum urea 30 mg. per cent, and the prothrombin time after massive vitamin-K administration was 16 seconds with a control of 12 seconds. The venous phase of a superior mesenteric arteriogram revealed a patent superior mesenteric vein and reversed flow down the portal vein from the liver.

The establishment of the Teflon shunt reduced the jejunal vein pressure from 37 to 25 cm. H_2O. Postoperatively there was an early recovery without signs of encephalopathy. Barium-swallow examination and oesophagoscopy 3 months after surgery revealed no evidence of oesophageal varices. There was no recurrent bleeding during the first postoperative year or evidence of encephalopathy, but the biochemical indices of liver function continued to deteriorate.

Case 2.—A female, aged 75 years, was first known to have cirrhosis when she underwent cholecystectomy in February, 1967. Over the next 4 years she suffered several severe haematemeses which required blood transfusions. She was again admitted to hospital in February, 1971, with a massive haemorrhage requiring the transfusion of 15 pints of blood. After the passage of a Sengstaken tube immediate control of bleeding was obtained, but there was recurrent bleeding after the tube was removed and the patient was transferred to St. James's Hospital. The Sengstaken tube was replaced, and after a further 4 pints of blood had been transfused the patient was operated upon and a Teflon shunt was inserted without technical difficulty. Four litres of ascitic fluid were removed at surgery.

Immediately prior to operation the serum bilirubin was 2·6 mg. per cent, serum albumin 2·5 g. per cent, serum urea 60 mg. per cent, and the prothrombin time had returned to normal after vitamin-K administration.

Postoperatively the patient remained well for 72 hours, after which she slipped into a Grade II hepatic coma which responded slowly to neomycin and colonic wash outs.

During the 12 months after operation the patient ha taken 2 g. of neomycin daily without further signs o encephalopathy. Barium-swallow examination shows n varices and there have been no further episodes of gastrointestinal bleeding. Although biochemical tests of live function continue to deteriorate, there has been n reaccumulation of ascites.

Case 3.—A female, aged 57 years, had 1 year previousl undergone a laparotomy at another hospital for wha appeared to be obstructive jaundice. However, a shrunke cirrhotic liver was found and the patient remaine jaundiced during the next 12 months. She next presente with continued haematemesis and hepatic precoma an was treated with intravenous Pitressin and a transfusion o 12 pints of blood. However, the bleeding continue unabated and the patient was transferred to St. James' Hospital where she was found to be severely jaundice (total bilirubin 24·8 mg. per cent) and disorientated and t have stigmata of chronic liver disease. The abdomen wa grossly distended with ascites and there was pitting oedem of the lower half of the body.

A barium-swallow examination showed oesophagea varices, the serum electrolytes and urea were markedl abnormal (sodium 122 mEq./l., chloride 81 mEq./l., ure 179 mg. per cent), and the serum albumin was low (2·4 g per cent).

Although the patient continued to vomit large amount of fresh blood, surgery was withheld for several days i order to try to improve her general condition. However, i became clear that the outlook was very poor withou surgery and, in the hope that portal decompression migh be life-saving, a Teflon mesenteric caval shunt wa established without further investigation. No technica difficulties were experienced.

Postoperatively the initial course was good for 48 hour but thereafter she rapidly became comatose and die 72 hours after surgery. Post-mortem examination reveale the Teflon graft to be partially obstructed by thrombosi with resultant venous congestion of the small intestine This failure was almost certainly due to narrowing of th inferior vena caval anastomosis by one stitch picking u the back wall about one-third of the distance along th suture-line.

Case 4.—A male, aged 57 years, was first diagnosed a suffering from alcoholic cirrhosis in 1959 but was relativel untroubled until 12 years later when he presented a another hospital with an uncontrollable haematemesi from oesophageal varices. After a trial of medical treatment and having received 10 pints of blood, the patien underwent a porto-azygous disconnexion and splenectom which were initially successful in averting bleeding However, 6 weeks later haemorrhage recurred, and durin the next 4 weeks a further 12 pints of blood were transfused and it was attempted to control the haemorrhag by a Sengstaken tube and intravenous Pitressin. Th patient was then transferred to St. James's Hospital wher he was found to be jaundiced (serum bilirubin, 8·9 mg per cent) and to have stigmata of chronic liver disease. pronounced liver flap was present with mild disorientation The abdomen was soft with evidence of ascites and th liver was enlarged three fingers' breadth below the costa margin. There was marked ankle oedema.

Investigations revealed a haemoglobin of 7·1 g. per cent platelet count of 67,000 per c.mm., serum albumin o 3 g. per cent, prothrombin time after vitamin-K administration of 19 seconds (control 15 seconds), and serum ure of 105 mg. per cent. A coeliac axis arteriogram demonstrated filling of the portal and superior mesenteric vein during the venous phase.

Vomiting of large quantities of bright-red bloo continued and surgery was carried out. No unusua technical problems were encountered and the post-shun pressure in a jejunal vein was reduced to 20 cm. H_2O from a pre-shunt pressure of 35 cm. H_2O.

Six hours after operation the patient collapsed and became comatose. Neomycin and colonic wash-out produced no improvement, and a tracheostomy was performed on the fourth postoperative day. Melaena occurred continuously for 1 week, necessitating repeated blood transfusions. The bleeding did not recur but bronchopneumonia and renal failure supervened and the patient died $2\frac{1}{2}$ weeks postoperatively.

Case 5.—A male, aged 32 years, had been operated on 6 years previously for bleeding oesophageal varices. At laparotomy an extrahepatic portal vein thrombosis had been found but an attempt at a definitive portacaval shunt had been made. However, the shunt had not effectively decompressed the portal system and bleeding had recurred 6 and 12 months later. Splenectomy had then been carried out but bleeding had recurred on several occasions, necessitating repeated blood transfusions.

After transfer to St. James's Hospital on the present admission a superior mesenteric arteriogram was carried out which, on subtraction films (*Fig.* 2), revealed a patent superior mesenteric vein although the portal vein appeared thrombosed. Liver-function tests showed no abnormalities.

A Teflon mesenteric caval shunt was constructed without technical difficulty, with reduction of the jejunal vein pressure from 35 to 22 cm. H_2O. The postoperative course was uneventful. Barium-swallow examination 3 months after operation revealed no trace of varices and there has been no recurrence of bleeding up to 9 months postoperatively.

DISCUSSION

Mesenteric caval shunts were introduced independently by Marion (1953) in France and by Clatworthy, Wall, and Watman (1955) in the United States of America. The operation was designed mainly to deal with patients with bleeding oesophageal varices in whom the portal and splenic veins were not available for anastomosis. Thus, the majority of patients selected for this procedure were children in whom the portal vein had thrombosed, or in whom the splenic vein was too small for shunting purposes, or who had already undergone splenectomy. The operation was also used in adult patients in whom a previously constructed portacaval shunt had thrombosed.

While the operation usually results in a wide shunt, certain technical difficulties are not unusual. In some patients the length of the vena cava is insufficient to curl easily around the lower border of the duodenum and difficulty is encountered in performing the anastomosis without distortion. Since the technique involves division of the vena cava there is venous stasis of the lower limbs and chronic oedema is to be expected. This has not proved a problem in younger patients, but adults have needed elastic support and diuretics in order to keep the oedema under control (Voorhees and Blakemore, 1962).

Possible advantages of a mesenteric caval shunt are that it is, in effect, a side-to-side shunt which in contrast to an end-to-side shunt could allow blood to drain from the liver if the haemodynamic situation requires it (Gliedman and Margulies, 1964). In other circumstances the shunt could allow continued portal flow to the liver and thus perhaps help to preserve residual hepatic function. As with splenorenal shunts, the mesenteric caval shunt is in a peripheral part of the portal system and postoperative encephalopathy should be relatively uncommon. However, mesenteric caval shunts have not found favour with the majority of surgeons. The largest series have been reported by Voorhees and Blakemore (1962) and Gliedman (1965). While the results in each study were satisfactory in the relief of variceal bleeding, there was no clear advantage over the portacaval shunt for the uncomplicated case of chronic liver disease.

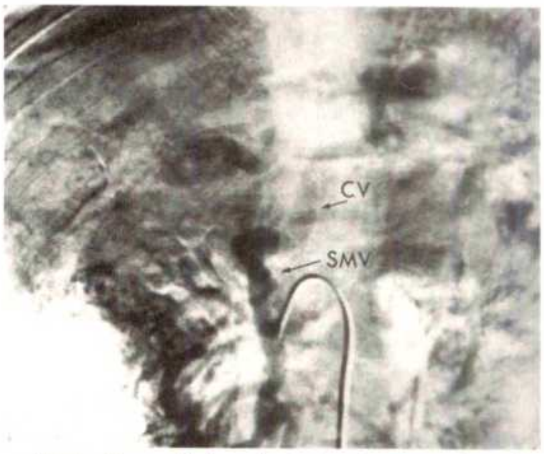

FIG. 2.—*Case* 5. Radiograph showing the venous phase of a superior mesenteric arteriogram outlining the superior mesenteric vein (S.M.V.) and a large collateral vein (C.V.) extending towards the cardio-oesophageal junction. No filling of the portal vein is demonstrated.

Interposed grafts of autogenous veins, homologous arteries, or synthetic materials such as Teflon and Dacron have been used in surgery of the portal venous system. Experimental studies suggest that autogenous veins and Teflon grafts give the most satisfactory results although routine anticoagulation may be necessary to ensure continued patency (Foster, Jolly, Symbas, and Dively, 1965). In the clinical situation vein-grafts have been used to bridge the gap between the portal vein and inferior vena cava in the hilum of the liver (Reynolds and Southwick, 1951; Foster and others, 1965). This technique may be advantageous where a side-to-side shunt is proposed and the portal vein is found to be short and the caudate lobe of the liver enlarged. Rousselot (1952) suggested that splenorenal shunts could be simplified if vein-grafts were used. However, while the early results in 4 patients were satisfactory, it has been reported that all of these grafts ultimately thrombosed.

Construction of mesenteric caval shunts by interposed grafts using a Teflon prosthesis has been reported by Lord and others (1970). Of the 7 patients studied by Lord and others (1970), in 1 case the shunt eventually thrombosed but the remaining patients were apparently in good health, although it is not clear whether these patients had been suffering from chronic liver disease originally. Read, Thompson, Wise, and Murphy (1970) reported 9 mesenteric caval shunts using vena caval homografts. In 2 of the patients the shunts ultimately thrombosed but 4 patients survived without further bleeding. Drapanas (1972) has reported the use of an interposition Dacron mesenteric caval shunt in 25 cirrhotic patients with an operative mortality of 8 per cent. Although the mean follow-up time of these patients is only

19 months, there has been an encouraging lack of re-bleeding and encephalopathic complications. Investigation of 15 of these patients has shown complete success with regard to long-term patency of the graft.

Our own experience with Teflon mesenteric caval shunts is limited to 5 patients with bleeding varices. One patient with extrahepatic portal vein thrombosis had undergone two unsuccessful attempts at portal decompression. A Teflon mesenteric caval shunt caused a considerable reduction in the portal hypertension with resolution of the varices without the need to divide the vena cava. The other 4 patients had exsanguinating haemorrhages from oesophageal varices and all had severe disturbance of liver function, with jaundice, ascites, and hypo-albuminaemia. It was hoped that a mesenteric caval shunt would decompress the portal system sufficiently to control the bleeding, and at the same time help to preserve liver function by not shunting all the portal blood away from the liver. It was also hoped that it would prove to be a simpler operation, but it must be admitted that at this stage of our experience this procedure had not reduced the operating time required or the degree of operative dissection in these very ill patients. The 2 patients with the severest degrees of liver decompensation died following the operation and in 1 there was clear evidence of further bleeding. The other 2 patients have made good recoveries and follow-up barium-meal and endoscopic studies have shown disappearance of the oesophageal varices. The mortality in these patients seems to be no greater than for the relatively simple Boerema-Crile operation, which requires a later definitive operation, or for emergency portacaval anastomosis with its attendant disadvantages (Wantz and Payne, 1961; Rothwell-Jackson and Hunt, 1971).

It seems possible that the Teflon mesenteric caval shunt might avoid the problems of lower-limb venous stasis in addition to having the other advantages of a mesenteric caval shunt. The experience of Lord and others (1970) would suggest that long-term patency of the graft can be achieved. It is also our impression that the procedure can be performed in the emergency situation without recourse to investigations to demonstrate patency of the portal and splenic veins. The main place for this type of operation will undoubtedly be in the management of patients with portal and splenic vein thrombosis, but the technique may also be useful when an emergency laparotomy has been carried out for gastro-intestinal bleeding and the surgeon is faced with unsuspected portal hypertension. In addition, we suggest that further assessment of its use as an emergency procedure in poor-risk patients is warranted.

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CIRCULATORY PATTERNS IN THE NORMAL HAND

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SUMMARY

Circulation in 100 apparently normal hands was studied clinically by the use of the Allen test and ultrasonically with a Doppler flowmeter. Circulatory dynamics in the hand were found to follow a very variable pattern, the ulnar artery being the dominant source of supply in most hands. It was concluded that collateral circulation in the hand would generally maintain viability of the fingers when either the radial or ulnar artery was occluded at the wrist. In 9 per cent of hands, however, there was evidence of more drastic disturbance of the circulation on occlusion of the ulnar artery, and in 6 per cent the same finding was made upon occlusion of the radial artery. The Allen test was positive in only 3 per cent of the hands, and in each case the ultrasonic examination confirmed the dependence of the digital circulation on a single artery at the wrist. It is suggested that these variations in collateral adequacy in the hand may explain ischaemic phenomena seen in some patients with the 'hammer-hand' syndrome, in a few patients after radial artery cannulation for monitoring purposes, and in a somewhat higher percentage of patients having arteriovenous fistulae constructed at the wrist for long-term haemodialysis. It is also suggested that patients undergoing procedures which will distort radial artery haemodynamics in the hand should be screened to test collateral adequacy.

THE radial artery at the wrist is a frequent site of surgical assault. It is convenient and relatively simple to cannulate the radial artery at this point when an indwelling arterial catheter is to be used for monitoring purposes. The radial artery is also readily accessible for the construction of arteriovenous fistulae in patients requiring long-term haemodialysis. It is assumed that the collateral circulation in the hand is generally adequate to cope with the haemodynamic disturbances thus created. Indeed, the hand is well supplied with arterial blood and communications between the radial and ulnar artery are provided through the dorsal arterial arch, the deep palmar arch, and, most important of all, the superficial palmar arch. The superficial palmar arch is completed on the radial side usually by junction with the radialis indicis or the princeps pollicis arteries and this communication is often small, measuring less than 2 mm. in diameter (McCormack, Cauldwell, and Anson, 1953).

There is increasing information to suggest that interruption of the radial artery flow may be less benign than has been assumed. Serious ischaemia of the hand with tissue loss has been reported in a relatively small percentage of cases following radial artery cannulation for monitoring purposes (Samaan, 1971), and in a somewhat larger number of cases following the construction of arteriovenous fistulae for maintenance haemodialysis (Storey, George, Stewart, Tiller, May, and Sheil, 1969; May, 1972). Although the percentage of patients who are prone to serious ischaemia may be low, tissue loss under such circumstances represents a major disaster.

The ulnar artery at the wrist is less prone to iatrogenic damage, but is particularly susceptible to trauma where it lies in relation to the hook of the hamate in the palm of the hand (Barker and Hines, 1944). The syndrome of digital ischaemia resulting from thrombosis of the superficial palmar branch of the ulnar artery at this site following prolonged use of the hand as a hammer has recently attracted considerable attention (Conn, Bergan, and Bell, 1970; Little and Grant, 1972; Millender, Nalebuff, and Kasdon, 1972). An industrial study has suggested that relatively asymptomatic examples of this 'hammer-hand' syndrome may be fairly common (Little and Ferguson, 1972), and that the development of symptomatic ischaemia may depend on individual variations in collateral adequacy between the radial and ulnar arteries.

In order to investigate possible means of predicting digital ischaemia after arterial damage at the wrist we have conducted a study of 100 hands, using clinical and ultrasonic methods of examination.

MATERIAL AND METHODS

Fifty randomly selected normal volunteers were used in this study. None of them had obvious clinical abnormalities affecting their hands, either on questioning or physical examination.

Clinical Examination.—All the hands were clinically examined by the Allen test (Allen, 1929), using strict criteria. The Allen test is carried out as follows. The patient is asked to clench his fist as tightly as possible so as to drive the blood out of his hand. The radial and ulnar arteries are then firmly compressed at the wrist. The fingers are partly straightened so that they are extended and relaxed. Hyper-extension of the fingers can produce a false-positive test. The hand appears bloodless and ischaemic while the two arteries are held compressed. When one artery is released there is a rapid return of pink coloration to the hand under normal circumstances. Return of this colour is complete in less than 5 seconds. The two arteries are individually examined in this way. A positive Allen test is said to occur when colour does not return to the hand within 5 seconds of release of one or other artery.

Ultrasonic Examination.—An E.M.I. Type 64 Ultrasonic Flow Velocity Detector, operating at 10 MHz. and delivering a 2-mm. beam, was used to identify pulsatile flow in each of the interdigital arteries in the three interdigital clefts of each hand. Once pulsatile flow had been located, first one artery, then the other was compressed at the wrist, and a record was kept showing whether pulsatile flow was abolished by compression of either artery. It was thus possible to determine the dependence of pulsatile flow in each interdigital cleft on radial or ulnar artery inflow.

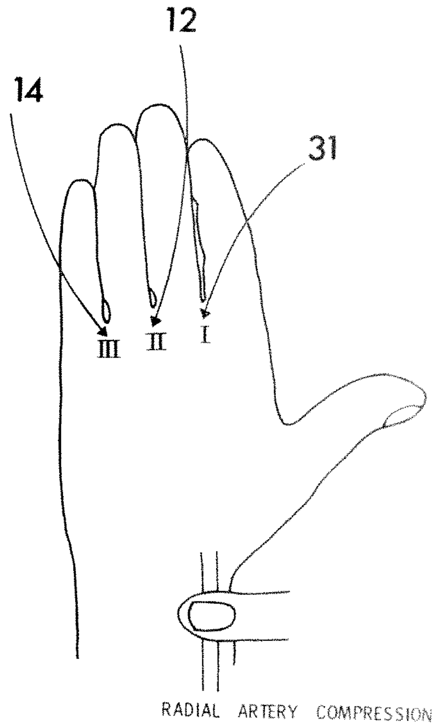

FIG. 1.—The number of times that interdigital pulsatile flow was abolished in each cleft by radial artery compression.

RESULTS

There were 19 men and 31 women in this survey. The mean age was 32 years, with an age range of 18–67 years. Thirty-four subjects were light or occasional smokers, 7 smoked between 10 and 20 cigarettes a day, and the remaining 9 subjects smoked 20 or more cigarettes each day. Smoking habits amongst these people without evidence of clinical arterial disease did not seem to have any bearing on the circulatory patterns in the hand.

Ultrasonic Examination.—The findings of the ultrasonic examination can be summarized as follows:—

1. Radial artery compression abolished pulsatile flow in 57 of the 300 interdigital arteries examined. The cleft between the index and middle fingers (cleft I) was affected in 31 cases, that between the

middle and ring fingers (cleft II) in 12 cases, and that between the ring and little fingers (cleft III) in 14 instances (*Fig.* 1).

2. Ulnar artery compression abolished pulsatile flow in 75 of 300 clefts. Cleft I was affected in 25 cases, cleft II in 28 cases, and cleft III in 22 cases (*Fig.* 2).

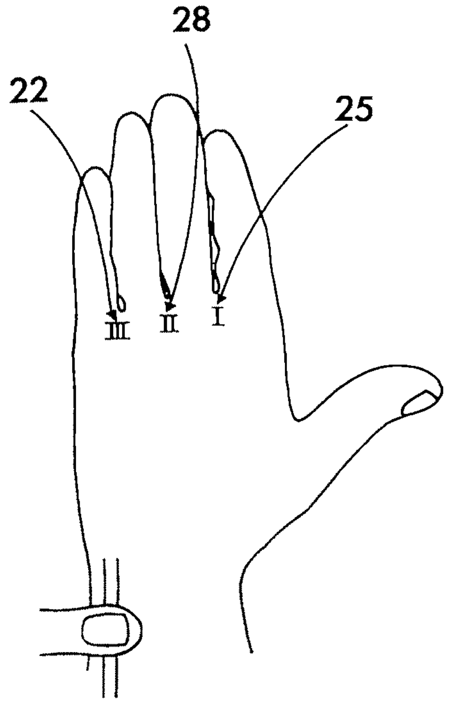

Fig. 2.—The number of times that interdigital pulsatile flow was abolished in each cleft by ulnar artery compression.

3. Radial artery compression abolished pulsatile flow in at least one cleft in 38 of 100 hands.

4. Ulnar artery compression abolished pulsatile flow in at least one cleft in 46 of 100 hands.

5. Ulnar artery compression abolished pulsatile flow in all three clefts in 9 of 100 hands.

6. Radial artery compression abolished pulsatile flow in all three clefts in 6 of 100 hands.

Allen Test.—Using the strict criterion of return of colour within 5 seconds, there were 3 positive Allen tests. In 2 instances the Allen test suggested that the radial artery supply to the hand was deficient, in that revascularization did not occur within 5 seconds after release of the radial artery while ulnar artery compression was sustained. In the remaining case release of the ulnar artery did not produce revascularization while compression of the radial artery was sustained. In the 2 hands in which the radial artery supply was thought to be deficient on the basis of the Allen test, compression of the radial artery made no difference to the ultrasonically detected pulsatile flow in the interdigital clefts, but pulsatile flow disappeared on compression of the ulnar artery, confirming circulatory dependence on the ulnar artery. In the 1 remaining hand in which the ulnar artery supply was felt to be deficient, compression of the radial artery abolished pulsatile flow in all three interdigital clefts.

DISCUSSION

The collateral circulation in the hand is important in three situations. Direct trauma to the arteries at the wrist is fortunately fairly rare except in suicidal attempts. When one or other artery is divided at this point, surgeons generally ligate with equanimity. Damage to the superficial palmar branch of the ulnar artery where it crosses the hook of the hamate (the 'hammer-hand' syndrome) may, however, be a potent cause of disability (Conn and others, 1970). Since it has been shown that some individuals with this injury have relatively few symptoms (Little and Ferguson, 1972), it is necessary to seek an explanation for the variation from individual to individual. While propagation of thrombus and micro-embolism to the digital arteries may account for more extreme forms of digital ischaemia, variations in the collateral supply may equally well explain some of the variation encountered.

Samaan (1971) reported 3 cases of digital ischaemia after the insertion of a radial artery catheter for pressure monitoring in patients undergoing cardiac surgery. In 2 cases frank gangrene of the fingers occurred, and in 1 case amputation above the wrist became necessary. These 3 cases were noted in a series of 'about 800 cases of open-heart surgery'.

The haemodynamic situation created by an arteriovenous fistula at the wrist for long-term dialysis is much more complicated. Diversion of radial artery flow will obviously be important, but a situation can develop in which reverse flow occurs in the radial artery distal to the fistula to such an extent that a 'steal' situation is created (Bussell, Abbott, and Lim, 1971). Gangrene of the fingers developing some time after the fashioning of such an arteriovenous fistula is being reported with increasing frequency (May, 1972). Once again, the circulatory pattern in the hand is likely to be an important determinant of this form of ischaemia.

Preoperative assessment of the circulatory dynamics in the hand is obviously difficult. It would be hard to justify routine arteriography, with its attendant risks, and an arteriogram has the shortcoming of producing a static picture which may well conceal the dynamics of the circulation. The Allen test seems to provide some useful information, but it is probably a relatively crude test. It is too early to say how useful ultrasonic examination will prove to be, but a prospective study has been set up to see whether any prediction can be made concerning the development of ischaemia in patients undergoing arteriovenous fistula formation at the wrist. Clearly, ultrasonic examination can only provide indirect information, but it has the theoretical advantage of testing the dynamics of the collateral circulation in the hand.

It would be unwise to base anything more than tentative conclusions on the data so far accumulated. It seems that circulatory dynamics in the hand follow a very variable pattern, and that ischaemia following occlusion of either artery may manifest itself in any finger. The ulnar artery seems to be the dominant source for digital arterial blood, as judged by abolition of the interdigital artery pulses on compression of the ulnar artery in 75 of the 300 clefts examined, compared with the 57 interdigital arteries affected by compression of the radial artery. The loss of pulsatile flow in at least one of the interdigital vessels, which occurred in 38 hands on compression of the radial artery and in 46 cases on compression of the ulnar artery, was of patchy distribution and did not follow any particular pattern. This suggests that collateral circulation will generally maintain viability of the fingers following occlusion of the radial or ulnar arteries, since abolition of pulsatile flow in all three interdigital arteries was relatively uncommon. In 9 per cent of the hands, however, ulnar artery compression did abolish pulsatile flow in all three interdigital clefts. Interruption of the ulnar artery flow under these circumstances could possibly lead to ischaemia in any finger. In 6 per cent of the hands radial artery interruption similarly produced abolition of pulsatile flow in all the interdigital clefts, and might likewise be expected to produce digital ischaemia. In only 3 of these 15 hands was the Allen test positive.

It is suggested that modes of investigation as mentioned in this paper should become part of the routine examination of patients who are likely to undergo procedures which may compromise the blood-flow in the radial artery. It is particularly important to bear in mind the frequency with which damage occurs to the superficial palmar branch of the ulnar artery over the hook of the hamate amongst subjects in heavy labouring jobs. Loss of flow in this vessel may lead to serious ischaemia if the radial artery flow is interrupted at the wrist.

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THERMOGRAPHY IN THE DIAGNOSIS OF OCCLUSIVE VASCULAR DISEASE OF THE LOWER LIMB

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SUMMARY

An assessment of the diagnostic accuracy of thermography in arterial disease of the lower limb is reported. By comparing the arteriographic and thermographic appearances of 52 patients, three independent observers had overall agreement of interpretation in approximately 50 per cent of cases. Factors found to limit accuracy were increasing subcutaneous fat thickness and localized disease with good collateral circulation.

FEMORAL arteriography as a diagnostic procedure is not without risk. Local haemorrhage, arterial thrombosis, peripheral embolism, plaque dislodgement, subintimal dissection, aneurysm formation, and guide-wire fracture are among its well-described sequelae (Grainger, 1965; Ansell, 1968). Lang (1963), in a review of 11,402 Seldinger procedures, reported 7 deaths and 81 serious complications. The hypothesis that thermography could be used as an alternative less hazardous method for locating the site of arterial blockage and assessing 'peripheral run-off' has been evaluated in this study.

MATERIAL AND METHODS

Sixty patients (58 males and 2 females) were subjected to thermographic studies of lower-limb blood-flow. Fifty-two of these patients had, in addition, femoral arteriography performed.

Each patient was warmed in a confined draught-free space by a source of radiant heat. A toe-knee temperature as near as possible to 28° C. in the ischaemic limb(s) was achieved. The patient was then moved into a specially constructed room at a constant ambient temperature of 16° C. Scanning was by Pyroscan Mark II with a scanning time of 35 seconds, which gave at a distance of exactly 2 ft. (60·96 cm.) a spatial resolution of 3 mm. Thermograms and toe-knee temperatures were recorded at 2-minute intervals over 40 minutes or until the ischaemic toe temperature fell to 21° C. Comparison of the thermographic and arteriographic appearances was then made by three independent observers who had no access to the clinical records of the case. The suspected site of the arterial blockage and assessment of the collateral circulation and peripheral run-off were recorded.

In addition, certain parameters possibly affecting the diagnostic accuracy of thermography were recorded; subcutaneous fat content expressed as skin-fold thickness using Harpenden callipers (Edwards, Hammond, Healy, Tanner, and Whitehouse, 1955) was estimated at the level of the adductor hiatus in each limb. This point was chosen as it is most frequently involved in occlusive disease (Watt, 1966) and therefore at this site subcutaneous fat insulation could be expected to have its greatest diagnostic impact in the majority of cases. Estimate of the extent of the disease on arteriography was made and recorded as the 'occlusive vascular score' according to the following scale:—

Grade I: Local segmental (either upper or lower segments involved) with good collateral circulation, score 1.

Grade II: Segmental disease with poor collateral circulation, score 2.

Grade III: Extensive (both upper and lower segments involved) disease with poor collateral circulation, score 3.

Grade IV: Extensive disease with no collateral circulation, score 4.

RESULTS

Of the 52 patients undergoing both arteriography and thermography, approximately 8 per cent of the thermograms were of such poor technical quality that no interpretation of the arterial pattern could be made. On comparing the arteriograms and thermograms of the remaining cases, observer agreement with accurate localization of the arterial block was achieved in 50 per cent of cases. Similarly, in 58 per cent of the cases observer agreement was found between the state of the collateral circulation and peripheral run-off on arteriography and thermography.

Table I.—CORRELATION BETWEEN SKIN-FOLD THICKNESS AND ACCURACY OF THERMOGRAPHY

SKIN-FOLD THICKNESS (mm.)	NO. OF CASES	NO. IN WHICH THERMOGRAPHY WAS SUCCESSFUL	PERCENTAGE ACCURACY
8·3	6	6	100
8·5	7	6	85·71
9·0	7	6	85·71
9·5	3	2	66·66
10·0	2	1	50·00
10·5	3	1	33·33
12·0	7	1	14·28
13·0	9	1	11·11
13·3	4	0	

$r = -0·974$, $P < 0·001$.

Table II.—CORRELATION BETWEEN SEVERITY OF ARTERIAL DISEASE AND ACCURACY OF THERMOGRAPHY

GRADE OF DISEASE	NO. OF CASES	TOTAL SCORE*	NO. IN WHICH THERMOGRAPHY WAS SUCCESSFUL	PERCENTAGE ACCURACY
I	6	6	0	0
II	7	14	1	14·28
III	9	27	3	33·30
IV	26	104	20	77·00

* *See* text for full description.
$r = 0·971$, $P < 0·001$.

Subcutaneous fat thickness varied from 8·3 to 13·3 mm., with a mean of 10·46 mm. (S.D., 1·89). A negative correlation was found between the percentage diagnostic accuracy and the subcutaneous fat thickness of the adductor hiatus (*Table I*; $r = 0·974$, $P < 0·001$), the percentage accuracy of thermography falling from 100 to 0 per cent with increasing subcutaneous fat thickness.

When the diagnostic accuracy of thermography was correlated with the extent of the disease expressed as the 'occlusive vascular score' (*Table II*) the accuracy rose from 0 to 77 per cent with increasing score, i.e., increasing severity of disease ($r = 0·971$; $P < 0·001$).

DISCUSSION

Many claims have been made as to the value and diagnostic accuracy of thermography in widely disparate clinical situations. Accuracy in diagnosis of 85–95 per cent has been claimed in thyroid disease (Samuels, 1972a); 90 per cent in parathyroid disease (Samuels, 1972b); 94·5 per cent in the localization of perforating veins (Patil, Williams, and Lloyd Williams, 1970), and 88·6 per cent in carotid artery occlusion (Capistrait, 1971). Claims as to the place of thermography in the diagnosis of breast carcinoma have ranged from the enthusiastic (accuracies of 100 per cent (Swearingen, 1965) and 87 per cent (Wallace and Dodd, 1968)) to the guarded (accuracy of 53 per cent (Furnival, Stewart, Weddell, Dovey, Granville, Evans, and Forrest, 1970)). It is significant that diagnostic accuracy has been found to be always greatest in situations where difference in infra-red emission could not be obscured by variable subcutaneous fat insulation. The wide observer variance in accuracy of thermographic diagnosis in breast carcinoma could be accounted for by the variable fat density of the breasts studied in different series.

The results of our study show that in general thermography is a poor diagnostic substitute for femoral arteriography. It would appear that this is because in lower-limb occlusive disease accuracy is limited by the insulating capacity of the subcutaneous fat and the higher thermal background provided by segmental disease with good collateral circulation.

Acknowledgements.—We wish to thank Mr. C. R. Helsby, under whose care the patients were admitted, Mr. A. Cuscheri, and Mr. D. Annis for their encouragement and advice in preparing this paper.

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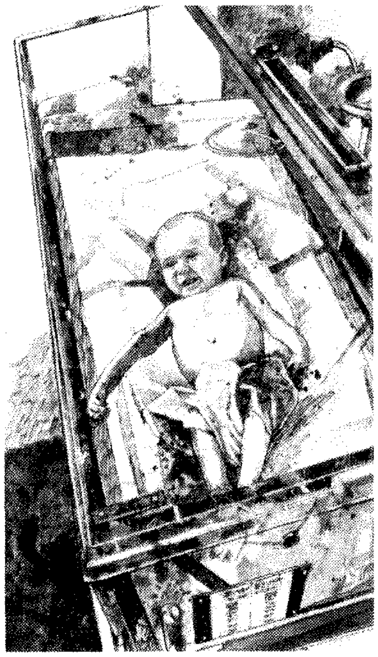

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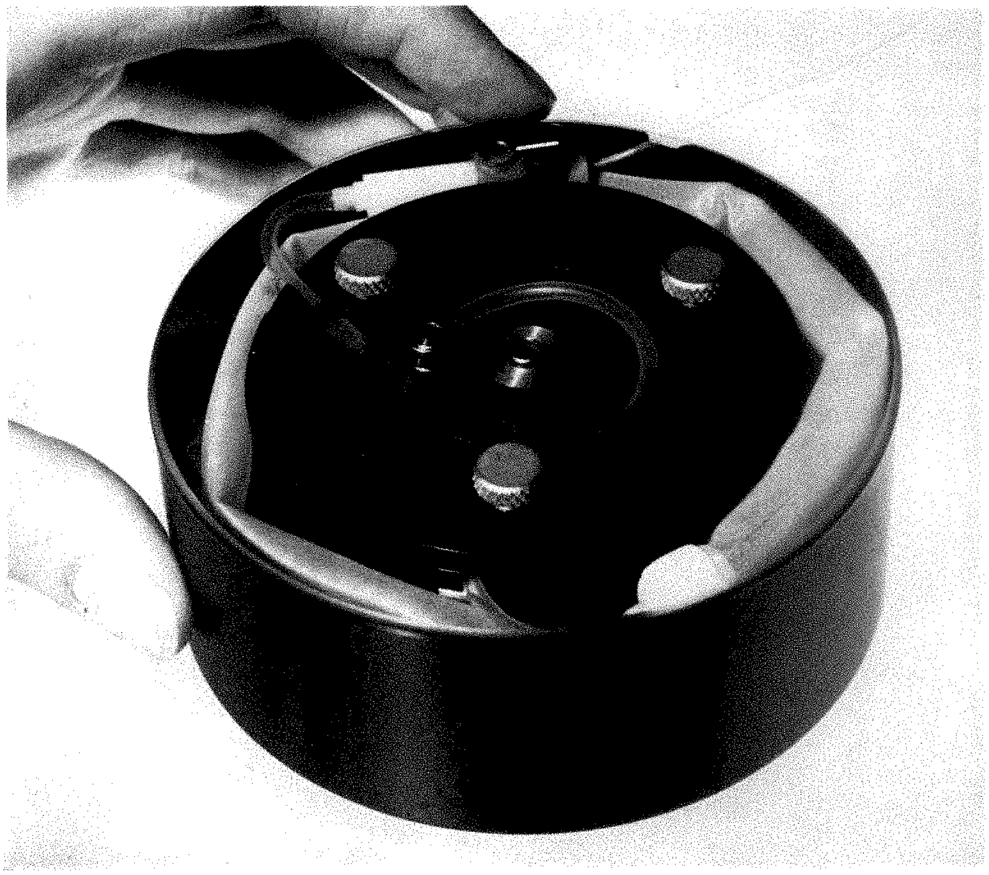

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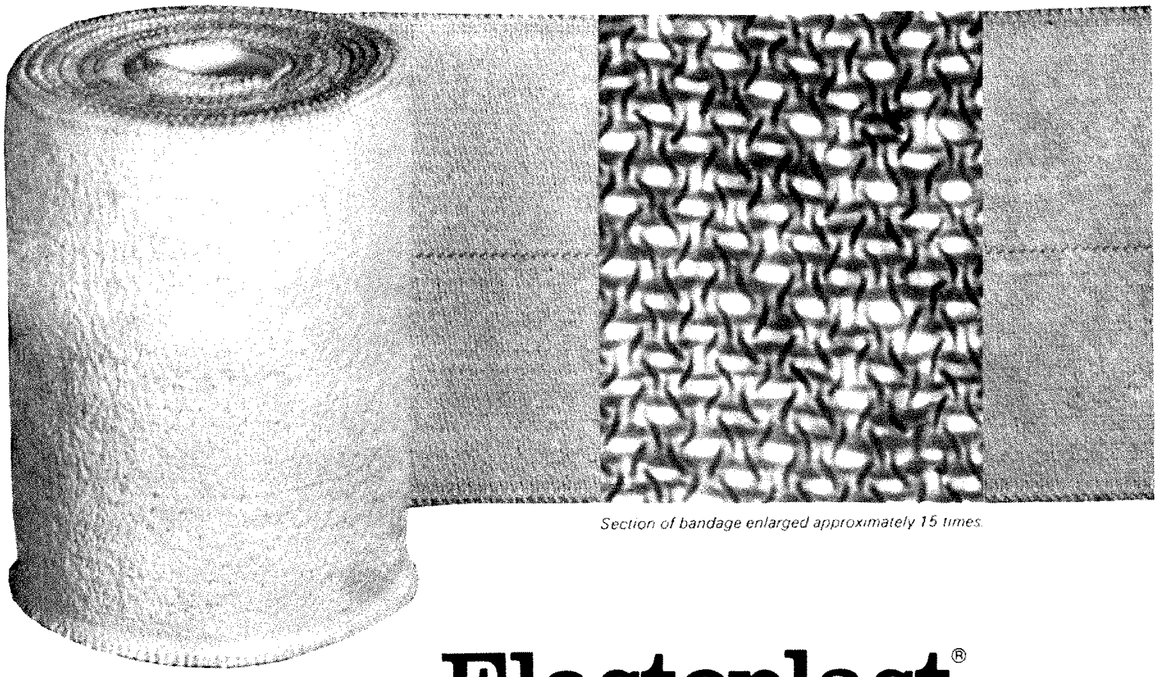

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BLUNT ABDOMINAL INJURY: A REVIEW OF 59 CONSECUTIVE CASES UNDERGOING SURGERY

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SUMMARY

1. A consecutive series of 59 patients undergoing laparotomy as a result of blunt abdominal trauma is reported.

2. Road-traffic accidents were the most common cause of blunt abdominal trauma and frequently produced a complex pattern of associated injuries.

3. There were 8 deaths, giving a mortality-rate of 14 per cent.

4. The number of associated injuries was the most important single factor influencing the mortality-rate.

5. Delay in diagnosis occurred in 14 patients, and this may contribute to the high mortality-rate of blunt abdominal injury.

6. A high index of suspicion, thorough and repeated clinical assessment, and willingness to resort to laparotomy are the main principles in the diagnosis of blunt abdominal injury.

OVER the past 15 years greater understanding of the physiopathology of shock has resulted in improvement in the resuscitation and management of severely injured patients. These advances have been responsible for the relatively recent decline in the mortality-rate of penetrating abdominal injury (McLeod and Brown, 1966). Nevertheless, the mortality-rate of blunt abdominal trauma has remained in the region of 6–23 per cent (Aho and Rastima, 1971). The failure to achieve a significant reduction in the mortality of non-penetrating abdominal injury is probably related to the progressive increase in high-speed road-traffic accidents producing major abdominal visceral injury in association with multiple other injuries (Macbeth, 1966). In addition, the difficulty in early diagnosis of the visceral injury, particularly in patients with multiple injuries, may lead to delay in the institution of appropriate treatment. In some cases symptoms and signs of visceral injury only become apparent hours or days after the initiating trauma. This delay in presentation also contributes to the higher mortality-rate of non-penetrating abdominal trauma.

In this paper we report a consecutive series of 59 patients who underwent surgery for blunt abdominal injury. The importance of early diagnosis is emphasized and the reasons for delay are discussed.

CLINICAL MATERIAL

Patients.—The 59 patients reviewed were treated between December, 1966, and June, 1972. Forty-two of the patients (71 per cent) were male. The age incidence is shown in *Fig.* 1. Two-thirds of the patients were in their second or third decade.

Aetiology.—The types of accident producing the abdominal injuries are listed in *Table I.* Road-traffic accidents were responsible for the injuries to 76 per cent of the patients in this series. Only 3 of the 45 victims of traffic accidents were pedestrians. The remaining 14 patients (24 per cent) were involved in domestic, sporting, or industrial accidents.

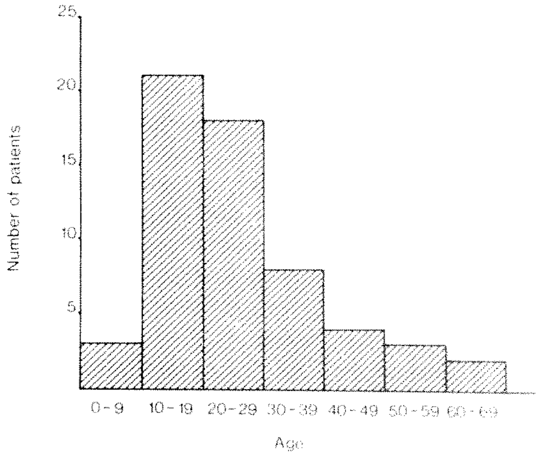

FIG. 1.—Age incidence of the present series.

Table I.—AETIOLOGY OF BLUNT ABDOMINAL TRAUMA

Type of Accident	*No. of Patients*
Traffic	45
Domestic	6
Industrial	4
Sporting	4
Total	59

Table II.—SITES OF ABDOMINAL VISCERAL INJURY

Site of Injury	*No. of Cases*
Liver	28
Spleen	19
Kidney	11
Diaphragm	6
Small bowel	6
Large bowel	6
Mesentery	6
Urethra	4
Gall-bladder	2
Bladder	2
Pancreas	2
Stomach	1
Aorta	1
Total	94

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Abdominal Injuries.—The incidence of injury to the different abdominal organs is listed in *Table II*. In many patients more than one viscus was damaged. The liver, spleen, and kidney were the organs most frequently involved, accounting for 58 (62 per cent) of the 94 visceral injuries recorded, although virtually every abdominal organ appears on the list.

All but 3 of the 28 cases of liver injury had associated major damage to at least one other organ. Crushing injury sustained in the front seat of a motor vehicle was the usual aetiology. A detailed analysis of 20 of these patients has been recorded elsewhere (Blumgart and Vajrabukka, 1972).

In general, rupture of the spleen appeared to be associated with a lesser or more localized trauma and a smaller proportion of these injuries was due to traffic accidents. Hepatic injury coexisted in 5 cases and renal injury in 4 of the patients with rupture of the spleen.

Table III.—ASSOCIATED INJURIES AND MORTALITY

SITES OF INJURY	NO OF PATIENTS	NO OF DEATHS	MORTALITY-RATE (per cent)
Abdominal alone	12	0	0
Abdominal + orthopaedic	12	0	0
Abdominal + craniocerebral	8	1	13
Abdominal + thoracic	3	0	0
Abdominal + orthopaedic + craniocerebral	6	1	17
Abdominal + orthopaedic + thoracic	3	0	0
Abdominal + craniocerebral + thoracic	4	1	25
Abdominal + craniocerebral + thoracic + orthopaedic	11	5	45
Total	59	8	14

Orthopaedic injury. Fracture of one or more long bones or the pelvis.

Craniocerebral injury: includes facial fracture and scalp and facial lacerations. One case had cerebral injury

Ten of the 11 patients with a ruptured kidney had associated injuries to other abdominal organs. In the remaining patient minor trauma had led to the rupture of a hydronephrotic kidney. The renal damage itself was not severe in the majority of cases and surgical intervention was usually necessitated by the associated injuries. Nephrectomy was performed in only 2 patients, both of whom had gross renal disruption. Rupture of the membranous urethra in association with a fractured pelvis occurred in 4 cases and intraperitoneal rupture of the bladder in 2 cases. One of the latter patients had also sustained a rupture of the gall-bladder and has been reported previously (Blumgart, 1969).

Diaphragmatic injury was always due to major crushing trauma. All 6 patients with diaphragmatic injury had severe multiple injuries to the thoracic and upper abdominal viscera.

The small intestinal injuries were associated with high-speed traffic accidents. Three patients were found to have a laceration of the second part of the duodenum at laparotomy. In each of these patients there were associated abdominal visceral injuries. The ileum was the site of rupture in 2 patients and the jejunum in 1. Large-bowel injury also occurred in 6 patients and in 3 it was associated with fracture of the pelvis. Mesenteric injury usually accompanied intestinal injury, but in 1 case an isolated mesenteric tear was the sole lesion found at laparotomy.

Pancreatic injury occurred twice in the series. One of these 2 patients had severe multiple injuries elsewhere including damage to the stomach and duodenum, while the other had sustained an isolated pancreatic injury following local trauma to the left side of the abdomen (*Case* 5). Evidence of pancreatitis was found at post-mortem examination in 2 fatal cases (one with liver injury and the other with multiple injuries to the chest and abdomen). In neither of these cases was there direct evidence of pancreatic rupture.

One patient had ruptured a pre-existing abdominal aortic aneurysm when he had fallen on to his abdomen (Bolton and Blumgart, 1972).

Associated Injuries (*Table III*).—Only 12 (20 per cent) of the patients in this series did not have extra-abdominal injuries.

Fractures of long bones or pelvis were the most common of the associated injuries, occurring in 32 patients (54 per cent). A common combination was fracture of an upper limb bone and rupture of an upper abdominal viscus. In particular, 5 of 9 patients with severe injury of the right lobe of the liver had sustained fractures of the right upper limb. Fracture of the pelvis occurred in 10 patients. In 4 cases this was associated with rupture of the membranous urethra and in another 3 with rupture of the colon.

Twenty-nine patients (49 per cent) had associated head injuries. The majority of these injuries were relatively minor, comprising concussion and/or facial and scalp lacerations. Only 3 patients had fractures of the skull, and in only 1 case was there evidence of significant cerebral injury when contused occipital lobes were found at post-mortem examination.

Thoracic injuries occurred in 21 patients (36 per cent) and 9 of these required tracheostomy and assisted respiration. Fractures of the ribs were present in nearly all of these cases, but only 5 patients had significant flail segments. In 9 of the 21 patients there was a pneumothorax and 7 had sustained contusions or lacerations of the lung(s). Two patients sustained damage to the thoracic aorta. One of these died as a result of rupture of a traumatic aneurysm of the aorta sited just distal to the ligamentum arteriosum. The other patient was found to have an intimal tear of the thoracic aorta at post-mortem examination.

Diagnosis.—In general, diagnosis was based on clinical features similar to those outlined by Mathieson (1962), supplemented at times by radiological findings. Only rarely was abdominal paracentesis used, and in 1 such patient a ruptured spleen was found following a negative four-quadrant tap. In cases of doubt, repeated examinations and review of the findings usually resolved the problem. In the few patients where doubt still remained, laparotomy was performed.

Only one negative laparotomy was performed. This patient was under the influence of alcohol and had upper abdominal tenderness in association with multiple fractured ribs.

A clinical diagnosis of intra-abdominal injury requiring surgery was made within 8 hours of admission in 45 of the 59 patients in this series. In

14 cases the diagnosis was delayed for more than 8 hours following admission to hospital (*Table IV*).

RESULTS

Eight of the 59 patients died, a mortality-rate of 14 per cent (*Table III*). All the fatal cases were the result of road accidents. The mortality-rate appeared to be directly related to the number and severity of the injuries sustained. It is significant that all 12 patients with abdominal injury alone survived. Where there was a combination of abdominal visceral damage and injuries to the thorax, head, and limbs, 5 patients out of 11 died, a mortality-rate of 45 per cent. Two of the 14 cases where there was delay in diagnosis and treatment died. The mortality-rate of this small group is 14 per cent and does not differ significantly from that of the whole series.

During the 5½-year period of the series 20 cases of penetrating abdominal injury were also treated with no deaths.

DIFFICULTIES IN DIAGNOSIS

Analysis of the injuries sustained by the 14 patients whose diagnosis was delayed for longer than 8 hours (*Table IV*) reveals two groups of clinical situation responsible for the delay. In the first group abdominal signs were initially absent or insignificant after injury. However, with persistence of fluid leak into the peritoneal cavity, signs of shock or peritonitis became manifest usually 12–48 hours after injury. This type of 'slow-leak' picture was associated with the diagnostic delay in 3 of the patients with ruptured liver, in 1 with ruptured spleen, in 1 with ruptured duodenum, and in 1 patient with combined rupture of the gall-bladder and urinary bladder.

Table IV.—TYPE OF INJURY IN PATIENTS IN WHOM THERE WAS DELAY IN DIAGNOSIS

Type of Injury	*No. of Patients*
Ruptured liver	4
Ruptured spleen	4
Ruptured colon	3
Ruptured pancreas	1
Ruptured gall-bladder	1
Ruptured duodenum	1
Total	14

The second type of clinical picture resulted when either there was no initial leak or the leak became temporarily sealed off. Delayed rupture then followed days or weeks later and produced rapid development of generalized peritonitis or led to a faecal fistula. Delayed visceral rupture of this type was seen in 3 of the cases of ruptured spleen, 3 cases of ruptured colon, and 1 case of ruptured liver.

The following case histories are illustrative of the difficulties encountered in the diagnosis of such cases.

CASE REPORTS

Case 1.—A 58-year-old woman was involved in a road-traffic accident. She was concussed initially but complained of pain in the right hypochondrium when seen in the casualty department of another hospital. On examination at this time her pulse and blood-pressure were within normal limits. No abdominal signs were noted and she was admitted for observation. Sixteen hours later she became hypotensive, developed generalized abdominal pain and tenderness, and was transferred to our care. At laparotomy there was a rupture of the second part of the duodenum, a contused segment of ileum, and a small haematoma of the liver. The pancreas did not appear to be damaged. Repair of the duodenum was performed but she died on the fifth postoperative day in a state of refractory hypotension associated with bacteriaemic shock and acute renal failure. It seems likely that the initial delay associated with continued leakage of intestinal contents contributed to the ultimate fatal outcome.

Case 2.—A 13-year-old boy fell from a milk van. On admission he was fully conscious and complained of pain in the right hypochondrium. His general condition was good, with a pulse-rate of 64 per minute and a systolic blood-pressure of 105 mm. Hg. There was local tenderness in the right hypochondrium but no rigidity. The diagnosis of ruptured liver was considered but in view of the minimal symptoms and signs he was treated conservatively and laparotomy was not performed. Sixteen hours later he developed a tachycardia and the abdomen became more tender with rigidity in the right upper quadrant. At laparotomy there was a large haemoperitoneum resulting from an extensive injury to the right lobe of the liver which necessitated right hepatic lobectomy. There was also a right perirenal haematoma. Postoperatively there was some transient respiratory difficulty followed by an uneventful recovery.

COMMENT.—Despite the very extensive liver injury in this patient, 16 hours elapsed before sufficient blood had accumulated in the peritoneal cavity to give definite signs of peritoneal irritation and hypovolaemia.

Case 3.—A 67-year-old man complained of pain in the right iliac fossa following a road-traffic accident. On examination he was dyspnoeic, drowsy, and hypotensive (blood-pressure, 80/50 mm. Hg). There was bruising in both flanks and some tenderness on palpation in the right iliac fossa. Rhonchi and coarse crepitations were audible in both lungs. Radiographs confirmed the clinical diagnosis of fractured pelvis and fractured left humerus. The chest film showed increased basal markings bilaterally and emphysema. No rib fractures were visible.

As a major problem appeared to be acute respiratory distress, the patient was admitted to a respiratory unit and treated with oxygen, antibiotics, bronchodilators, and physiotherapy. There was some persistent lower abdominal tenderness which was attributed to the fractured pelvis. On the fifth day after admission he suddenly developed severe generalized abdominal pain, accompanied by distension and diarrhoea. On examination there was generalized abdominal tenderness and rigidity. Laparotomy revealed a perforation of the anterior wall of the caecum. The perforation was exteriorized. His recovery was slow owing to his chronic pulmonary disease. Three months later the caecostomy was closed surgically and the patient is now mobile and well.

Case 4.—A 31-year-old man fell 5½ m. while bricklaying, landing on his hands and left side. On admission he complained of pain in both wrists and clinically there were bilateral Colles's fractures. Examination of his abdomen revealed tenderness in the left hypochondrium but no other abnormality was found. Radiographs confirmed the clinical diagnosis of bilateral Colles's fractures. These were reduced and he was observed for 48 hours prior to discharge from hospital when his abdominal tenderness had subsided. Nine days later he was readmitted complaining of pain in the left hypochondrium and left shoulder tip. On examination he was pale. His pulse was 90 per minute and blood-pressure 100/60 mm. Hg. There were tenderness and guarding in the left upper quadrant. Delayed rupture of the spleen was suspected and a splenic arteriogram performed via coeliac axis catheterization confirmed the clinical diagnosis (*Fig.* 2). Splenectomy was performed and he made an uneventful recovery.

COMMENT.—In this patient symptoms and signs of visceral injury were absent 2 days after rupture of the spleen. The well-known potential dangers of such cases leading to diagnostic delay and increased morbidity and mortality are apparent.

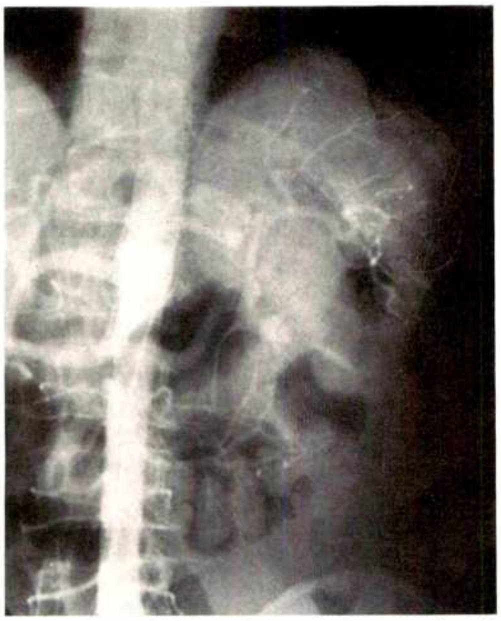
FIG. 2.—*Case* 4. Splenic arteriogram showing separation of the lateral splenic vessels from the diaphragm with loss of a clear-cut splenic margin.

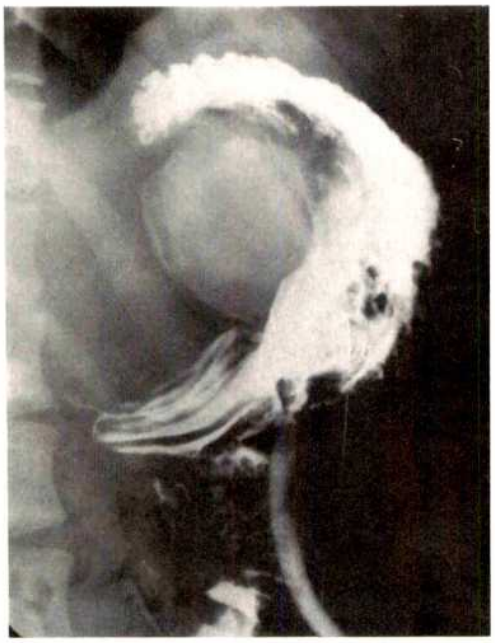
FIG. 4.—*Case* 5. Barium-meal film showing the relationship of the contrast-filled pancreatic pseudocyst to the stomach.

Case 5.—A 21-year-old man was kicked in his left side during a rugby match. On admission he complained of pain in the left upper quadrant and left shoulder tip. His pulse was 72 per minute and blood-pressure 140/80 mm. Hg. There was mild tenderness in the left upper abdomen. Radiographs of the chest and abdomen were within normal limits. He was considered to have a bruised abdominal wall and was admitted for observation. Over the next 12 hours he vomited four times and his tenderness increased. A clinical diagnosis of ruptured spleen was made. At laparotomy there was bruising in the splenic hilum and a retroperitoneal exudate about the tail of the pancreas. The spleen was mobilized to inspect the tail of the pancreas and then removed. A diagnosis of pancreatic contusion producing traumatic pancreatitis was made. A large tube drain was laid beside the tail of the pancreas and the wound was closed. Postoperatively he remained unwell with persistent upper abdominal tenderness, a left pleural effusion, and elevated serum-amylase levels. Large volumes of amylase-rich fluid passed through the drainage tube. A sinogram (*Fig.* 3) and barium-meal film (*Fig.* 4) confirmed the presence of a pseudocyst of the pancreas. Posterior cystogastrostomy was carried out 24 days after the original laparotomy. The patient then made an uninterrupted recovery.

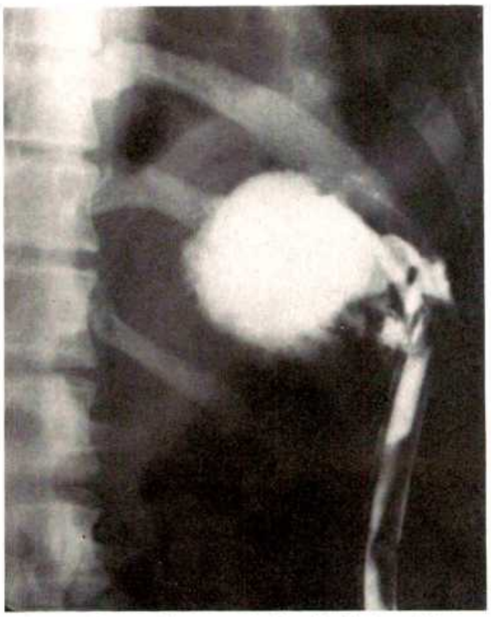
FIG. 3.—*Case* 5. Sinogram via the tube drain outlining a pancreatic pseudocyst.

Case 6.—A 23-year-old man was run over by a tractor. On admission he was shocked with a blood-pressure of 70/50 mm. Hg. There was tenderness in the left loin, haematuria, and absent bowel-sounds. Plain radiographs revealed fractures of the right transverse processes of the upper four lumbar vertebrae. An intravenous pyelogram showed no excretion of dye by the left kidney. His condition improved after resuscitation, but 36 hours later he again became hypotensive and developed generalized abdominal tenderness. At laparotomy the lower pole of the left kidney was found to be avulsed and a nephrectomy was performed. There was also an extensive retroperitoneal haematoma which had ruptured through the posterior peritoneum just medial to the descending colon. There was no apparent damage to the descending colon or any of the other viscera. Twenty days after the operation he was readmitted with faeces discharging through his left loin incision, the fistula presumably resulting from delayed rupture of the descending colon. The fistula was treated conservatively and closed spontaneously 10 weeks after the injury.

COMMENT.—This case, the full details of which have been reported elsewhere (Wightman, 1967), did not have any macroscopic abnormality of the colon at laparotomy, although there was an adjacent mesenteric tear. Presumably the fistula was related to focal ischaemia of the colonic wall.

DISCUSSION

The sex ratio, age incidence, and mortality-rate in this series are similar to those of recent reports (Macbeth, 1966; Divincenti, Rives, Laborde, Fleming, and Cohn, 1968). Massive blood-loss and refractory hypotension were prominent features in 7 of the 8 deaths. The other patient (*Case* 1) did not have major blood-loss but developed persistent hypotension and terminal renal failure.

A particularly high mortality-rate of 45 per cent was found in our series among patients with combined injuries to the abdomen, head, chest, and limbs. McLeod and Brown (1966) also recorded a high mortality-rate of 57 per cent in a small group of patients with major injuries to the abdomen, head, and chest.

Williams and Zollinger (1959) found that in half of their fatal cases of non-penetrating abdominal injury there was significant delay in diagnosis and treatment. In this series we have suggested two patterns of injury associated with delay in diagnosis. Our numbers are too few to permit meaningful statistical analysis of the effects of such diagnostic delay. However, there were 2 deaths in the group where diagnosis was made more than 8 hours after admission, and in both the fatal outcome was related to the diagnostic delay. In *Case* 1 surgery was not performed until 16 hours after admission. The second death in this group occurred in a man who was referred 48 hours after admission. He was anuric following hypotension as a result of severe hepatic injury. Right hepatic lobectomy was performed but he died 14 days postoperatively with unresponsive renal failure and gastro-intestinal haemorrhage. There appears to be little doubt that earlier recognition and diagnosis of intra-abdominal injury will result in an improvement in the mortality-rate.

Sometimes extra-abdominal injury may mask the abdominal visceral damage. In particular, a diminished level of consciousness in association with craniocerebral injury may obscure the signs of peritoneal irritation. Although 29 of our patients had sustained varying degrees of head injury, many of these were relatively minor and only 6 patients were unable to give some details of history on admission. Thus, in our series the presence of concomitant head injury did not appear to contribute significantly to the difficulties of diagnosis. The low incidence of major head injury is surprising. A likely explanation is that the association of major cerebral and abdominal injury is the result of very severe trauma and often leads to a rapidly fatal outcome. Also, major cerebral injury is frequently due to acceleration/deceleration forces rather than crushing trauma and the abdomen may be spared significant injury in these circumstances, where the upper part of the body absorbs the major forces of impact.

Many patients had ingested alcohol before injury, but it is of interest that this only contributed to delay in diagnosis in 1 case.

The main problem for the clinician in the diagnosis of blunt abdominal injury is to make a decision as to laparotomy in the presence of minimal abdominal symptoms or signs.

A detailed accurate history from the patient or a witness may provide valuable clues as to the likely patterns of injury. If this is not available, examination of the body wall may reveal contusions or abrasions overlying the site of visceral injury.

Determinations of haemoglobin, haematocrit, and leucocyte count are of little value in the first 4 hours after injury. However, they do provide a useful baseline for comparison with subsequent values. Serum-amylase levels are raised in patients with traumatic pancreatitis and this estimation should be performed when there has been blunt trauma to the upper abdomen (Northrup and Simmons, 1972).

Blood-pressure on admission was frequently within normal limits, possibly because the majority of road-accident victims are young and rapidly compensate for a hypovolaemic state. However, pallor, sweating, restlessness, and tachycardia were usually present. Patients admitted in a state of hypotension usually had major blood-loss or serious multiple injuries as a result of road-traffic accidents.

Persistent pain and signs of peritoneal irritation were the most reliable clinical features and occurred in the majority of patients in this series. However, physical signs may be minimal or absent. In cases where there is real doubt, repeated clinical examinations are probably of more value than ancillary investigations (Williams and Zollinger, 1959; Mathieson, 1962). Increase in pain or tenderness or development of tachycardia indicates the need for laparotomy. Although anaesthesia and laparotomy in a patient with multiple injuries are not without side-effects, we consider a negative laparotomy to be preferable to the dangers of an unrecognized visceral injury.

Some authors (Morris, 1966; Stephens and Conolly, 1967) have reported that abdominal paracentesis by the method of a four-quadrant tap can give valuable diagnostic aid. Using this technique in a study of 304 patients with blunt abdominal injuries, Perry, DeMeules, and Root (1970) found the incidence of false-negative and false-positive taps to be only 4 per cent. In our experience false-negative taps have occurred and we do not routinely use the technique for this reason. Root, Hauser, McKinley, LaFave, and Mendiola (1965) used peritoneal lavage as an aid to the diagnosis of abdominal visceral injury and found no false negatives in a series of 28 patients. Peritoneal lavage was not performed in our series although it is possible that it might have been of use in some patients.

Plain radiographs of the chest or abdomen are sometimes of value, particularly in the diagnosis of ruptured diaphragm (*Fig.* 5). They may also be useful in demonstrating the presence of free gas in the peritoneal cavity. However, perforation of a hollow viscus can be present without free gas in the peritoneal cavity and in addition the necessary views may be difficult to obtain in an ill patient. A ground-glass appearance on supine films is seen in only a small proportion of cases with free fluid in the peritoneal cavity. Loss of the psoas shadow is indicative of a retroperitoneal fluid collection. Fractures of the lower ribs may be associated with injuries to the upper abdominal viscera. However, ruptures of the liver and spleen frequently occur without rib fractures. In a review of 153 patients with fractures of the left lower ribs, Bollinger and Fowler (1956) found the incidence of splenic injury to be only 3·9 per cent. They also found that only 6 of 24 cases of ruptured spleen had associated left lower-rib fractures. Arteriography has been recommended in the severely injured patient (Freeark, Love, and Baker, 1968) to delineate the site(s) of bleeding. In the acute case this procedure should not delay laparotomy which is therapeutic as well as diagnostic. However, in 2 patients with suspected delayed rupture of the spleen we found splenic arteriography by coeliac axis catheterization (Nusbaum, Baum, Blakemore, and Finkelstein, 1965; Redman, Reuter, and Bookstein, 1969) to provide confirmatory diagnostic evidence of the splenic injury. A third patient not in this series with left upper quadrant pain and tenderness was spared a laparotomy by a normal splenic arteriogram.

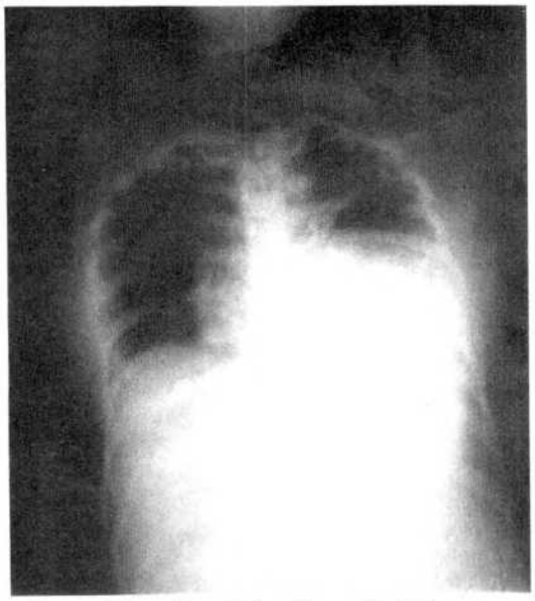

FIG. 5.—Chest radiograph of an 18-year-old girl illustrating rupture of the left leaf of the diaphragm.

Delayed rupture of a subcapsular haematoma is a common complication of splenic injury (Bollinger and Fowler, 1965; Watkins, 1960). These reports suggest that delayed rupture occurs in between 14 and 33 per cent of patients with splenic injury and may occur at any time up to several months following the initial trauma. In our series the longest interval between trauma and delayed rupture was 12 weeks and the shortest was 48 hours. Terry, Self, and Howard (1956) have reported that the latent period is less than 7 days in 50 per cent of patients and less than 2 weeks in 75 per cent. Thus, it has been suggested that patients who have sustained left upper abdominal trauma should be observed in hospital for 2 weeks after the injury. We would recommend splenic arteriography in such patients. Sizer, Wayne, and Frederick (1966) reported an increased mortality in patients with delayed rupture of the spleen. This underlines the importance of early diagnosis. In our small group of patients with delayed rupture of the spleen there was no mortality.

We found an unexpectedly high incidence of delayed rupture of the large bowel. This condition is unusual, although there have been previous reports in the literature (Hicken and Carlquist, 1944; Wightman, 1967). It is possible that some cases may represent misdiagnosis rather than late perforation. Nevertheless, delayed perforation of the colon does occur. It may be caused by the formation and rupture of an intramural haematoma, by crushing of the bowel wall with subsequent necrosis, or by local interruption of the arterial supply or venous drainage resulting in ischaemic necrosis. The initiating force is usually considerable, and rupture of the colon is often associated with fractures of the pelvis and/or vertebral column. The possibility of delayed rupture of the colon should be considered in all cases of crushing injury to the abdomen.

Pancreatic injury is uncommon. Symptoms and signs are often absent initially. The damage is frequently more extensive than the surgeon suspects. A recent comprehensive review (Northrup and Simmons, 1972) has emphasized the problems of early diagnosis, recognition at laparotomy, and treatment of pancreatic injury. Possibly our *Case* 5 might have been saved a second operation by the recognition of the major duct injury and the performance of a distal pancreatectomy at the initial laparotomy.

The high mortality-rate of blunt abdominal injury is largely due to severe multiple associated injuries. Some reduction may be possible through the prompt and energetic treatment of shock, and the improved co-ordination of management and early diagnosis, using repeated and thorough clinical assessment of the abdominal signs coupled with a willingness to resort to laparotomy.

Acknowledgements.—The patients reviewed were all treated at the Sheffield Royal Infirmary, Nottingham General Hospital, and Cardiff Royal Infirmary. One of us (L. H. B.) was associated with the treatment of all the cases but many were admitted under the care of the following surgeons to whom we record our thanks: Mr. C. P. D. Jones, Mr. J. F. Sheehan, Mr. T. Field, Mr. J. Swan, Mr. H. N. Renyard, Mr. J. Wightman, Mr. D. L. Crosby, and Mr. J. L. Craven. Mr. J. Wightman of Chesterfield Royal Infirmary gave permission to quote details of *Case* 6.

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COMMON ILIAC VEIN COMPRESSION SYNDROME OCCURRING IN SIBLINGS

BY W. M. JONES, I. TAYLOR, AND C. J. STODDARD
ROYAL INFIRMARY, SHEFFIELD

SUMMARY

Two sisters displaying the common iliac vein compression syndrome are reported. It is suggested that this syndrome may be congenitally determined, which would explain the increased familial incidence of deep-vein thrombosis.

CASE REPORTS

Case 1.—K. B., a 40-year-old woman, was admitted with a 1-month history of cramp-like pains occurring in the left leg associated with moderate ankle swelling. She had also noted occasional episodes of chest pain with dyspnoea which was unrelated to exercise. There was no haemoptysis. She was not taking an oral contraceptive and there was no history of recent inactivity. Her mother had died suddenly in 1961, following an episode of severe chest pain which had been preceded by 1 week's history of left calf pain.

On examination the patient had a markedly swollen left leg, calf tenderness, and a positive Homan's sign. All the peripheral pulses were palpable and the remainder of the examination was unremarkable. An initial diagnosis of deep-vein thrombosis was made and she was anticoagulated with heparin and maintained on Warfarin. A venogram performed through the left femoral vein showed left iliac vein compression (*Fig.* 1). At the completion of this investigation the patient complained of severe left chest pain and dyspnoea. A lung scan was performed, and poor perfusion of the left posterior base, consistent with a pulmonary embolus, was demonstrated.

It was decided to examine the iliac veins to determine the local pathology. At operation a triangular fibrous band was seen to be constricting the left common iliac vein where it was crossed by the right common iliac artery. This band was divided and a segment was excised. A venotomy was performed and an intraluminal band crossing the vessel obliquely was divided. In an attempt to widen the lumen the vein was closed using a vein-patch graft. The immediate postoperative period was uneventful and the patient was discharged home on the thirteenth postoperative day.

Case 2.—A. N. (sister of *Case* 1), aged 56 years, presented with an 8-month history of intermittent pain and swelling in the left leg. During this time she had had three separate episodes of haemoptysis. On two occasions, once in 1949 following an operation and once in 1958 following a period of bed-rest, she had developed a left deep-vein thrombosis.

On examination the left leg was swollen and the calf was tender to palpation. An intra-osseous venogram performed

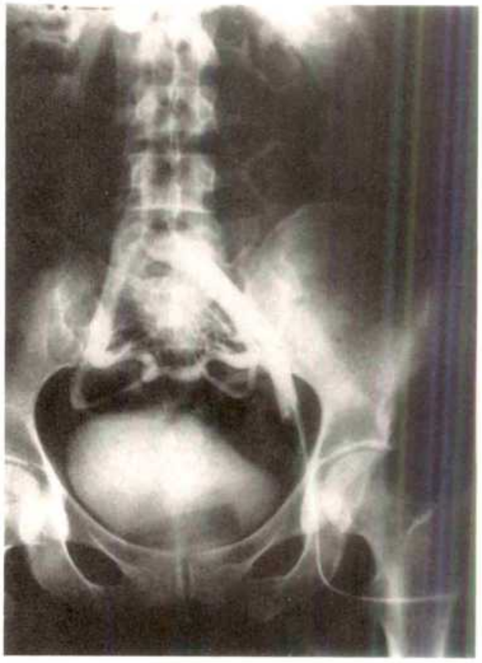

FIG. 1.—*Case* 1. Transfemoral venogram showing the left common iliac vein compression syndrome. Note the large pelvic collateral vein.

through the greater trochanter showed a noticeable obstruction of the left common iliac vein with a large pelvic collateral vessel (*Fig*. 2).

At operation the left common iliac vein was occluded across its junction with the inferior vena cava by a distinct fibrous band. The left common iliac vein appeared to be replaced by a mass of small tributaries as far as the left internal iliac vein. No further surgery was feasible and the abdomen was closed.

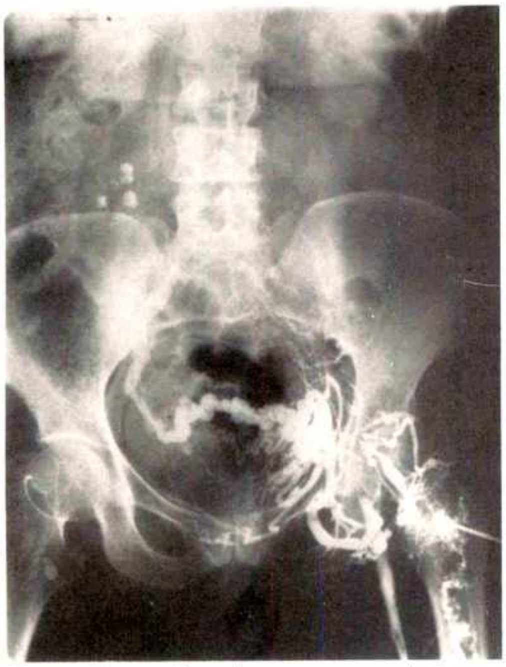

FIG. 2.—*Case* 2. Pertrochanteric venogram showing non-filling of the left common iliac vein. A large pelvic collateral vein is present which communicates with the right common iliac vein.

DISCUSSION

Compression of the left common iliac vein by the right common iliac artery has been recognized for many years (McMurrich, 1906; Erhlich and Krumbhaar, 1943). This flattening and widening of the lumen of the common iliac vein combined with an intraluminal band determine the predominance of left-sided iliofemoral thrombosis (May and Thurner, 1957; Cockett, Lea Thomas, and Negus, 1967; Mavor and Galloway, 1967).

The aetiology of the intraluminal bands is a subject of dispute. McMurrich (1906) suggested that they were a persistence of an embryological condition. Veins develop as multiple venous channels most of which later disappear, but fragments remain and manifest themselves as intraluminal bands. Other workers believe them to be of acquired origin, arising by local pressure resulting in the organization of thrombus and fibrosis. Their constant position, always lying immediately behind the artery, makes an acquired origin a possibility (Negus, Fletcher, Cockett, and Lea Thomas, 1968).

The reported cases, however, suggest that hereditary factors may be responsible for the presence of the bands and so play a part in the development of iliofemoral thrombosis. Histologically they resemble congenital bands since they consist of smooth muscle and fibrous tissue (Negus and others, 1968). Cockett and others (1967) found a family history in 13 out of 57 patients with iliofemoral thrombosis. Erhlich and Krumbhaar (1943), in a study of unselected autopsies, found a 4·7 per cent incidence of bands in 127 children and babies.

It is suggested that the added insult of an intraluminal congenitally determined band in the presence of an extrinsic compression is the factor which precipitates iliofemoral venous thrombosis.

Acknowledgements.—We would like to thank Mr. Clifford Jones, Consultant Surgeon, Royal Infirmary, Sheffield, for help in the preparation of this report. We are indebted to the Photographic and Radiology Departments, Royal Infirmary, Sheffield.

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In Memoriam

Sir Clement Price Thomas, K.C.V.O., F.R.C.S., F.R.C.P.

(1893–1973)

SIR CLEMENT PRICE THOMAS, a pioneer of thoracic surgery, called the 'King's Surgeon' because of his successful operation on King George VI in 1951, is remembered and loved by a host of people, not only by medical men and women, nurses, and patients, but by the members of many national institutions who elected him to high office. To have attained presidencies, such as those of the British Medical Association, the Royal Society of Medicine, the Association of Thoracic Surgeons, the Welsh National School of Medicine, the Medical Protection Society, and the Association of Surgeons of Great Britain and Ireland, amongst others, demands a man of great qualities, of exceptional stamina and leadership, and of loyalty to the particular institution that had asked him for devotion and guidance. His international and national achievements in thoracic surgery are widely acknowledged.

Although he died at the age of 79, he never appeared to be an elderly man; he underwent a serious operation many years ago with courage and with cheerfulness, having characteristically chosen as his surgeon a man junior to himself. Then, as more recently following an eye operation, he was determined to return to work in the committee room, and in his beloved garden.

He was always genial, humorous, and welcoming, maintaining to the end of his life a vivacious interest in the establishments with which he had been associated. After his school-days at Caterham, he spent a short period at the University College of South Wales before joining the Army to serve as a private in the R.A.M.C. in the First World War from 1914 to 1918. As an active consultant in thoracic surgery to the Army and Royal Air Force in the Second World War he was deeply involved in the treatment of Forces personnel who had suffered wounds or injuries to the chest.

He entered the Westminster Hospital Medical School with an Entrance Scholarship. He qualified in 1921 and gained the Fellowship of the Royal College of Surgeons in 1923. Elected to the staff of his hospital, he formed a valuable partnership with Tudor Edwards, which flourished also at the Brompton Hospital and at Midhurst. Both were 'general surgeons' but found the time and energy to develop thoracic surgery, ultimately becoming 'specialized'. Price Thomas was a fine teacher of students, both undergraduate and postgraduate; he played an important role in the training of younger men who have become thoracic surgeons and who owe much of their success to the stimulating effect that he provided; his devotion to Wales was exemplified by his many visits to Sully Hospital, which was then in the charge of the Welsh National Memorial Hospital.

In the thirties and forties Clement Price Thomas provided a most valuable link between leading thoracic surgeons, such as Tudor Edwards and J. E. H. Roberts, and the group of younger men who were always the object of his encouraging affection and whom he instructed by word and precept.

In the 1930–60 period when surgery played a large role in the treatment of pulmonary tuberculosis he was accepted throughout the world as a leader both in the field of thoracoplasty and of resection procedures. At the Brompton Hospital, Midhurst, and at Sully he established centres of excellence and encouraged many surgeons, now no longer young, to overcome the difficult days that faced them before the discovery of streptomycin. His success in the surgical treatment of lung cancer and other tumours and of bronchiectasis was remarkable. The advancement of cardiac surgery was not actively possible for him to achieve as he was nearing the time of retirement from clinical surgery. However, in addition to being the first surgeon in Great Britain to operate on coarctation of the aorta, he was wise and generous in providing every opportunity for his younger colleagues to develop this field, particularly at the Westminster Hospital, thus laying the foundations of the fine cardiovascular department which has been so successful.

Sir Clement's large experience of general surgery before becoming 'specialized' made him valuable to the Royal College of Surgeons, where he was happy, gaining respect and affection as a Member of Council and subsequently Vice-President.

The surgical world has been enriched by the late Sir Clement; an optimistic outlook on life, nurtured by a strong religious belief, and a capacity for surgical work of an exhausting nature were sustained by a splendid sense of humour and of loyalty. He was helped by a wonderful wife, who, by her gentleness and affection for his friends and patients, shared his love for mankind at all times.

The Service of Thanksgiving for his life and work, held in Westminster Abbey on 30 May, 1973, was a moving ceremony, attended by a large congregation.

SHORT NOTES OF RARE OR OBSCURE CASES

'SPONTANEOUS' RUPTURE OF THE DIAPHRAGM DURING DELIVERY

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SUMMARY

A case of 'spontaneous' diaphragmatic rupture occurring during a normal delivery and resulting in herniation, incarceration, and gangrene of the stomach and omentum is described. Resection of incarcerated viscera was followed by complete recovery. To the best of our knowledge this is the first report of such a complication of a 'normal' delivery.

TRAUMATIC rupture of the diaphragm may occur as a result of blunt or penetrating injury to the chest or abdomen. The condition is well documented in the medical literature (Bekassy, Dave, Wooler, and Ionescu, 1973).

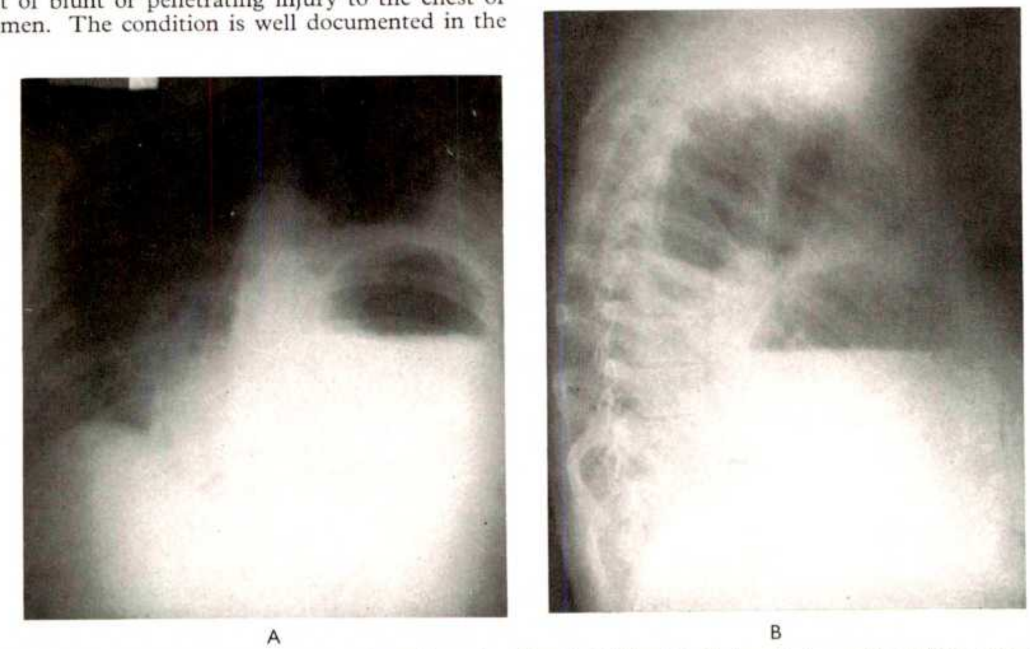

FIG. 1.—Postero-anterior (A) and lateral (B) chest radiographs. Note the fluid level in the herniated stomach and displacement of the oesophagus to the right (nasogastric tube in situ). The lateral view shows two fluid levels, one in the stomach and the other at a lower level which is due to free fluid in the left pleural cavity.

A congenital or traumatic defect in the diaphragm may become symptomatic during pregnancy or in the postpartum period. There have been only 14 such cases reported since 1916 (Granzow, 1927; Fishbeck, 1928; Delee and Gilson, 1941; Diddle and Tidrick, 1941; Salgado, 1944; Thompson and LeBlanc, 1945; Yenen, 1946; Bourgeois and Hood, 1949; Pearson, Pillsbury, and McCallum, 1950; Osborne and Foster, 1953; Grage, MacLean, and Campbell, 1959).

'Spontaneous' rupture of the diaphragm may occur as a result of severe instantaneous effort. Except for 5 cases reported from this department (Bekassy and others, 1973), there has been only 1 other published case of 'spontaneous' rupture of the diaphragm (Salomon, Feller, and Levy, 1969).

The present case is unique as it occurred during an otherwise normal delivery. To our knowledge this is the first such case reported.

CASE REPORT

A 25-year-old primipara was admitted to hospital 38 hours after a 'normal' full-term delivery. She had had a normal antenatal course and denied any previous trauma or symptoms referable to gastro-intestinal, respiratory, or cardiac disease. During the labour she had felt nauseated and immediately thereafter she had developed continuous vomiting, dyspnoea, and constant pain in the left interscapular area which increased on inspiration.

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* Requests for reprints to M. I. Ionescu.

On examination the patient looked ill and was apyrexial and the conjunctivae were pale. Her heart-rate was 200 per minute and regular. The respiration was shallow and the rate was 40 per minute. Examination of the chest revealed signs of collapse of the left lower lobe. There was generalized tenderness in the abdomen. The uterus was small and firm. Intestinal sounds were present. Her haemoglobin was 13·6 g. per cent and the white-cell count 36,500 per c.mm. with 80 per cent polymorphonuclear leucocytes. The serum sodium was 142 mEq./l. and potassium 4 mEq./l. Analysis of the blood-gases showed P_{CO_2} 24 mm. Hg, P_{O_2} 55 mm. Hg, *p*H 7·45, standard bicarbonate 20·0 mEq./l., and base deficit 5·5 mEq./l. A postero-anterior chest radiograph showed a fluid level in the left hemithorax, and the oesophagus was displaced to the opposite side (*Fig.* 1). A diagnosis of rupture of the diaphragm with herniation of the stomach causing high intestinal obstruction was made and the patient was taken immediately to the operating theatre.

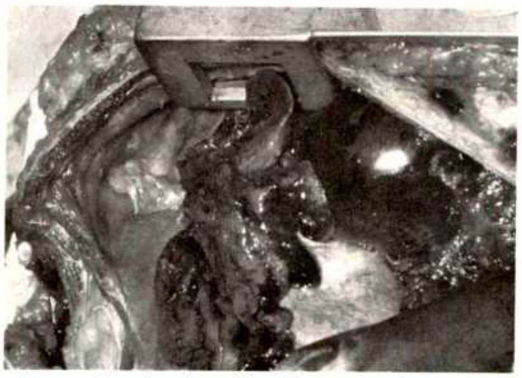

FIG. 2.—Operative view of the left pleural cavity showing the herniated gangrenous stomach and omentum through a fresh tear in the central part of the left diaphragm.

The left chest was opened at the upper border of the seventh rib. About 800 ml. of foetid sanguineous fluid were aspirated from the pleural cavity. The left lower lobe was collapsed. The herniated three-quarters of the stomach together with a large portion of the greater omentum were found to be gangrenous and incarcerated through a rupture of about 3 cm. in diameter situated in the tendinous part of the diaphragm (*Fig.* 2). The chest incision was extended into the abdomen and the diaphragm was incised radially up to the site of rupture, releasing the incarcerated viscera. Three-quarters of the body of the stomach together with the greater omentum were resected. The only healthy parts of the stomach were the cardia with a small segment of the fundus and the pyloric antrum. They were anastomosed with a double layer of continuous sutures. The reconstructed remnant of the stomach was reattached to the transverse mesocolon and the diaphragm was repaired with a double layer of interrupted and continuous silk sutures. Intravenous fluids were given for 7 days postoperatively. The patient made an uneventful recovery and left the hospital on the seventeenth day.

DISCUSSION

'Spontaneous' rupture of the diaphragm is very rare. Five such cases in a group of 19 patients with rupture of the diaphragm seen in this hospital since 1940 have been reported (Bekassy and others, 1973). To the best of our knowledge only 1 other case of 'spontaneous' rupture has been described (Salomon and others, 1969) and none has been reported complicating a 'normal' delivery. Silent diaphragmatic rupture due to previous injuries and congenital defects of the diaphragm have been known to become symptomatic during pregnancy or in the immediate postpartum period. Fourteen such cases have been reported in the literature.

In the present case there was no history of previous injury and the location and appearance of the rupture were such as to exclude a congenital abnormality. Furthermore, a chest radiograph performed 3½ years previously showed no abnormalities of the diaphragm and lungs (*Fig.* 3).

The 'spontaneous' rupture of the diaphragm probably results from a sudden sharp rise in the intra-abdominal pressure, pushing the diaphragm up and tearing its fibres at the least supported part. During the later months of pregnancy the diaphragm is considerably stretched, rendering it more vulnerable to sudden pressure changes. Asynchronous diaphragmatic contractions during labour may create areas of unequal tension, contributing to its rupture.

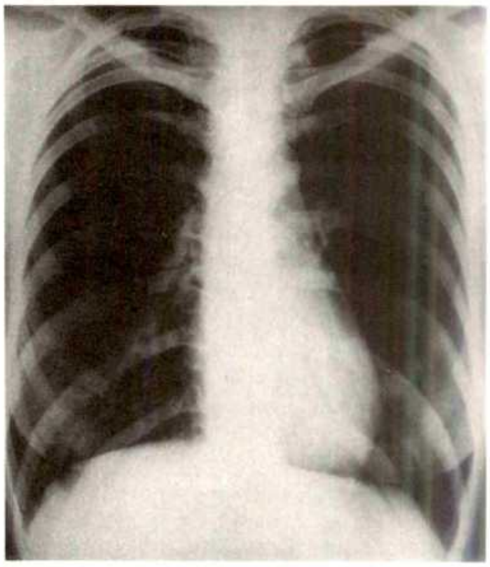

FIG. 3.—Postero-anterior chest radiograph performed 3½ years prior to admission to hospital.

The liver probably protects the right hemidiaphragm by even distribution of the pressure over its entire surface. The peripheral fibres of the diaphragm are supported by the thoracic cage especially when they are more intimately apposed to the chest wall when the diaphragm is suddenly pushed up. The highest part of the left hemidiaphragm is least supported. This possibly accounts for the spontaneous rupture occurring at the centre of the dome. It has been suggested that the site of the rupture in the left leaflet of the diaphragm correlates well with the embryological area of weakness in the posterior and lateral leaflets (Salomon and others, 1969). This, however, does not explain rupture at the centre of the dome in an apparently normal diaphragm.

The diagnosis of 'spontaneous' rupture of the diaphragm is difficult and it should be suspected in patients with uncertain abdominal or respiratory symptoms following instantaneous effort. Radiological examination of the chest and abdomen seems to be the most useful investigation in such cases. Any unusual abnormality on plain radiographs calls for a barium-swallow or barium-enema examination to elucidate the diagnosis further.

Diagnostic pleural aspiration is a hazardous procedure if a diaphragmatic rupture is suspected. Inadvertent injury to the herniated spleen during a diagnostic pleural aspiration, necessitating its subsequent removal, has been reported (Salomon and others, 1969).

In the patient reported here the rupture occurred during a normal delivery and it was followed by chest pain, dyspnoea, and symptoms of high intestinal obstruction. The correct diagnosis was established when chest radiographs showed the herniated stomach and displacement of the oesophagus to the opposite side.

Once the diagnosis is made immediate operation should be performed as there is danger of incarceration and gangrene of the herniated viscera. A mortality of 58·3 per cent has been reported in diaphragmatic hernia complicating pregnancy or the postpartum period (Osborne and Foster, 1953). In doubtful cases an exploratory thoracotomy would seem to be preferable to a laparotomy especially when there is no trauma and no associated abdominal visceral lesions. It is easier to deal with the incarcerated viscera through the thoracic cavity and the incision can be extended into the abdomen if necessary. The repair of the diaphragm is best achieved by a double layer of non-absorbable sutures.

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ACUTE TUBERCULOUS ABSCESS OF THE THYROID GLAND

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SUMMARY

A case is reported of acute tuberculous abscess of the thyroid gland in a young woman. The rarity of this presentation is discussed in the context of the other forms of tuberculous thyroiditis.

Tuberculosis of the thyroid gland is a rare condition and presentation of the disease as an acute abscess is even more uncommon. The case of a young woman with primary tuberculosis of a congenitally malformed thyroid gland in whom an acute abscess destroyed much of the existing thyroid tissue is reported.

CASE REPORT

A 25-year-old married Scots woman was referred to Charing Cross Hospital on 1 Sept., 1972, with a history of pain and swelling in the right side of the neck for 1 week, associated with a fever, general malaise, and a little loss of weight. She had not been abroad recently and there had been no known contact with tuberculosis. On examination there was a tender swelling, the size of a hen's egg, that did did not move freely on swallowing, in the right anterior triangle of the neck. There were no signs of thyrotoxicosis and the provisional diagnosis was haemorrhage into a thyroid cyst.

A chest radiograph was normal but a radiograph of the neck showed tracheal deviation to the left. The white-cell count was normal but the erythrocyte-sedimentation rate was 50 mm. per hour (Westergren) and electrophoresis of the plasma proteins showed an increase in α_2- and γ-globulins. The Paul-Bunnell test was negative. A thyroid scan showed a 'cold' mass in the right lobe and no accumulation of radioactivity in the left lobe, which raised the suspicion of a generalized thyroid disorder.

On 15 Sept. the lump in the neck was explored by a standard thyroid approach. The isthmus and left lobe were absent except for a small nodule of tissue at the lower pole. The right lobe was adherent to the strap muscles and mostly replaced by an abscess containing creamy pus. The abscess was deroofed and drained and pus continued to discharge for several weeks.

Microscopy of the wall of the abscess showed partial destruction of thyroid follicles by tuberculoid granulomas and the pus gave no growth on routine culture. A Mantoux test at this time was just positive at a 1 in 10,000 dilution. Six weeks later acid- and alcohol-fast bacilli were grown from the pus and treatment with streptomycin and Pasinah was started.

DISCUSSION

Tuberculosis of the thyroid gland has been recognized for more than a century, but although the first diagnosis in a living patient was made in 1893 (Bruns, 1893), the majority of cases have been discovered at post-mortem examinations. It is a very rare condition; of 20,758 partial thyroidectomies performed between 1920 and 1931, tuberculous infection was found in 21 cases, an incidence of 0·1 per cent (Rankin and Graham, 1932). In 1952, out of 2114 partial thyroidectomy specimens, only 2 cases were reported (Levitt, 1952), and only 2 cases were discovered among 74,393 patients who underwent thyroid biopsies at an Italian centre between 1941 and 1970 (Bolis, 1970). Most of the patients have been middle-aged females.

The infection of the thyroid may be primary or in association with tuberculosis elsewhere in the body and there is disagreement about which is the more common condition. There are at least five pathological varieties:—

1. Multiple lesions throughout the gland in association with miliary tuberculosis (Rankin and Graham, 1932).
2. A goitre, often with much caseation (Andretta, 1968).
3. Cold-abscess formation sometimes presenting on the surface (Rankin and Graham, 1932).
4. Chronic fibrosing tuberculosis which is difficult to distinguish from De Quervain's thyroiditis (Andretta, 1968);
5. Acute abscess formation is the rarest form (Goldfarb, Schifrin, and Graig, 1965) and the danger of making the wrong diagnosis of carcinoma has been stressed (Crompton and Cameron, 1969).

Disorders of thyroid function are not common but hyperthyroidism does occur and hypothyroidism has been reported (Rankin and Graham, 1932).

The case presented here is an unusual variety of a rare disease. The patient was a young woman with no known contact with tuberculosis and no evidence of tuberculosis involvement of the respiratory or urinary tracts. The onset was sudden and was associated with fever and a painful swelling in the neck. The operative findings suggested acute infection with an organism such as *Staphylococcus*. The correct diagnosis was suggested by the histopathology and was confirmed bacteriologically, but the Mantoux test was only weakly positive, suggesting recent conversion. The patient was euthyroid, but the destruction of the right lobe by the infection combined with the virtual absence of the other lobe (also a rare condition) make it likely that she will become hypothyroid.

We suggest that, with the persistence of tuberculosis in this country, unusual forms and presentations of the disease should not be forgotten.

Acknowledgements.—We are grateful to Dr. R. Jewkes for the thyroid scan, to Dr. K. C. Chong for the histopathology report, and to Dr. H. Andrews for the bacteriological studies.

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REVIEWS AND NOTICES OF BOOKS

Maladie de Dupuytren. Edited by R. TUBIANA and J. T. HUESTON. 10½ × 8¼ in. Pp. 185. Illustrated. 1972. Paris: Expansion Scientifique Française. 85F.

As the results of the treatment of Dupuytren's disease are rather disappointing it is interesting to read the lectures given at a symposium in Paris by outstanding hand surgeons from several countries.

There is a difference of opinion about the necessity of partial or radical removal of the palmar fascia, but the extension on the fingers is the main cause for recurrences. The operation is anatomically difficult particularly because of the closeness of the neurovascular bundle.

The incision in the distal palmar crease is no longer used, longitudinal incisions offering better primary healing.

Grafting of the skin, especially of the fingers, is advocated by many, as necrosis of the skin is not an exception, while the disease sometimes involves the cutaneous tissue.

The extrapalmar symptoms such as contracture of the plantar fascia and Peyroni's disease draw attention to the theory of a congenital disposition.

Non-surgical therapy, using enzymes (trypsine-hyaluronidase) in the case of the hand, and drugs (the cytostatic agent methylhydrazine in Peyroni's disease), offers alternative therapeutic possibilities.

No doubt the surgical treatment should only be undertaken by experienced hand surgeons.

Abraham Colles 1772–1843 Surgeon of Ireland. By MARTIN FALLON, O.B.E. (Mil.), M.A., M.Ch., F.R.C.S.I., F.A.C.S., Perth. 8¼ × 5½ in. Pp. 238 + xii, with 19 illustrations. 1972. London: William Heinemann. £2·25.

EPONYMS are unfashionable, but it is unthinkable that a fracture of the lower end of the radius could ever become dissociated with the name of Abraham Colles.

In this sensitive biography by Martin Fallon, which in fact is the life and times of Abraham Colles, the author portrays vividly a remarkable man, not only as a surgeon with an extraordinary versatility but also as a great leader and teacher who brought honour and distinction to the Dublin School of Medicine in the early nineteenth century. He was twice elected President of the Royal College of Surgeons of Ireland and he also held the Chair of Anatomy, Physiology, and Surgery of the college. Those were the days when Robert Graves, William Stokes, Robert Adams, and John Cheyne made their great contributions to medicine. They were golden years. It is salutary to be reminded in this age of the computer that many of the great advances in medicine can be attributed to the thoughtful interpretation of accurate clinical observation.

This book is much more than a biography. The author has taken great pains to make it so and has succeeded admirably. Around the life of Abraham Colles he has woven a tapestry of events and personalities which provides a background for this astonishing man. It is a most enjoyable book and one that will appeal not only to the orthopaedic surgeon but also to all those interested in the history of medicine.

Die rückenmarksnahen Anästhesien. Edited by H. NOLTE and J. MEYER, Minden. 9 × 6 in. Pp. 105 + vii. Illustrated. 1972. Stuttgart: Georg Thieme Verlag. DM.26.

THIS German work records the proceedings of an international symposium in Minden in 1972. The problems associated with spinal and epidural anaesthesia are discussed in relation to anatomy, physiology, and indications and contra-indications. The approach is somewhat didactic and the text in many places reminds one of a synopsis type of book relieved only in its rather dull presentation by two cartoons. It may be of interest to the anaesthetist with special interest in this field.

Spezielle Chirurgie für die Praxis. Volume II, Part 3. Edited by F. BAUMGARTL, Augsburg, K. KREMER, Dusseldorf, and H. W. SCHREIBER, Hamburg. 10¼ × 7¼ in. Pp. 528 + xii. Illustrated. 1972. Stuttgart. Georg Thieme Verlag. DM. 270.

THIS book is one of a series of beautifully illustrated works on surgery. This volume includes abdominal surgery in children and sections on urology and gynaecology. The text is in German, but the illustrations are self-explanatory and well worth looking at. The text follows the conventional style and deals with indications for surgery and operative technique. It is a practical manual but with good references. The presentation makes for ease in reading, and it will find favour with surgeons in training.

Surgical Treatment of Developmental Jaw Deformities. By EDWARD C. HINDS, B.A., D.D.S., M.D., F.A.C.S., F.A.C.D., Houston, and JOHN N. KENT, B.A., D.D.S., Houston. 10 × 8 in. Pp. 258 + xi. Illustrated. 1972. London: Henry Kimpton. £14·60.

THE indications for skeletal surgery in the treatment of facial deformity are becoming more widely recognized and an extensive literature dealing mainly with techniques already exists. Coincident with this, the demand for this type of surgery is increasing.

The various facets of the subject are brought together by Hinds and Kent in such a way that this book presents itself as a comprehensive review of much value both to the student as well as to the surgeon practising in this difficult and exacting field.

The early chapters spell out the importance of an exact knowledge of the anatomy, both normal and pathological, and the various interests of the surgeon and dentist are very well presented.

Considerable emphasis is put upon the importance of case 'work up' where the problems of skeletal growth and dental function are found to be parameters requiring minute attention. Cephalometry, photography, and dental study models are the techniques required in diagnosis.

The standard surgical procedures which are carried out on the maxilla and the mandible are well described and clearly illustrated. There is sufficient technical information for any surgeon suitably trained and equipped or working with a dental colleague to embark on corrective skeletal procedures although he will find that the more exotic Le Fort osteotomies are not really convincingly described.

The section on splintage is short and anyone unaccustomed to arch bar or cast metal caps would find himself in difficulties. This, however, indicates the importance of teamwork in this field.

The bibliography is comprehensive and offers access to any aspect of the subject, and the book can certainly be recommended for inclusion in the library of anyone interested in facial surgery.

Gastro-intestinal Pathology. By BASIL C. MORSON, V.R.D., M.A., D.M., F.R.C.S., F.R.C.Path., St. Mark's Hospital, London, and I. M. P. DAWSON, M.A., M.D., F.R.C.P., F.R.C.Path., Westminster Medical School, London. 10 × 7 in. Pp. 676 + xii. Illustrated. 1972. Oxford: Blackwell Scientific Publications. £12.

THIS is a book for both the pathologist and the clinician. There has been a need for a concise textbook of the pathology of the alimentary tract, and the authors have done a great service by setting their experience in clinical perspective. Each section of the book is devoted to an organ, and deals first with the normal situation, then common pathology, followed by a consideration of developmental anomalies and disease. It has liberal references, providing an up-to-date starting point for the young clinician or research worker; yet these do not obtrude into the text for the general reader. There are valuable sections on the assessment of biopsies of the alimentary tract, particularly orientated to their clinical significance.

Among the many excellent sections, those on gastritis, the sections on polyps and neoplasms of the colon, as well as the chapter on inflammatory bowel disease reflect the unique contribution of the authors who help to guide us in the significance of pathological findings in these conditions which pose so many problems in management for the clinician. There are carefully selected and beautifully produced illustrations, and the presentation of the book is without criticism.

The task of presenting a textbook is arduous and the tendency is to reproduce the standard model. The authors have rejected this temptation and have given their views of the significance of pathological contribution to the clinical problem. We need more books of this type. This book is essential reading for all gastroenterologists. It should become the standard reference book for pathology of the alimentary tract. All clinicians will find it helpful in the management of patients with alimentary disorders, and the cost should not detract from the need for the clinician to include this as an essential part of his personal library.

Manual of Surgical Therapeutics. Second edition. Edited by ROBERT E. CONDON, M.D., M.S., Iowa, and LLOYD M. NYHUS, M.D., Chicago. 8½ × 5¼ in. Pp. 385 + xii. Illustrated. 1972. Edinburgh: Churchill Livingstone. £3·25.

THIS is an excellent book; being a mere 385 pages long, it starts with the advantage that undergraduate students, junior hospital staff, and others can hope to find time to read it. There are seventeen chapters, some of which contain several sections by different authors. For example, Chapter 1 is on the evaluation and management of trauma and comprises 66 pages divided into eight sections, all by different authors. Other chapters are shorter, for instance, massive upper gastro-intestinal haemorrhage is disposed of in 4½ pages by Professor Nyhus. Despite the multiple authorship there is a remarkable uniformity in style and presentation with succinct sentences, short, numbered paragraphs, and free use of italics and heavy type; no doubt this is the work of the editors. They are to be congratulated for producing a concise book which promotes clear thought and logical, effective action.

Drug therapy in surgical patients is a notable feature of the book; British readers will have to translate the names of some drugs. They will note some absences: 'parenteral fat emulsions are not currently available in U.S.A.', but readers will be rewarded by finding that even in Chicago pills and injections are not everything: 'Cranberry juice, 240 ml., twice daily will keep the urine *p*H acidic.'

Progress in Pediatric Surgery. Volume 4. Edited by P. P. RICKHAM, Zürich, W. CH. HECKER, Munich, and J. PRÉVOT, Nancy. 8¾ × 6 in. Pp. 164. Illustrated. 1972. Munich: Urban & Schwarzenberg. DM.45.

THIS is the fourth volume of a series. It begins with C. E. Koop's 1971 Simpson Smith Lecture on neuroblastoma; an interesting and stimulating account of the author's experience and views on the treatment of this baffling and lethal tumour. In it he emphasizes the poor results of present methods of treatment and the lack of improvement in the past 15 years and the importance of removing, even by crude surgical means, the bulk of the tumour. He cites evidence for the importance of the immune response of the individual host against the tumour and suggests that all that much of conventional treatment by radiotherapy and chemotherapy achieves is an impairment of the host's natural resistance and some prolongation of survival at the expense of increased illness.

Pleuropulmonary circulation in neonates and infants is a different process to that found in adults and is discussed by Geley and Hartl from Linz, Austria. They discuss the aetiology of empyema of the pleura in the neonate, particularly staphylococcal pneumonia, and how they have reduced the mortality by suction drainage of the abscess at a much earlier stage than had been attempted previously, with an associated reduction in the need for thoracotomy from 30 per cent to 5 per cent and the improvement in subsequent expansion of the lungs by positive-pressure inflation with decortication if this form of treatment fails. The long-term results were also much improved by early suction drainage.

J. Prévot and his colleagues from Nancy, France, deal with the treatment of very-long-segment Hirschsprung's disease in which the whole of the colon and distal ileum are aganglionic. They discuss the diagnostic problems of this form of Hirschsprung's disease and their own experience with it in 7 patients and 1 in whom they used the technique of Lester Martin, in which a long length of normally innervated distal ileum is pulled down to the anus and then is anastomosed side to side to the rectum and colon from the splenic flexure of the pelvic floor. This operation was designed in the hope that it would reduce the morbidity and mortality resulting from excision of the whole colon in the neonate.

In his 1971 Forshall Lecture in Genoa Soave described his experience with the use of the transverse colon to bridge the gap between the two ends of the oesophagus in oesophageal atresia when this was too wide for a primary anastomosis. Soave describes his experience with the use of the transverse colon in 27 patients, with a 19 per cent mortality-rate, the colon being anastomosed to the distal end of the upper pouch and the proximal end of the distal pouch.

Moosa, in describing 16 patients with acute pancreatitis seen at the Alder Hey Hospital, Liverpool, between 1954 and 1970, has stated that he believes that now that this condition is known to occur in children many more patients are being recognized than in the earlier part of the period covered by his series. He points out that the clinical features, the complications, and the way in which the disease should be treated in children are similar to those in adults although the aetiological factors are different. So also is the prognosis in children which is usually good. Only 1 of their patients had recurrent pancreatitis and only 1 died.

Finally, Lawson discusses the results of treatment of obstruction due to the resection of too little of the aganglionic segment of Hirschsprung's disease in 28 patients and suggests that forcible dilatation of the anal canal and the distal residual segment should be tried and that if this treatment fails a vertical internal sphincterotomy may be necessary to produce relief.

The papers in this volume are of most interest to paediatric surgeons who are directly concerned with the problems which are described, but in the sense that the number of survivors from the successful treatment of these various anomalies and diseases is steadily increasing, they have some general interest for all surgeons who have to deal with children later in life, either for the late complications of neonatal operations or for other conditions which are not associated with their original anomalies.

Symposium on Aesthetic Surgery of the Face, Eyelid, and Breast. Edited by FRANK W. MASTERS, M.D., Kansas, and JOHN R. LEWIS, jun., M.D., Atlanta. 11 × 8½ in. Pp. 222 + xii. Illustrated. 1972. London: Henry Kimpton. £16.

THIS is the fourth volume in a series on plastic and reconstructive surgery. The previous volumes reported symposia on head and neck cancer, maxillofacial injuries, and the hand. This volume documents a symposium held at Phoenix, Arizona, in November, 1970, organized by the Educational Foundation of the American Society of Plastic and Reconstructive Surgeons. There are thirty-eight contributors.

Of the two introductory chapters, the first, on the psychological aspects of aesthetic surgery, is helpful but too short; however, there is further coverage of this topic in later chapters. The second chapter gives some hints on how to run a cosmetic surgery practice.

Surgery of the ageing face is covered in thirteen chapters. The section commences with a brief review of the anatomy and physiology of ageing skin; following this the indications and contra-indications for rhytidectomy are discussed and a standard operative technique is described. There is a comprehensive list of complications and how to avoid them. Completing this section there are two detailed chapters on the 'chemical peel'.

The five chapters on blepharoplasty include a clear description of a standard technique and an account of several useful modifications.

The aesthetic surgery of the breast is dealt with in the final fourteen chapters. This part starts with a short history and comprehensive bibliography of cosmetic and reconstructive breast surgery and continues with a brief account of the anatomy and a rather lengthy description of the thermographic and radiographic appearances of the breast. There follows a description of the types of breast prosthesis available and the techniques of breast augmentation. The complications of this procedure are mentioned. Breast reconstruction following subcutaneous mastectomy for fibrocystic disease is fully discussed and methods of nipple reconstruction are described. Breast reduction by the methods of nipple transplantation and transposition is detailed and suggestions for how to tailor the surgery to the type of deformity are given. The chapter on the complications of breast reduction is too brief.

The presentation of this book is good but there is wasted space and repetition. Illustrations are plentiful although many of the 'before' and 'after' photographs are not strictly comparable and in one diagram (*Fig.* 24-9) the titles are transposed.

It is a book that should be read by all who are engaged in the aesthetic surgery of the face and breast.

Perfusion Techniques in Biochemistry. A Laboratory Manual. By B. D. Ross. 9½ × 6½ in. Pp. 479 + xv. Illustrated. 1972. London: Oxford University Press. £11·50.

THIS book is for the specialist and might usefully be available in all laboratories carrying out work on organ-perfusion systems. There is an immense amount of detail about technique with many hints to the worker who is new to this field. More valuable, however, is the consideration of the advantages and limitations of techniques which is so necessary to the novitiate, yet often so hard to find.

It is a closely packed volume which should act as a standard reference for this type of work. It is carefully illustrated and has excellent references. The general principles section deals with the characteristics of perfusion media and even includes a part on items such as cannulae. The sections on perfusion of individual organs frequently itemize more than one technique, so that the experimental research worker can choose the one which is most suited to his needs.

It is not a book for general reading. The research worker in this field will find it a most excellent guide and reference book.

Immunization in Tuberculosis. Forgarty International Center Proceedings No. 14. Edited by Dr. CARL C. CHAMBERLAYNE. 9 × 6 in. Pp. 252 + v. Illustrated. 1972. Bethesda: U.S. Department of Health, Education, and Welfare. $3.

THIS book reflects the use of anti-tuberculous vaccines by the United States Public Health Service. It reviews

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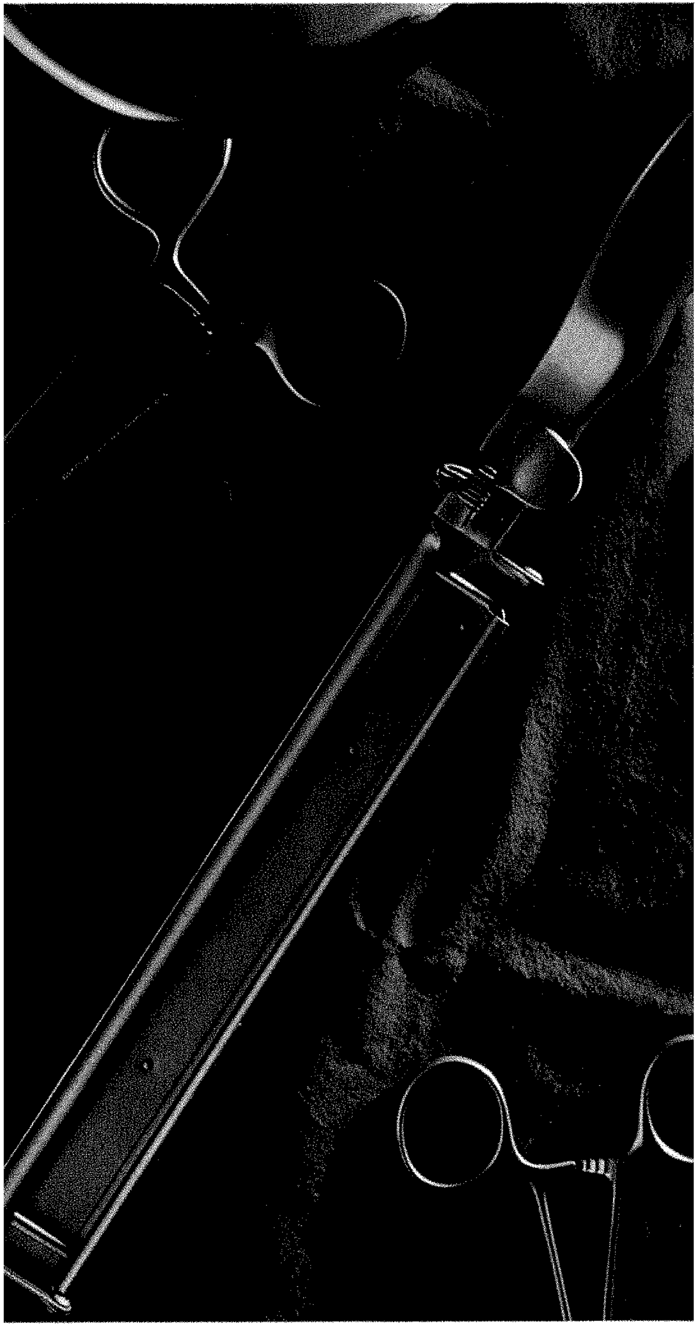

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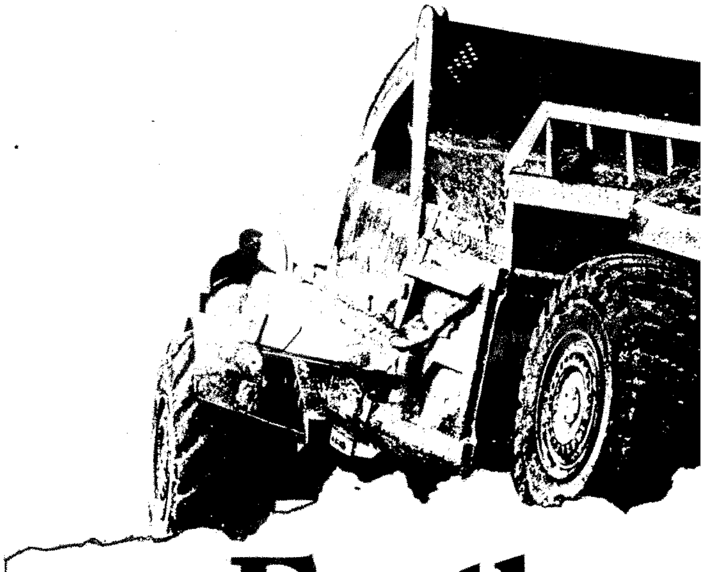

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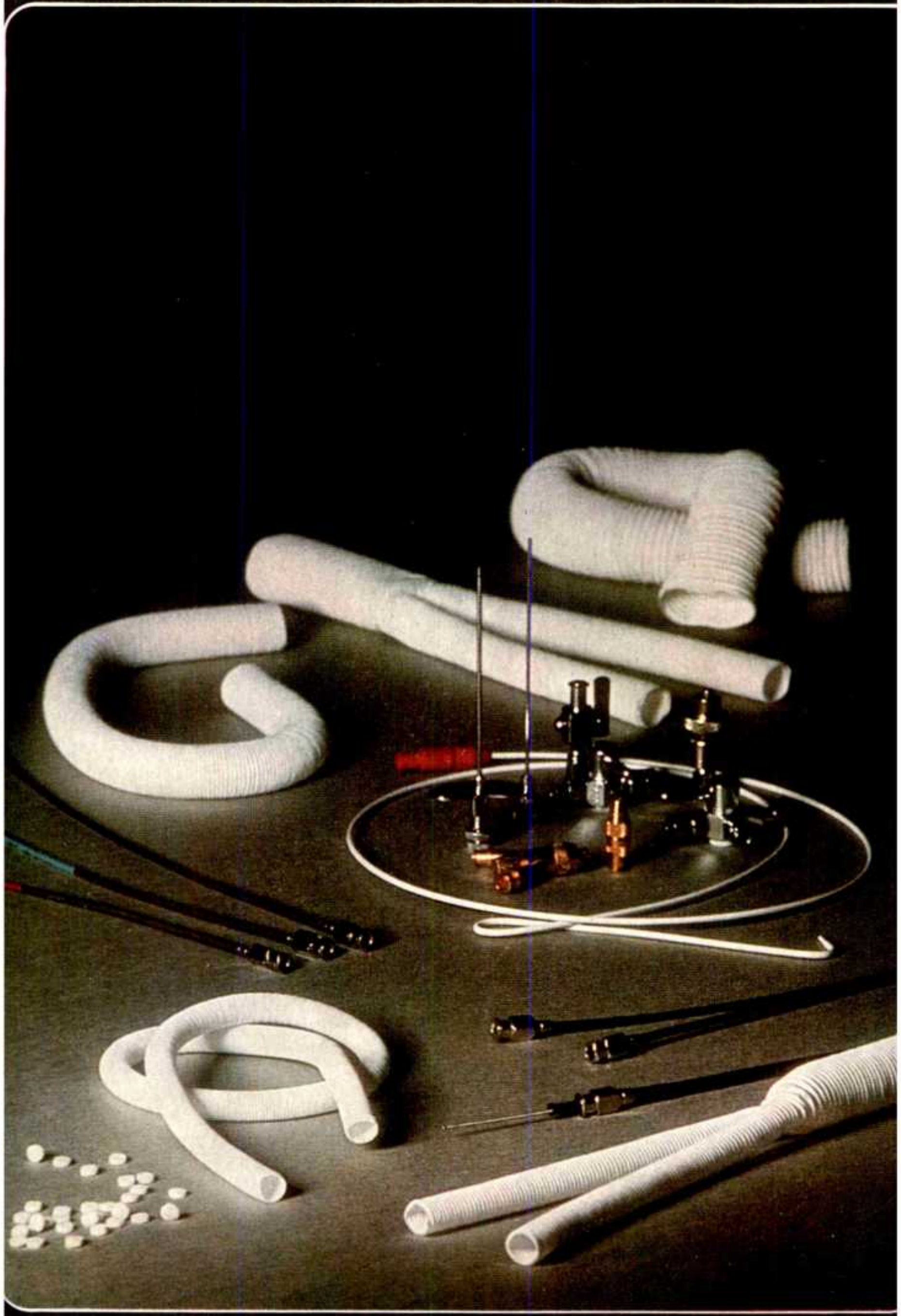

Cardiovascular catheter and grafts

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1 *Brit med J* (1969), **4**, 470
2 *Postgrad med J* (1969), **45**, Supplement (November), 91
3 *S Afr med J* (1970), **44**, Supplement (August), 17
4 *Med J Aust* (1971), **1**, 526

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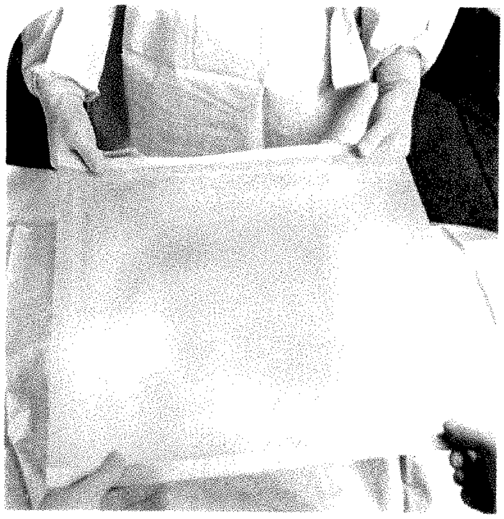

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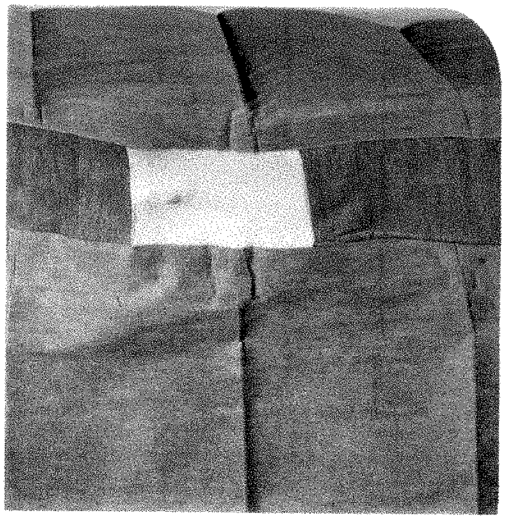

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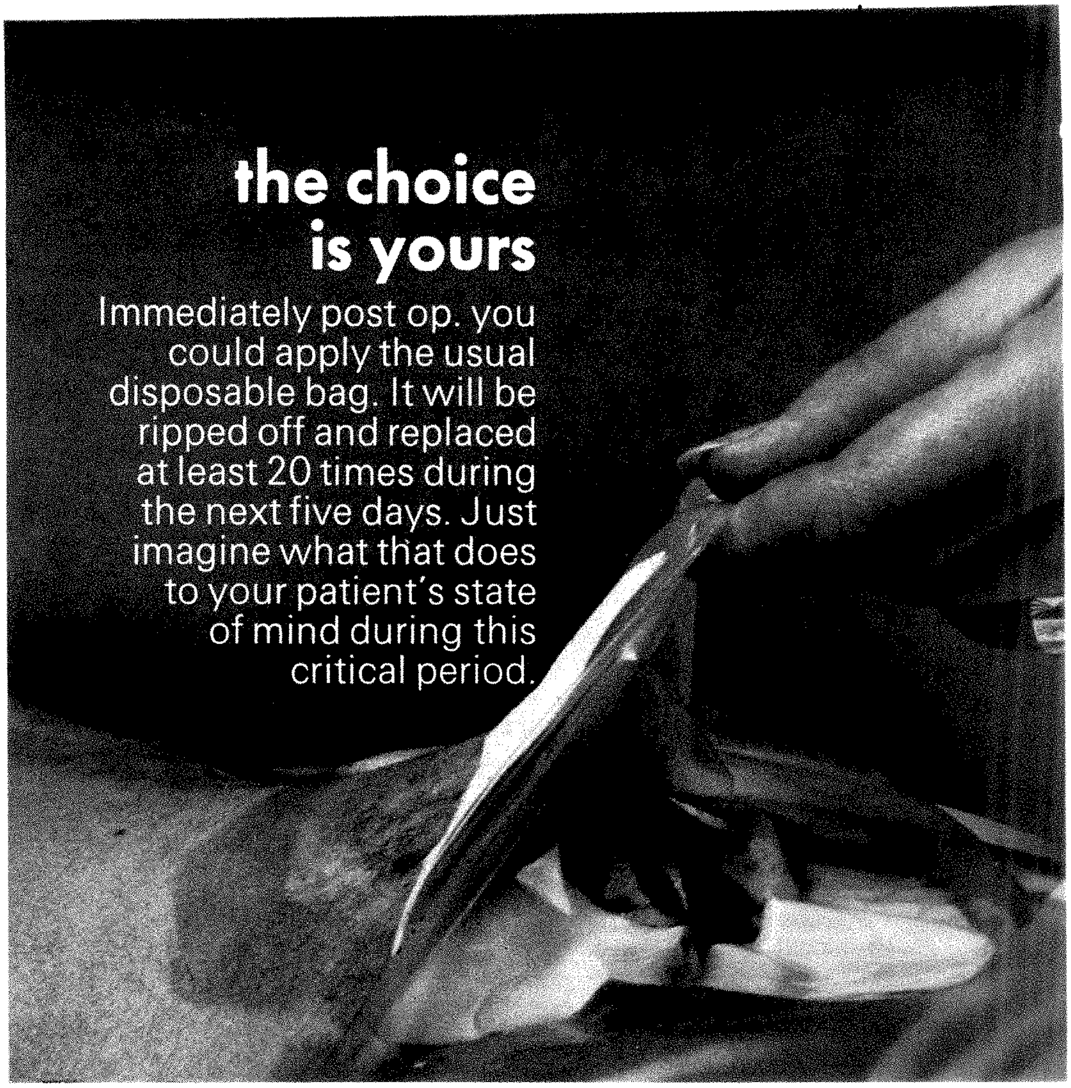

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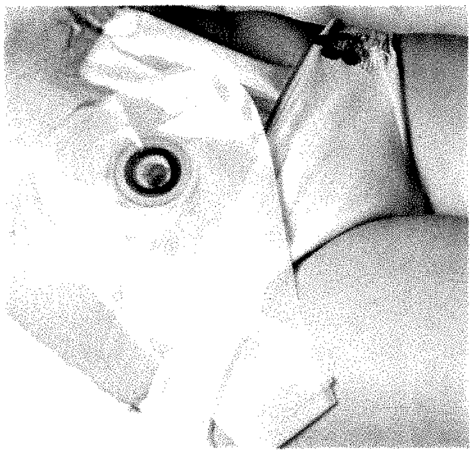

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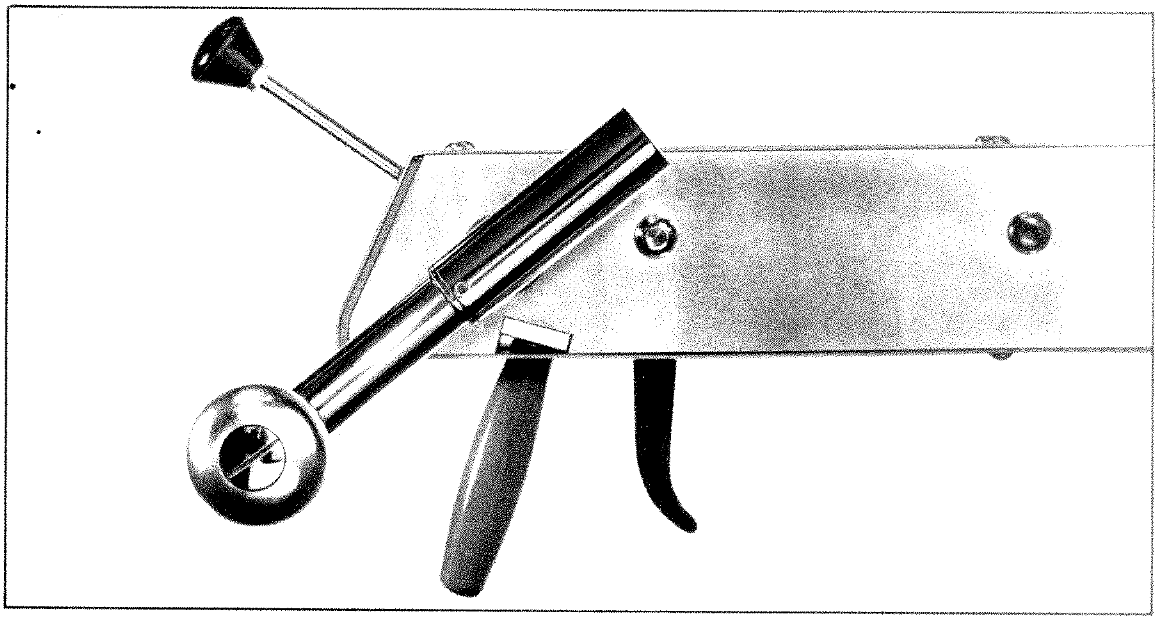

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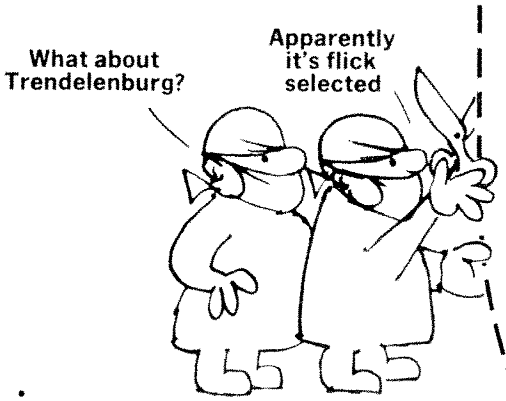

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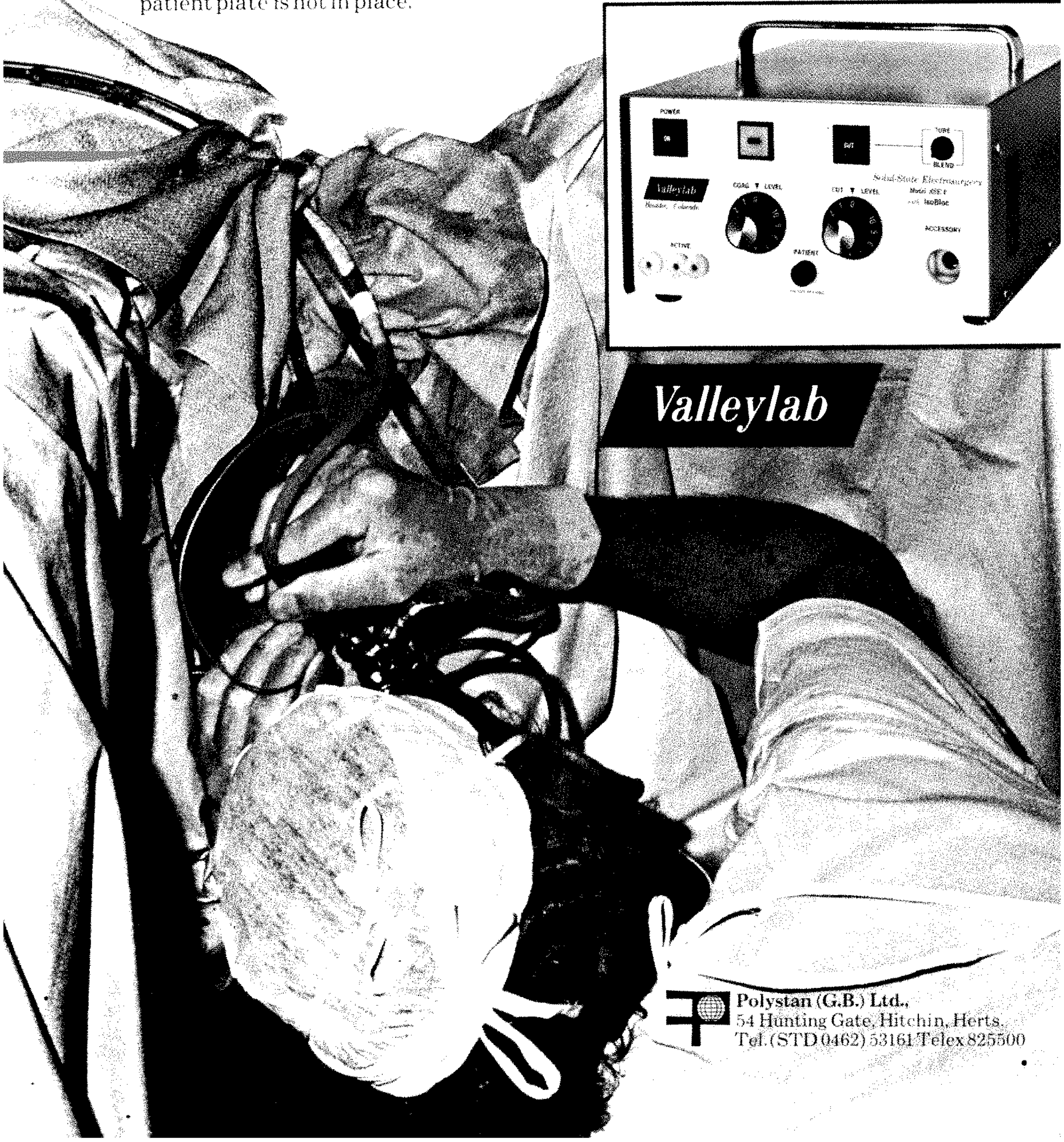

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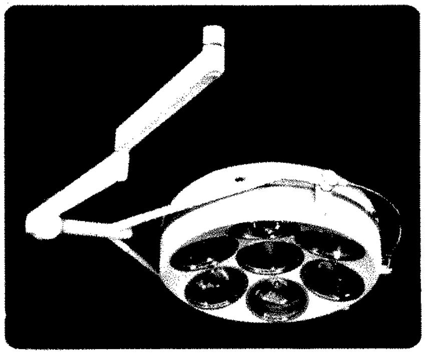

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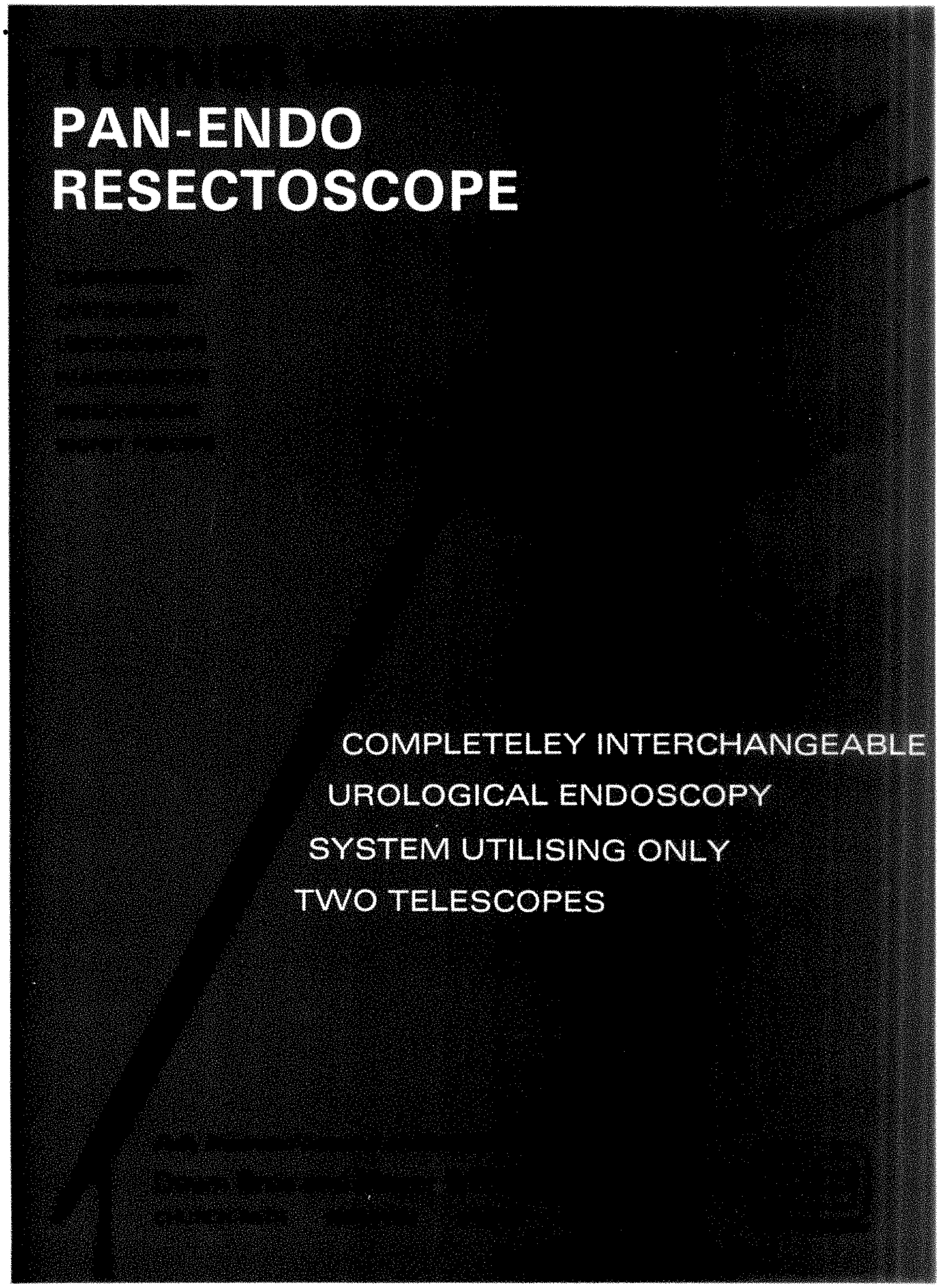
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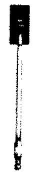

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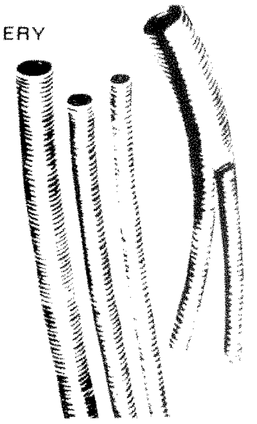

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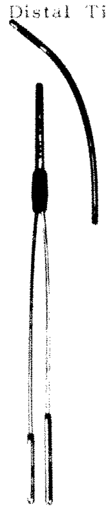

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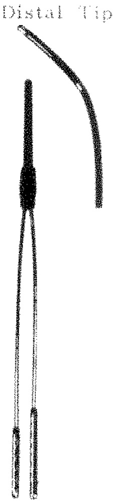

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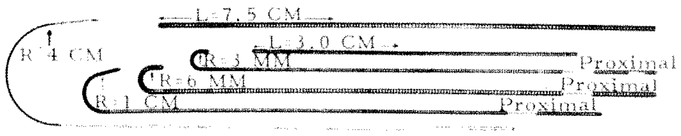

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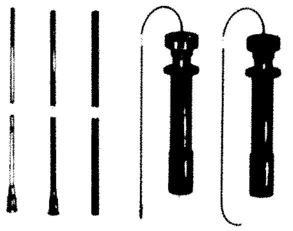

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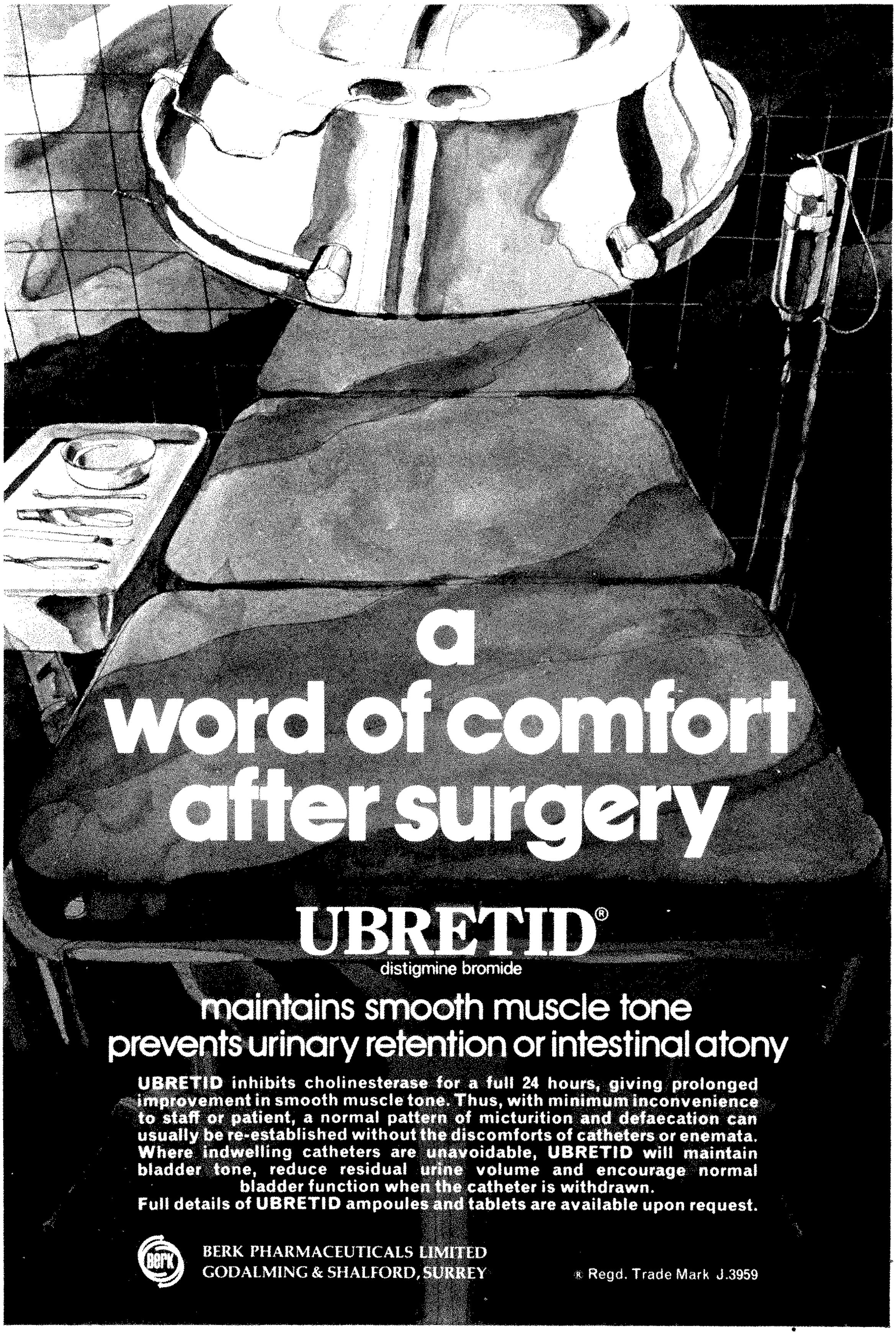

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SENIOR REGISTRAR IN GENERAL SURGERY, THE UNITED LIVERPOOL HOSPITALS

SUMMARY

Two patients with a particular type of isolated injury to the left colon produced by the lapstrap of a seat belt are described. The literature on this subject is reviewed and the features and management of these injuries are discussed, with particular reference to the delay in presentation often seen in such patients and to the frequent association with ischaemic damage which makes proximal colostomy advisable where primary repair is undertaken.

Of 4 patients presenting at a major accident centre with closed injuries of the left colon, there were 2 in whom a seat belt appeared to have been responsible for the injury. These 2 patients are reported and the features of seat-belt injuries of the colon are described together with a review of the literature and a discussion of the management of this type of injury.

CASE REPORTS

Case 1.—A 42-year-old lorry driver was admitted to the Accident Centre at Walton Hospital, Liverpool, on 18 March, 1970. He had been driving a car which had been in collision with another car 14 hours earlier. He had been wearing a lapstrap and diagonal belt type of seat belt.

He had sustained a head injury and after regaining consciousness he had noticed some discomfort in his left lower abdomen which he had attributed to the tightening of his seat belt at the time of impact. This sensation had rapidly passed off and he had felt well enough to return home without attending hospital.

Twelve hours later (2 hours prior to admission) the discomfort had returned and had slowly increased in severity, being latterly aggravated by movement and by coughing. He had therefore attended the Accident Centre.

He stated that he had passed both flatus and faeces per rectum since the accident and at the initial examination the only positive finding was of localized moderate tenderness without guarding in the left lower quadrant of his abdomen. Straight radiographs of his abdomen showed no abnormality. It was felt that he had suffered a contusion of his abdominal wall from his seat belt but nevertheless he was detained in hospital under observation.

His condition did not change for 6 hours but then he developed a pyrexia associated with a tachycardia, and further examination disclosed a slight but definite increase in his still-localized abdominal tenderness with, more significantly, the appearance of associated guarding.

With this evidence of intraperitoneal injury laparotomy was undertaken, being commenced 9½ hours after admission and 23½ hours after the injury.

At operation, apart from an area of minor contusion of the lower ileum, the only finding was that the lower descending colon was gangrenous over a length of 7 cm. The colon was intact although perforation was imminent, and the damaged segment was exteriorized by the method of Paul and Mikulicz through a separate incision in the left lower quadrant, and resected at skin level after closure of the main wound.

The postoperative course was uneventful and the colostomy was closed on the twentieth day. The patient was allowed home 13 days later and when seen subsequently he was found to have made an excellent recovery.

Histological examination of the excised colon showed nothing other than ischaemic changes due to trauma.

Case 2.—A 39-year-old engineer was admitted to the Accident Centre on 20 March, 1970. He had been driving a car which had collided with another vehicle 3 hours earlier. He had been wearing a lapstrap and diagonal belt type of seat belt.

Following the accident he had walked away unaided, and although he had noticed some left-sided abdominal discomfort he had returned home immediately. During the next 3 hours the discomfort had steadily increased and in the hour prior to admission he had vomited and had felt pain at the tip of his left shoulder. There was no other injury, but he stated that he had been treated with a steroid preparation for ulcerative colitis in the past, although he had been well and had not required any such treatment for the previous 5 years.

Examination showed that he was moderately shocked with evidence of peritoneal irritation in the left half of his abdomen. A transverse band of bruising was noted on the left side of his abdomen caused by the seat-belt lapstrap.

A diagnosis of intraperitoneal injury and bleeding was made and laparotomy was undertaken 4 hours after the accident.

At operation a haemoperitoneum of 1 litre was aspirated and free faecal material was removed from the left side of the abdominal cavity. The descending colon was almost completely severed in its upper third and multiple minor contusions of the small bowel were also noted. The bleeding had come from torn paracolic vessels. There was no evidence of active ulcerative colitis. The damaged ends of the colon were resected and these were then exteriorized as a double colostomy on the left side of the abdomen.

The postoperative course was normal and the patient was allowed home on the fourteenth day. Histological examination of the excised colon showed no evidence of ulcerative colitis and full investigation during the recovery period was normal. His colostomy was closed 3 months later and he has subsequently made a full recovery.

REVIEW OF THE LITERATURE

In 1952 DuBois, discussing the Viking aeroplane crash of 1950, described, in addition to other major injuries, severe intra-abdominal damage to the solid viscera and the great vessels owing to acute flexion of the victim over the lapstrap safety harness in use.

During the past decade considerable interest has been shown in the United States of America in what has become popularly known as the 'seat-belt syndrome', where a variety of injuries may be produced by the sudden tightening of a seat belt in road accidents, including intra-abdominal damage (Shennan, 1973). This latter type of injury is particularly likely to occur when such belts are worn improperly (Sube, Ziperman, and McIver, 1967).

The first description of this type of abdominal injury is credited to Kulowski and Rost (1956), who reported 1 case of traumatic contusion of the terminal ileum due to a seat-belt lapstrap which was followed by adhesion formation and repeated bouts of intestinal obstruction. Subsequently, a number of similar reports have been published and it is clear from these that the jejunum and ileum with their mesentery are the most frequently damaged structures (Garrett and Braunstein, 1962, 1 case; Sube and others, 1967, 2 cases; Shamblin, 1968, 2 cases; Witte, 1968, 5 cases). Other viscera have been injured by seat belts including the bladder and kidney (Garrett and Braunstein, 1962), the gravid uterus (Rubovits, 1964), common bile-duct (Spitz, 1971), pylorus (Shamblin, 1968), and duodenum (McLeod and Nicholson, 1969).

Seat-belt injuries of the colon are most uncommon and the first case of isolated colon injury by this mechanism was recorded by Tolins (1964). Williams, Lies, and Hale (1966) reported 1 patient with sigmoid mesocolon damage where the colon itself was intact, and Blumenberg (1967) described a patient with delayed ischaemic perforation of the sigmoid colon occurring 72 hours after injury. Witte (1968) reported that 1 of his 5 patients with seat-belt injury of the jejuno-ileum had also sustained multiple lacerations of the sigmoid colon and mesocolon. Towne and Coe (1971) reported 4 patients with seat-belt injuries of the left colon and in 2 of these patients associated major damage to the small bowel was present. Sube and others (1967) described a unique injury to the sigmoid colon where the serosa and muscularis layers are torn away leaving an intact mucosal tube and which they termed the 'sleeve-stripping injury'.

DISCUSSION

Both the patients reported in this paper were the drivers of cars and were wearing seat belts of the lapstrap and diagonal belt type. Both were involved in a head-on collision with another vehicle and their seat belts probably prevented multiple injuries being sustained by them. Each patient was able to walk away from the accident apparently without serious harm but were later seen to have sustained isolated severe damage to the descending colon caused by the seat-belt lapstrap on impact.

The features of interest demonstrated by these 2 patients were:—

1. Initial discomfort at the site of the injury experienced immediately after the accident but attributed by both patients to the seat belt and therefore causing them no early concern. This was followed by a variable latent period, of 12 hours in the patient with ischaemic damage and of 3 hours in the patient with actual colon rupture.
2. A consequent delay in seeking advice even in the patient with faecal soiling.
3. The importance of close observation in doubtful cases with a suggestive history is illustrated by *Case* 1, as without doubt ischaemic perforation of the colon would have ensued had he been merely reassured and allowed to leave hospital.
4. A progressive increase in the clinical picture, the rapidity being clearly related to the type of lesion present. Maximal signs occurred over the site of the colon injury in both patients but the clinical evidence of intraperitoneal injury took considerably longer to develop in the patient with traumatic ischaemia of the colon.
5. Bruising along the line of the seat-belt lapstrap was present in *Case* 2.
6. The isolated nature of the injury which involved the fixed part of the descending colon in both patients. Minor small-bowel contusion was present in both patients but in neither was this severe enough to have necessitated exploration itself.
7. The Paul-Mikulicz operation was particularly satisfactory in the patient with traumatic ischaemia as the basic lesion.
8. The favourable prognosis when the correct diagnosis is made without delay and treatment is instituted immediately.

Most reports of the 'seat-belt syndrome' where injury to either the large or the small bowel has occurred have stressed that delay in presentation is commonly seen (Williams and others, 1966). Sube and others (1967) described a delay in presentation of from 2 to 13 days in 4 of the patients whom they reviewed. Blumenberg's (1967) patient with traumatic ischaemia of the sigmoid colon presented 72 hours after injury. Towne and Coe (1971) reported a delay in the presentation of 3 of their 4 patients. These authors have emphasized the importance of close observation in this group of patients and recommended diagnostic abdominal paracentesis as being helpful (Williams and others, 1966; Sube and others, 1967; Towne and Coe, 1971).

There can be no doubt that delayed rupture of the colon following traumatic ischaemia is a definite entity, and although usually occurring before the fourth day it has been described considerably later (Gogler, 1962). With the more frequent use of car seat belts the possibility of colon damage existing in patients with seat-belt injuries should certainly be kept in mind.

MANAGEMENT

In *Case* 1 resection and anastomosis with proximal colostomy carried no advantage over the Paul-Mikulicz procedure which was used. The risk of further extension of the ischaemic process with breakdown of an anastomosis was an important consideration here and the Paul-Mikulicz operation was the method of choice with a highly satisfactory outcome.

Case 2 had significant faecal soiling at operation and there was the additional possibility of a severe exacerbation of his ulcerative colitis occurring and the risk of anastomosing colon involved by this disease to consider. Exteriorization was therefore the procedure of choice in this patient.

Witte (1968) performed simple primary repair in his patient with lacerations of the sigmoid colon, with a satisfactory outcome. Blumenberg (1967) performed a Paul-Mikulicz operation on his patient with delayed ischaemic perforation of the sigmoid colon and survival ensued. The experience of Towne and Coe (1971) is instructive. They described 4 patients with seat-belt injuries of the left colon of whom 2 had seromuscular tears of the sigmoid colon without penetration of the lumen. One of these patients had no other injury and simple oversewing was successful. The other patient also had severe damage to the ileum and its mesentery but the apparently minor superficial colon injury was treated by simple oversewing; postoperatively the colon repair broke down and the patient died. The 2 other patients in this series had perforating injuries of the left colon and both were treated by exteriorization; one of these patients, who had multiple associated injuries, died of renal failure on the tenth day, while the other patient recovered. These authors concluded that patients with seat-belt injuries of the left colon should have a proximal colostomy when primary repair is undertaken, even for seemingly trivial seromuscular tears.

It would seem that injuries of the left colon produced by seat belts might appear minor in extent and amenable to simple repair. However, there is a high incidence of associated ischaemic damage which may not be immediately obvious and which might be responsible for delayed breakdown of such a repair in the postoperative period. In view of this, proximal colostomy in addition to repair might be the treatment of choice even in the most minor injuries. For the same reasons the author would agree with Towne and Coe (1971) in suggesting that all transecting injuries produced by this mechanism should probably be exteriorized as a double colostomy and would add that for traumatic ischaemia of the left colon the Paul-Mikulicz procedure is particularly suitable.

CLASSIFICATION AND MECHANISM OF SEAT-BELT INJURIES

Sube and others (1967) classified seat-belt injuries of the abdomen according to the structure damaged and suggested three groups of injury which might occur alone or in combination:—

1. Superficial injury to the abdominal wall comprising cutaneous abrasions and bruising as well as muscular damage.
2. Intra-abdominal vascular injuries comprising tears of the mesentery or mesocolon with bleeding and including adjacent bowel ischaemia and possible delayed perforation.
3. Hollow visceral injury, usually the small bowel but less commonly the colon, stomach, bladder, and gravid uterus being damaged.

Towne and Coe (1971) described two types of bowel injury due to seat belts:—

1. Discrete perforations, usually at the anti-mesenteric border and often multiple, occurring at any level of the gastro-intestinal tract.
2. Complete or almost complete transections occurring particularly at or near points of fixation in the small and large bowels and due largely to shearing forces impinging against the vertebral column.

Discussing the way in which seat belts cause injury to the abdominal contents, Sube and others (1967) pointed out that a loosely worn belt was particularly concerned, and Towne and Coe (1971) emphasized that if the belt was worn at all loosely there was a tendency to slide forwards and under the lapstrap at impact, so-called 'submarining', so that instead of the force of impact being taken on the bony pelvic girdle it is exerted on the soft tissues of the abdomen and flank. Indeed such a shearing force applied to the flank may well be the major factor in transecting and ischaemic injuries of the fixed parts of the left colon.

It is certainly not the purpose of this paper to suggest that seat belts, properly worn, are dangerous. There is no doubt that the incidence of serious injury and death in road accidents has been dramatically reduced by their use. Garrett and Braunstein (1962) in America cited a reduction of 35 per cent, Lister and Milsom in Britain (1963) quoted a reduction of 51 per cent, and Shamblin (1968) stated that 5000 lives per year are saved by seat belts being employed.

Acknowledgements.—I am most grateful to Mr. G. J. Santer and Mr. D. Sykes for allowing me to publish these reports of their patients, and I would also like to express my thanks to Mrs. A. O. Mansfield and to Mr. David Annis for their interest and invaluable assistance.

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REVERSED AUTOGENOUS SAPHENOUS VEIN BY-PASS FROM THE COMMON TO THE DEEP FEMORAL (PROFUNDA FEMORIS) ARTERY

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SUMMARY

Extended deep femoral angioplasty is an invaluable method of saving a limb especially where a femoropopliteal vein by-pass is not possible because of a poor run-off. Atherosclerosis in the deep femoral artery often extends for more than 10 cm. In such cases we have preferred to perform a short vein by-pass than an extensive endarterectomy and patch graft. Our experience is described of 6 such cases, in 5 of whom amputation was avoided.

EXPERIENCE with revascularization of the ischaemic leg by extended deep femoral (profunda femoris) angioplasty has proved that such an operation is a simple and effective method of increasing the blood-supply and an indispensable technique where femoropopliteal by-pass grafting is either undesirable or impossible (Martin, Frawley, Barabas, and Rosengarten, 1972, Berguer, Cotton, and Sabri, 1973). In our continuing experience with reconstruction of the deep femoral artery we have met 6 instances in which our standard technique—endarterectomy and patching—did not seem an adequate solution, and therefore a vein by-pass was used instead. The discussion of this technique is the concern of the present report.

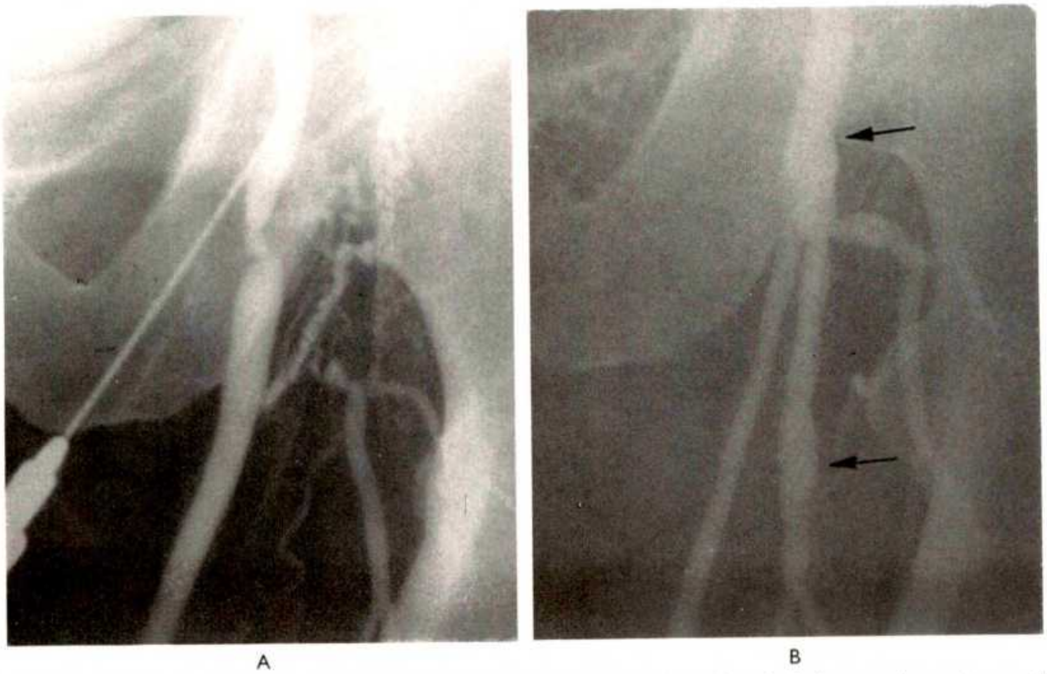

FIG. 1.—*Case* 1. A, Preoperative arteriogram showing complete occlusion of the deep femoral trunk. B, Postoperative arteriogram. The by-pass is between the arrows.

INDICATIONS

Four patients presented with rest pain, 1 of whom had ischaemic ulceration as well. Because of severe distal disease below the level of the knee they were not candidates for a femoropopliteal by-pass operation and were therefore facing amputation. The fifth patient had severe intermittent claudication (20 yards). The sixth patient underwent an aortofemoral endarterectomy to the level of the deep femoral artery on both sides. In spite of a good pulsation being produced in both the common and proximal deep femoral arteries, electromagnetic flow readings in the right common femoral artery were very low (45 ml. per minute). This figure represented the total outflow to the leg through the deep femoral artery since the superficial femoral artery was occluded. In this patient the right deep femoral artery was further exposed and a vein by-pass to the distal part of the deep femoral artery was carried out.

Frontal and oblique angiograms in these patients were of little help in determining the actual extent of the disease beyond the origin of the deep femoral artery. In 1 case the trunk was occluded (*Fig.* 1). In arteries of small calibre (3–5 mm. diameter) atherosclerotic plaques often cause drastic reductions in the cross-section area although angiograms fail to reveal their presence.

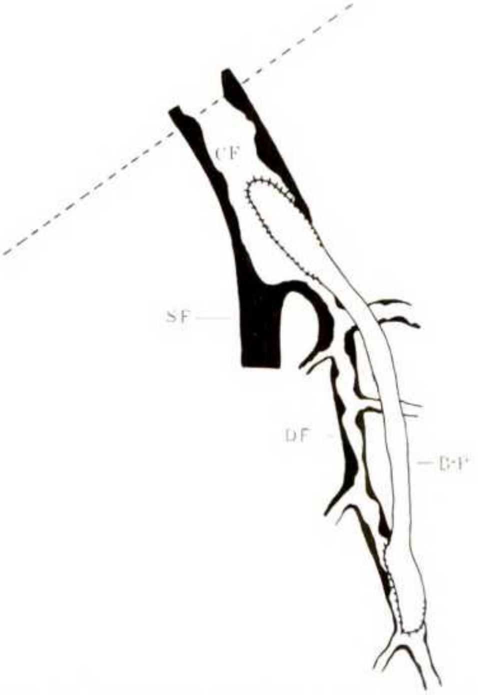

FIG. 2.—Schematic drawing of the common to deep femoral artery by-pass operation.

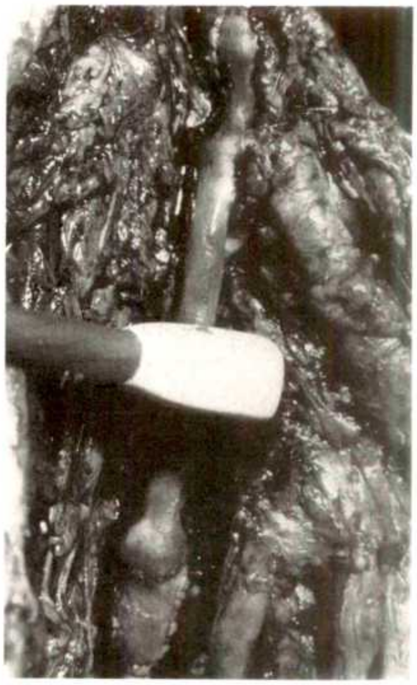

FIG. 3.—A completed by-pass with the flow transducer in place.

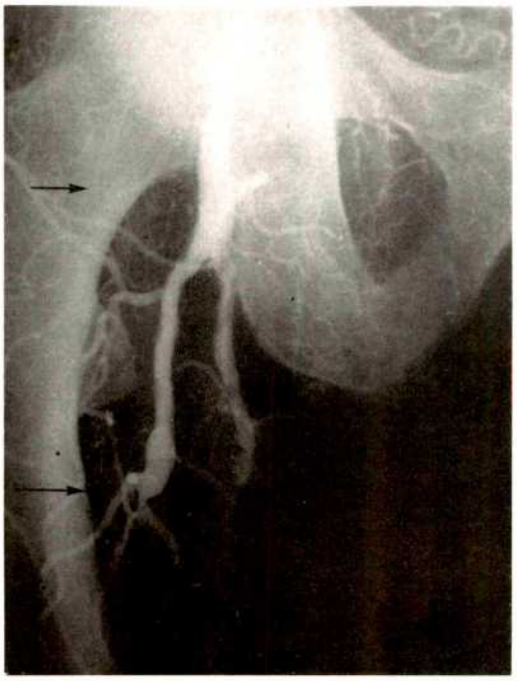

FIG. 4.—*Case* 2. Postoperative anteroposterior arteriogram showing the deep femoral by-pass (between the arrow levels).

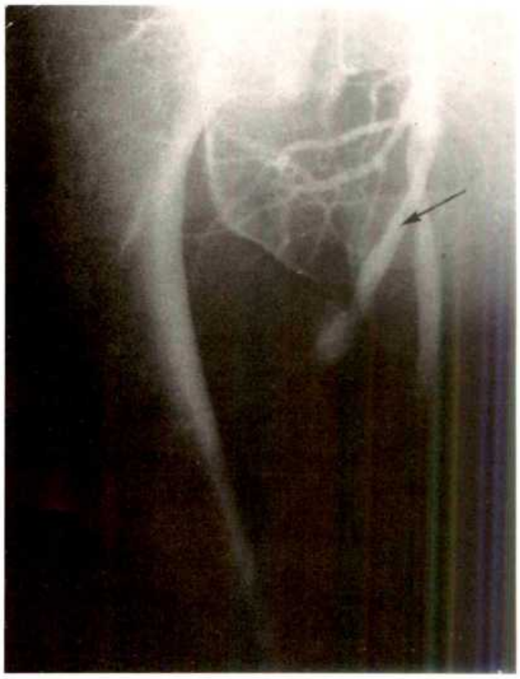

FIG. 5.—*Case* 4. Postoperative oblique arteriogram showing the functioning by-pass. The deep femoral trunk has occluded.

TECHNIQUE

Five operations were performed under general anaesthesia; one was done under local anaesthesia because the patient represented a high cardiopulmonary risk (*Case* 3). The approach was the same as that used for an extended deep femoral angioplasty (Berguer and others, 1973). The dissection of the deep femoral artery was pursued until a soft, clear segment was met. This meant dissecting as much as 14 cm. of the deep femoral artery in some cases. The branches of the deep femoral vein that cross the trunk of the parent artery were divided between ligatures. A segment of the proximal part of the saphenous vein was excised from its bed at the edge of the operative wound and reversed. The proximal arteriotomy was made over the common femoral artery, sometimes including the origin of the deep femoral artery (*Fig.* 2). The proximal end of the reversed vein was so fashioned as to provide a patch effect at the proximal anastomosis. The distal arteriotomy was made at the selected place in the non-involved distal deep femoral artery; no endarterectomy was done at this level. The graft was sutured end to side at both ends with 000000 Dacron material. Electro-magnetic volume-flow readings and qualitative flow-wave analysis were done before and after the procedure (*Fig.* 3).

Table I.—SUMMARY OF THE DETAILS OF THE PRESENT SERIES*

CASE	AGE (yr)	CONCOMITANT DISEASE	INDICATIONS	POSTOPERATIVE FLOW VOLUME (ml. per min)		RESULT
				By-pass Alone	By-pass + Deep Femoral Artery	
1. J. M.	53	Thrombo-angiitis obliterans, coronary artery disease†	Rest pain	—	170	Good
2. M. M.	72	Diabetes, coronary artery disease	Rest pain	70	—	Amputation‡
3. J. O.	62	Diabetes, coronary artery disease	Rest pain	28	128	Good
4. M. R.	71	Coronary artery disease	Rest pain and ulceration	72	—	Good
5 H. B.	67	Coronary artery disease	Intermittent claudication	96	128	Good
6. J. K.	59	—	Inadequate deep femoral outflow§	96	—	Good

* Preoperative flow data are not included because intravascular pressure variations and changing arterial wall thickness at the measuring point introduce substantial errors which invalidate comparative conclusions. Flow measurements have been made in the by-pass itself or in the common femoral artery, the superficial femoral artery being occluded Technical problems related to arterial wall thickness or inclusion of the anastomotic line in the flow transducer prevented simultaneous flow measurement in both sites in 4 patients.

† Previous history included bilateral cervical and bilateral lumbar sympathectomies, below-knee amputation (opposite leg) with poor healing and breakdown of the stump, and myocardial infarction.

‡ Patency of the graft, which was demonstrated by arteriogram, failed to relieve distal foot pain.

§ This patient underwent aorto-femoral endarterectomy on both sides for intermittent claudication. The indication for reconstruction of the right deep femoral was a post-endarterectomy volume-flow reading of 45 ml. per minute in the right common femoral artery (superficial femoral artery was occluded). Claudication was relieved postoperatively

RESULTS

The follow-up period extends from 1 to 10 months (mean, 4·1 months). The postoperative patency rate has been 100 per cent. The results are shown in *Table I*. We have not had any postoperative complications related to this technique except that *Case* 2 continued to have rest pain, necessitating a below-knee amputation. This man had diabetes and extensive infrapopliteal disease. The angiograms taken before the amputation (*Fig.* 4) show a patent graft; this might have helped in obtaining rapid healing of the stump.

The proximal end-to-side anastomosis preserves the flow through the proximal segments of the deep femoral to the femoral circumflex branches. Only in 1 case (*Case* 4) did the postoperative angiograms show the proximal part of the deep femoral trunk to have occluded (*Fig.* 5). In cases of occlusion of the origin of the deep femoral artery, flow to the circumflex branches may be re-established in a retrograde fashion via the by-pass.

DISCUSSION

In these 6 cases with extensive atheromatous disease along the deep femoral artery we have been reluctant to perform extensive endarterectomies and patching because: (*a*) the endarterectomy has to be done by the open method since the multiple branch orifices need to be cleared with precision, and (*b*) the resulting channel is haemodynamically unsound with its unavoidable patch dilatation and two long suture lines. Furthermore, it is difficult to find a suitable end-point to the endarterectomy if there is widespread atherosclerosis of the deep femoral artery. The expedient of placing tacking sutures at the end-point of an endarterectomy is not devoid of difficulty and risk in a vessel with a 2·5–3·5-mm. internal diameter such as the distal deep femoral artery.

The experience accumulated in surgical reconstruction of the superficial femoral artery has shown that the patency results of long endarterectomy with a patch are inferior to those obtained with autogenous vein by-pass (Darling, 1969). It is generally agreed that an autogenous vein by-pass provides a better arterial blood conduit in a medium-sized vessel than an endarterectomized wall covered with a patch attached by two long suture lines.

Reviewing the material published on surgery of the deep femoral artery, we have found only one report of a case, in a young man, of common to deep femoral artery by-pass (Billig, Callow, and Deterling, 1970), while two other papers mention this technique (Sproul, 1968; Youmans, Hopkins, and Derrick, 1969). Our short experience with this procedure inclines us to think that it deserves more attention. The question posed by this paper is whether a vein by-pass is preferable to endarterectomy when faced with extensive disease in the deep femoral artery. We have preferred the by-pass technique in such advanced cases in the light of previous experience with reconstruction of the superficial femoral artery and because of the technical difficulties and dangers inherent to endarterectomy in these circumstances.

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CLOSED INJURY OF THE EXTERNAL ILIAC AND COMMON FEMORAL ARTERIES*

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SUMMARY

Two cases of traumatic closed injury of the iliofemoral arterial segment incurred while working at sea are reported. These cases share many similarities which are discussed together with general observations on the management of such injuries. The need for repair utilizing the by-pass principle rather than direct procedures on the involved segment is stressed.

WOUNDS and injuries of arteries have been grouped into two categories (Kinmonth, Rob, and Simeone, 1962). These categories are summarized in *Table I*.

The type of lesion has a bearing on the prognosis. In acute lesions of major vessels there is a high probability that gangrene will occur. Chronic lesions lead to malfunction of the limb but gangrene is a more remote possibility.

Table I.—CLASSIFICATION OF WOUNDS OF ARTERIES

A. Acute arterial lesions
  1. Spasm: segmental or diffuse
  2. Contusion, involving one or more arterial coats
  3. Perforation and penetration
  4. Laceration, with partial or complete transection
  5. Thrombosis, occurring alone or, more usually, in association with the above

B. Chronic arterial lesions
  1. Traumatic aneurysm: true or false
  2. Arteriovenous fistula

The anatomical site of the injury must be taken into account. The iliofemoral arterial segment has a generous collateral potential, making closed injuries in this region less dramatic in their effects on the circulation of the distal ipsilateral limb.

The effect of such lesions is illustrated in the following case reports.

CASE REPORTS

Case 1.—M. M., a 27-year-old ship's purser, was admitted to hospital in November, 1971. Eight weeks previously he had been caught in a closing automatic door on his ship. His left lower chest, left hip, and thigh had been crushed. He had been admitted to hospital for immediate treatment where he had been kept for 2 weeks and then had been referred for vascular consultation because of suspected damage to his lower-limb vessels.

On admission he complained of weakness and dragging of the left lower limb but no pain. On examination he had diffuse swelling of the left groin and, to a lesser extent, of the thigh. There was no obvious wasting of the lower-limb muscles. The left femoral and popliteal pulses were absent but he had a palpable posterior tibial pulse and dorsal pulse in his left foot. The right-limb pulses were normal.

A clinical diagnosis of traumatic thrombosis of the left external iliac artery was made and the patient underwent translumbar aortography. This revealed complete occlusion of the left external iliac artery from its origin down to and including the common femoral artery. The superficial and deep femoral vessels were patent and filled through diffuse anastomotic channels from an enlarged internal iliac artery (*Fig.* 1).

At operation the iliac vessels were exposed through an oblique supra-inguinal approach. A vertical incision was made over the common femoral artery. The occluded vessels were found to be thrombosed and the walls were a dusky blue in colour. The proximal long saphenous vein on the left side was removed, prepared, and reversed. It was used as a by-pass graft from the common iliac to the distal common femoral artery which was patent opposite the profunda orifice.

The patient's postoperative progress was satisfactory, with restoration of the popliteal pulse and increase in pedal pulsation. A repeat aortogram was done a month later and showed the functioning graft. The internal iliac artery was diminished in size while the previously noted rich collateral circulation had greatly decreased (*Fig.* 2).

The patient's subsequent course has been satisfactory with no symptoms or signs of vascular deficit.

Case 2.—F. M., a 27-year-old captain of a fishing boat, was admitted in December, 1971, following an accident sustained the previous day at sea. He had been crushed between the cable of a fishing net and the side of the boat. Following this injury he had lost the use of his right lower limb and felt diminished sensation over the lower two-thirds of the leg and foot.

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* Based on a communication to the Vascular Society of Great Britain and Ireland in November, 1972.

On examination he was not shocked. The blood-pressure was 110/70 and the pulse-rate was 60 per minute and regular. A haematoma measuring 3 × 2 cm. was present over the anterior superior iliac spine and another haematoma measuring 6 × 3 cm. lay over the right inguinal canal. All the lower-limb pulses were absent on the right side including the femoral pulse. The right foot was slightly colder than the left but he had full movements of the ankle-joint and toes. There was impaired sensation to light touch and pin-prick from the middle third of the leg to the toes.

The patient was operated upon on the day of admission, preoperative angiography being omitted. The iliofemoral area was exposed by two incisions: (*a*) an oblique extraperitoneal approach to the iliac vessels, and (b) a hockey-stick-shaped incision over the right common femoral artery. The soft tissues of the right iliac fossa were stained by blood but no active haemorrhage was present. The artery from the common iliac bifurcation to the common femoral bifurcation was pulseless and stained a dark-red colour. The common femoral artery was opened opposite the profunda orifice. A Fogarty catheter passed easily to the ankle without evidence of distal thrombus. On passing the catheter proximally it met with an obstruction at the level of the inguinal ligament. A crimped 8-mm. Dacron tube was used as a by-pass. This was placed from the lower end of the common iliac artery to the femoral arteriotomy. Local heparin was used distally in the limb. On removal of the arterial clamps the graft functioned normally and pulses reappeared in the popliteal fossa and

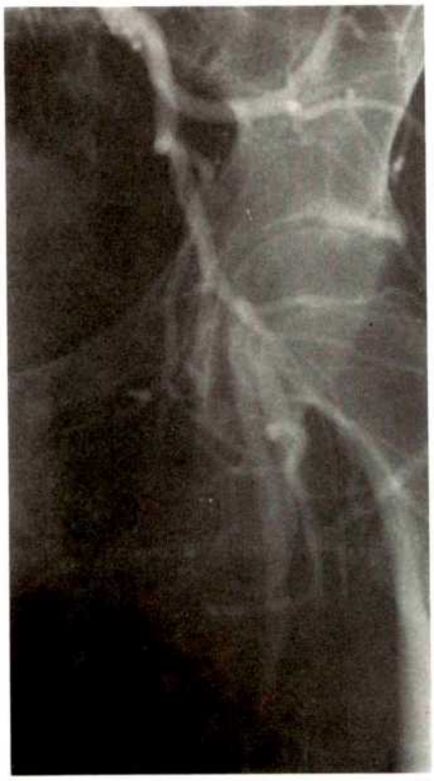

FIG. 1.—*Case* 1. Detail of the preoperative aortogram showing occluded external iliac and proximal common femoral arteries. Note the extensive collaterals from the enlarged internal iliac artery.

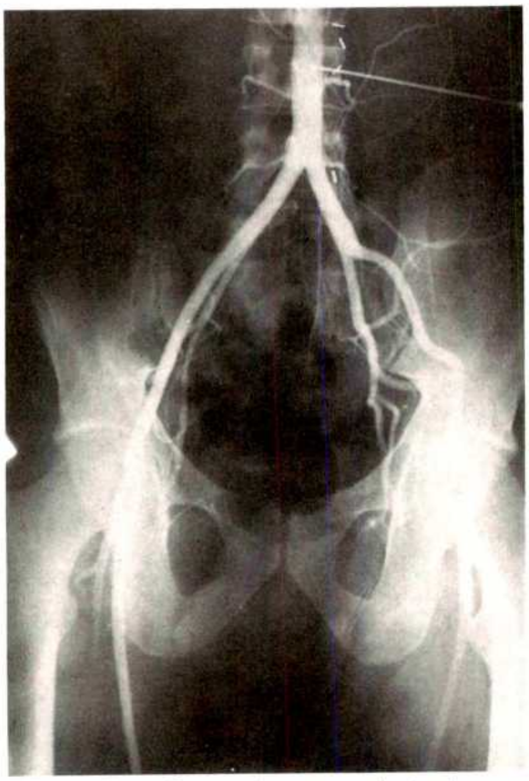

FIG. 2.—*Case* 1. Postoperative aortogram showing the patent iliofemoral vein-graft, the reduced size of the internal iliac arteries, and the difference in the groin collaterals from *Fig.* 1.

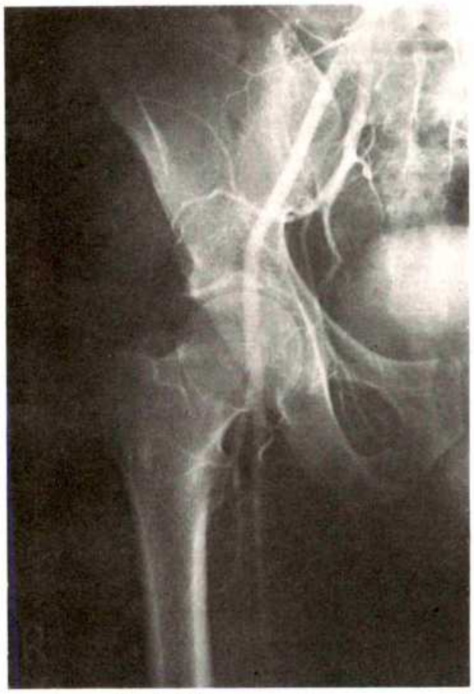

FIG. 3.—*Case* 2. Detail of the postoperative aortogram showing a patent prosthetic iliofemoral graft.

foot. The patient's postoperative course was uneventful. The skin sutures were removed on the eighth postoperative day. An angiogram performed on the thirteenth postoperative day showed a patent functioning by-pass graft (*Fig.* 3). His subsequent progress has been satisfactory and he has returned to sea.

DISCUSSION

Stiles (1965) reviewed the experience of injuries to the iliofemoral arterial segment at St. Mary's Hospital, London. The 4 cases described by this author occurred during the 1950's and were treated by thrombectomy, homograft, Orlon graft, and proximal ligation of a false aneurysm respectively. All had viable limbs on completion of therapy but all were found to have claudication at the 1-year follow-up visit. This author stresses the delay in referral of these cases, together with the need for arteriography following reconstruction to assess the adequacy of repair.

Eastcott (1969), in discussing the aetiology of iliac injuries, mentions the dangers of abdominal retractors and the over-tight application of a tape sling in addition to severe blunt violence to the groin.

The 2 cases described in this paper had severe contusion thrombosis of the iliofemoral artery. Their limbs were viable, although clinically ischaemic, when first seen. On exposure the involved vessels were dark blue in colour, swollen, and non-pulsatile. The lumen was totally occluded. This is the appearance of arterial contusion with intramural haemorrhage and intraluminal thrombosis. These vessels are unsuitable for thrombectomy or any form of direct repair. Use of the by-pass principle is mandatory and the selection of reversed vein or prosthetic tube-graft will depend on the individual surgeon's choice.

Early reconstruction in accordance with these principles resulted in normal limbs in these young men at 1 year following injury.

Acknowledgement.—We are grateful to Mr. K. Kearney, F.R.C.S., who referred *Case* 2.

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THE PREVENTION OF POSTOPERATIVE DEEP VENOUS THROMBOSIS WITH DEXTRAN 70

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SUMMARY

One hundred and six patients undergoing major surgery were given dextran 70—500 ml. during operation, 500 ml. on the following day, and then 500 ml. on alternate days until discharge. Of these patients, 1 developed a deep venous thrombosis after the operation (0·94 per cent). One hundred and one patients acted as control subjects and, of these, 10 developed deep venous thrombosis (9·9 per cent). This reduction in incidence of thrombosis is significant at the 2 per cent level, indicating that dextran 70, as macrodex 6 per cent in 5 per cent dextrose, in the régime given is a simple and effective means of reducing deep venous thrombosis after major surgery.

BYGDEMAN (1967) proposed the use of dextran 70 as an agent to prevent unwanted postoperative venous thrombosis. He suggested that 250-500 ml. of a 6 per cent solution daily would be adequate.

In trials to determine a suitable routine method of administration of dextran 70 to prevent postoperative deep venous thrombosis in the lower limb two series of patients were studied. The patients in the first series were given 500 ml. of dextran 70, as macrodex 6 per cent in 5 per cent dextrose, during operation and subsequently on alternate days until discharge. This dosage was not successful in preventing deep venous thrombosis to a significant degree, but was sufficiently encouraging to increase the dosage to 500 ml. of dextran 70 during the operation, 500 ml. on the following day, and thereafter 500 ml. on alternate days until discharge.

The second method reduced the incidence of deep venous thrombosis from 9·9 per cent in 101 control subjects to 0·94 per cent in 106 cases who were given dextran 70, a reduction which is significant at the 2 per cent level ($\chi^2 = 6{\cdot}56$).

MATERIAL AND METHODS

Patient Selection.—Male and female patients over the age of 45 years admitted for non-emergency major surgery were allocated to the same random series as used in a previous report (Carter, Eban, and Perrett, 1971). Similarly, all the patients with known varicose veins, peripheral arterial disease, cardiac or respiratory insufficiency, or a history of previous thrombotic episodes were excluded. No patient who had had major surgery within the previous 6 months was included.

Of 207 patients admitted to the trial, 106 cases (64 males and 42 females) were given dextran 70 as macrodex 6 per cent in 5 per cent dextrose, and 101 cases (65 males and 36 females) formed the controls who were given 4·3 per cent dextrose in 0·18 per cent saline in the same doses as the dextran 70.

Dextran 70 Dosage.—The treated group received 500 ml. of dextran 70 intravenously as a 6 per cent solution, the infusion starting immediately anaesthesia had been induced and lasting 4 hours or, if blood had to be given, being completed before blood was transfused. A further 500 ml. of dextran 70 were given on the day after operation within 24 hours of the intra-operative dose, and thereafter 500 ml. daily until discharge from hospital.

The controls received 500 ml. of 4·3 per cent dextrose in 0·18 per cent saline in identical volumes at the same times.

Diagnosis of Deep Venous Thrombosis.—The method of Flanc, Kakkar, and Clarke (1968) was used. Thyroid uptake of iodine was blocked with 100 mg. of sodium iodide not less than 1 hour before operation (intravenously) or more than 12 hours (orally) before giving 100 μc. of ^{125}I-labelled human fibrinogen (Radiochemical Centre). Both lower limbs were scanned with a Pitman 235 Isotope Localisator immediately before operation, just before the patient left the recovery unit, and thereafter daily until discharge from hospital.

Every case suspected of having a thrombosis had a venogram performed within 24 hours of the suspicion being raised.

Ambulation.—Every patient in this series was ambulant on the day after operation. Those with intravenous infusions or other encumbrances were walked around their bed at least three times daily until they were ambulant without help.

Table I.—DISTRIBUTION OF CASES BY SEX, AGE, AND SITE OF OPERATION

SITE	TREATED GROUP						CONTROL GROUP					
	Age (yr.)						*Age* (yr.)					
	45–50	51–55	56–60	61–65	66–70	71+	45–50	51–55	56–60	61–65	66–70	71+
Males												
Upper abdomen	4	1	4	3	4	3	4	0	10	5 (1)	1	2
Lower abdomen	1	4	6	9	7	10	2 (1)	2	7	7	7 (1)	12 (1)
Other	0	0	0	7	1	0	2	0	0	0	2	2
Total	5	5	10	19	12	13	8 (1)	2	17	12 (1)	10 (1)	16 (1)
Females												
Upper abdomen	4	0	5	4 (1)	4	7	2	1 (1)	3	2	2	11 (2)
Lower abdomen	0	1	2	6	0	5	1	3	0	0	1 (1)	8 (2)
Other	1	1	1	0	0	1	0	0	1	0	0	1
Total	5	2	8	10 (1)	4	13	3	4 (1)	4	2	3 (1)	20 (4)

Figures in parentheses indicate the number of cases of thrombosis.

RESULTS

Table I shows the distribution by age, sex, and site of operation of the 106 treated cases and the 101 controls. They are further analysed according to the site of operation to try to illustrate the relative risks between the different sites. It should be noted that in the males there is a preponderance of lower abdominal operations owing to the large number of prostatectomies in the series. There are only a few non-abdominal operations among the females as the cases of breast cancer in this unit are included in another study that precludes the use of ^{125}I.

In the males the incidence of thrombosis in the treated group is 0 in 64 cases and in the control group 4 in 65 cases. The value of P for this difference is 0·062, which is significant at the 10 per cent level but not at the 5 per cent level. In the females the incidence of thrombosis in the treated cases is 1 in 42 cases and in the controls 6 in 36 cases. The value of P is 0·034, which is significant at the 5 per cent level. Pooling both sexes gives an overall rate of thrombosis in the treated cases of 1 in 106 and in the controls of 10 in 101. This difference is significant at the 2 per cent level ($\chi^2 = 6·56$).

It is generally held that there is an increased risk of thrombosis in cases treated for malignant disease. *Table II* shows the distribution of such cases in this series. In males the incidence of thrombosis in the malignant cases was 0 in 11 against 4 in 54 in the non-malignant cases ($P = 0·47$). In females thrombosis occurred in 4 of 11 malignant cases and in 2 of 25 non-malignant cases ($P = 0·057$). There was, therefore, in this series a strong indication that thrombosis is more likely in females with malignant disease but no such indication in males.

No significant differences were found in the incidence of thrombosis attributable to age, type of anaesthetic (e.g., spinal/epidural or general), time spent on the operating table, or the need for blood transfusion or the quantity of blood given. There was no significant difference between the cases operated upon within 36 hours of admission (the majority) and those in hospital for periods of up to 23 days before surgery. None of the patients who were in hospital for any period of time was confined to bed before operation.

Table II.—DISTRIBUTION OF CASES BETWEEN MALIGNANT AND NON-MALIGNANT DISEASE

TYPE OF DISEASE	CONTROL GROUP		TREATED GROUP	
	Male	Female	Male	Female
Malignant	11	11 (4)	20	16 (1)
Non-malignant	54 (4)	25 (2)	44	26

Figures in parentheses indicate the number of cases of thrombosis.

The time of recognition of venous thrombosis was variable. *Table III* shows the distribution of the times of recognition. Previous experience with ^{125}I-fibrinogen localization of thrombosis suggested that the time of its recognition, presumably the time of its onset, could be as late as the tenth day after operation. For this reason dextran 70 was given throughout each treated patient's stay in hospital. *Table III* shows that although the majority of thromboses are recognized within 3 days of operation, 2 became apparent on the sixth day and 1 on the tenth postoperative day.

No case in this series developed thrombosis of the iliofemoral veins on either side.

Table III.—TIME OF ONSET OF THROMBOSIS

GROUP	AGE (yr.)	DAY AFTER OPERATION
Control Females	72	2
	68	3
	71	3
	81	3
	52	6
	85	6
Males	68	3
	45	3
	84	3
	64	10
Treated Female	67	7

DISCUSSION

The dextrans have been known to have an antithrombotic effect since 1959 (Borgström, Gelin, and Zederfeldt, 1959). Of the various dextrans, that with a molecular weight around 70,000 has been the most satisfactory in clinical use, as a 6 per cent solution. At this weight and concentration doses of the order of 250–500 ml. per day have not resulted in any tendency to unwanted bleeding or of overloading the circulation. Dextran is simple to use and, in the régime used in this series, requires no laboratory control.

Lambie, Barber, Dhall, and Matheson (1970) compared dextran 70 with Warfarin as methods of reducing postoperative deep venous thrombosis. In their series dextran was found to be more effective. Similarly Bonnar and Walsh (1972) found that in their series of major lower abdominal operations dextran reduced the incidence of deep venous thrombosis from 10·7 per cent in the control cases to 0·8 per cent in the treated cases.

In this series the reduction in the incidence of thrombosis has been from 9·9 per cent in the controls to 0·94 per cent in the cases which were given dextran 70. Previous (unreported) experience with dextran 70 had suggested that a single dose of 500 ml. during operation followed by 500 ml. on alternate days was not enough to reduce the incidence of thrombosis to a significant degree but was sufficiently encouraging to increase the dose to 500 ml. during operation, 500 ml. on the following day, and thereafter 500 ml. on alternate days until discharge. The result has been an overall significant reduction in thrombosis in treated cases although the males only showed a reduction in thrombosis at the 10 per cent level. The low incidence of thrombosis in the controls renders comparisons difficult, so that as thrombosis is more common in females a significance at the 2 per cent level is gained only by including both sexes in the assessment.

There appears, therefore, to be little doubt that dextran 70, used in the régime reported here, is effective in reducing thrombosis in the type of patient admitted to regional hospitals undertaking a wide variety of major surgical procedures on unselected patients.

Acknowledgements.—We wish to thank Pharmacia (Great Britain) Ltd. for their extensive financial support of this study and, particularly, Dr. Peter Allen of that company for his continuous help and for the statistical assessment; also the King Edward Memorial Hospital's League of Friends who purchased the Pitman 235 Isotope Localisator.

We are grateful to Sister Nancy Medlock and the staff of the intensive care unit and the chief theatre technician who carried out much of the limb scanning and allocated the patients to the random series.

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CARCINOID TUMOURS OF THE COLON

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SUMMARY

Four cases of carcinoid tumour of the colon are presented together with a brief review of the literature.

CASE REPORTS

Case 1.—A 70-year-old male presented with a 2-month history of anorexia and melaena. During this period he had lost 11 kg. in weight. He had had a partial gastrectomy for a perforated duodenal ulcer 14 years previously. On examination he was cachectic and clinically anaemic. Abdominal examination revealed a firm, irregular, mobile mass just above the level of the umbilicus. His haemoglobin was 8·3 g. per cent. The patient's condition improved considerably over the next 4 days, during which time he had a 5-unit blood transfusion. However, on the fifth day of his admission he collapsed with a further massive haemorrhage and died rapidly. Post-mortem examination revealed a carcinoid tumour of the splenic flexure measuring 4 cm. in diameter which involved the full thickness of the bowel wall; there were metastases in the para-aortic and coeliac nodes and also in the liver.

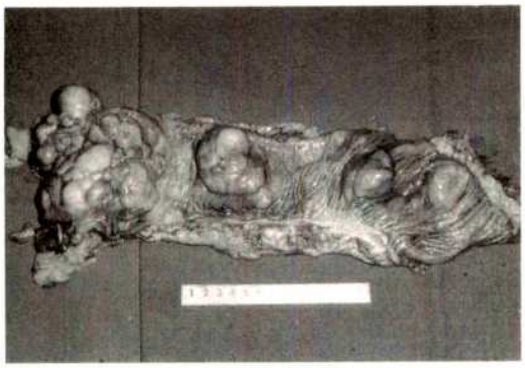

FIG. 1.—*Case* 4. The operative specimen showing one large tumour and several small ones.

Case 2.—A 51-year-old male was admitted with a 10-month history of intermittent colicky lower abdominal pain with no other associated symptoms. His family history revealed that a brother and sister had both died of carcinoma of the large bowel. On examination there was a tender, mobile mass in the right middle quadrant of the abdomen. Laboratory investigations showed an E.S.R. of 50 mm. per hour and a haemoglobin of 11·0 g. per cent. After a preoperative blood transfusion, laparotomy revealed a tumour in the ascending colon 4 cm. distal to the ileocaecal valve. There were no palpable metastases. A routine right hemicolectomy was performed, and histology of the operation specimen showed it to be a carcinoid tumour with no involvement of the local lymph-nodes. A postoperative urinary 5-hydroxy-indole acetic acid measurement was 3·3 mg. per 24 hours (normal < 10 mg. per 24 hours). The patient is well with no sign of recurrence 2 years after operation.

Case 3.—A 68-year-old female was admitted with a 6-week history of bilateral sciatica. During this time she had felt unwell and had lost 7 kg. in weight, although she had no other presenting symptoms. On examination there was a firm mobile abdominal mass just to the right of the umbilicus. Examination of the central nervous system revealed absent ankle reflexes. Laboratory investigations showed a haemoglobin of 12·0 g. per cent and an E.S.R. of 45 mm. per hour; protein concentration of the cerebrospinal fluid at a lumbar puncture was 80 mg. per cent; serial faecal occult-blood measurements were all positive. An electro-encephalogram showed a left midtemporal structural disturbance. Shortly after admission the patient developed papilloedema, became comatosed, and died. Post-mortem examination revealed a carcinoid tumour in the right half of the transverse colon about 2 cm. in diameter, with metastases in the mesenteric and coeliac lymph-nodes, in both adrenal glands, and in the liver. There were also metastases throughout the brain.

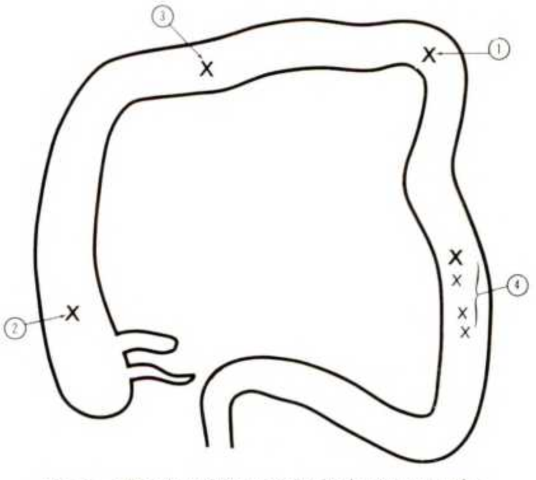

FIG. 2.—The sites of the tumours in the present series.

Case 4.—A 58-year-old female was admitted to a psychiatric hospital for assessment. She had a 20-year history of intermittent anxiety and depression; she had received regular out-patient psychiatric treatment and also three short spells of in-patient care. Repeated clinical examinations and biochemical investigations had revealed no abnormality. However, on this occasion routine examination showed a mobile mass in the left lower quadrant of the abdomen. She gave no history of symptoms referable to the gastro-intestinal tract and her lack of history was corroborated by her daughter with whom she was living. Laboratory investigations showed no abnormality, but a barium-enema examination revealed several filling defects in the descending colon, and at operation a large submucosal tumour was found in the descending colon with several small lesions below it (*Fig.* 1). There were no palpable lymphatic or hepatic metastases. A standard anterior resection was performed and histology showed the lesion to be a carcinoid tumour which had invaded the full thickness of the bowel wall, but with no involvement of the local lymph-nodes. A urinary

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5-hydroxy-indole acetic acid measurement postoperatively was 5·2 mg. per 24 hours. The patient is well with no sign of recurrence 1 year after operation.

DISCUSSION

Carcinoid tumours of the colon are extremely rare. Anthony and Drury (1970) collected 100 cases of carcinoid tumour in a 12-year period from 1956 to 1968 from the files of the Central Middlesex Hospital, the Middlesex Hospital, and St. Mark's Hospital, London, and did not find one such tumour in the colon. A review of 356 carcinoid tumours of the gastro-intestinal tract by MacDonald (1956) contained only 6 occurring in the colon, but he does not mention where abouts in the colon they arose.

Crittenden, Byllesby, and Dodds (1970) reported a carcinoid tumour presenting as an annular lesion in the ascending colon. Rosato, Anderson, and Andrus (1970) described 4 cases of carcinoid tumour of the colon, 2 in the ascending colon and 2 in the descending colon. Case (1969) reported a carcinoid tumour in the transverse colon. Of the 4 tumours presented here, 1 was in the ascending colon, 1 in the transverse colon, 1 at the splenic flexure, and 1 in the descending colon (*Fig.* 2). Thus, of the few reported cases, carcinoid tumours do not appear to show a predilection for any particular site within the colon. This is in strict contrast to adenocarcinomas of the colon, 70 per cent of which arise in the sigmoid colon and 15 per cent in the ascending colon.

Multiple primary tumours have occasionally been reported in association with carcinoid tumours of the gastro-intestinal tract; thus out of 72 cases reported by Kuiper, Gracie, and Pollard (1970), there were multiple tumours in 8 patients, although none of these was in the colon. In the present *Case* 4 the distal tumours were probably implantation metastases, although the possibility that they were multiple primaries cannot be eliminated.

In common with other gastro-intestinal carcinoid tumours those of the colon produce no early symptoms. They may present as an asymptomatic mass in the abdomen, as obstruction, as an incidental finding during laparotomy, or at autopsy. Even where there are extensive hepatic metastases the development of the carcinoid syndrome appears to be rare. Thus, in MacDonald's (1956) series, of 149 extra-appendicular carcinoid tumours, widespread hepatic metastases were present in 23 cases, and of these, only 3 patients had symptoms of the carcinoid syndrome. The 2 patients reported here whose tumours were discovered at autopsy and in whom there were extensive hepatic metastases did not have symptoms of the carcinoid syndrome. One striking feature in the symptoms of the 4 patients presented here was the marked weight-loss; 11 kg. in 3 months in *Case* 1, 14 kg. in 6 months in *Case* 2, and 7 kg. in 3 months in *Case* 3. Kuiper and others (1970) also drew attention to this feature, reporting weight-losses of 11, 11·3, and 45 kg. respectively in 3 patients with carcinoid tumours of the colon prior to diagnosis.

Several authors have reported a high incidence of a second neoplasm in association with carcinoid tumours. Thus, Moertel, Sauer, Dockerty, and Baggentoss (1961) reported an incidence of 29 per cent in a series of small-bowel carcinoid tumours, Foreman (1952) found a 47 per cent association, and Warren and Coyle (1951) reported a 33 per cent association of a second neoplasm with carcinoid tumours. In none of the cases reported here was a second lesion found.

As with other tumours of the colon the most important factor in determining the prognosis is whether or not there are hepatic metastases present at the time of exploration. Of 5 carcinoid tumours of the colon reported by Kuiper and others (1970), there were hepatic metastases at the time of operation in 3 patients all of whom died within 3 years, whereas the other 2 patients who did not have hepatic metastases were alive 10 years later.

Acknowledgements—I should like to thank Mr. P. H. Powley for permission to publish these cases and for his advice, and Professor D. G. Grahame Smith for his help in the management of *Case* 4.

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A STERILE 'USE-ONCE' CLIP APPLICATOR FOR SKIN CLOSURE

By DAVID ANNIS

LIVERPOOL ROYAL INFIRMARY

SUMMARY

A sterile disposable applicator for skin clips has been used for the closure of skin incisions in 117 consecutive operations. These have included most of the standard incisions in the head, neck, trunk, and limbs. The instrument has proved satisfactory in use, the skin incisions having healed satisfactorily with much time having been saved in their closure.

METAL clips have been used for the closure of skin incisions for more than 60 years. For the majority of surgeons their use has been limited to the closure of a very few incisions, mostly transverse and mainly in situations where the scar will ultimately be exposed. The collar incision for thyroidectomy is, of course, the incision for which many surgeons regularly use skin clips. However, a minority of surgeons have used skin clips for the entire range of surgical incisions.

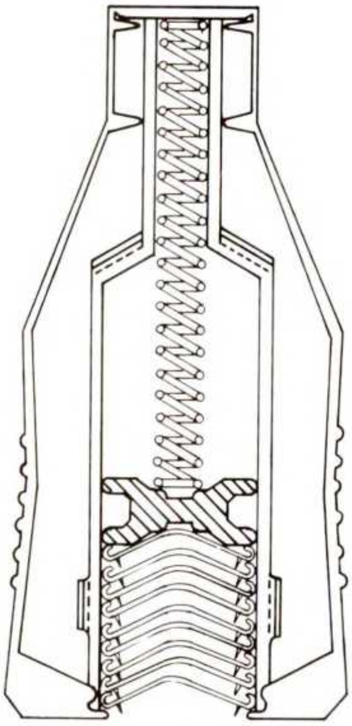

FIG. 1.—The applicator.

Michel and Kifa clips are held in their carriage and applied singly. There are instruments for holding a 'bank' of clips that present the clips in the jaws of the instrument ready for application. These instruments have the advantage of speed and economy of action, but require to be loaded and to be autoclaved before use.

A sterile pre-packed applicator containing 20 × 18-mm. double-toothed stainless-steel clips has been developed.* The applicator and its contents have been designed to be used for the closure of one skin incision, after which the applicator is discarded.

The device is illustrated in *Figs.* 1 and 2. A polycarbonate case containing 20 clips is presented in a double-wrapped sterile packet. A squeezing pressure on the sides of the device approximates the dogs that hold back the bank of clips and closes the presenting clip. Release of pressure frees this clip and allows the next clip to fall into place.

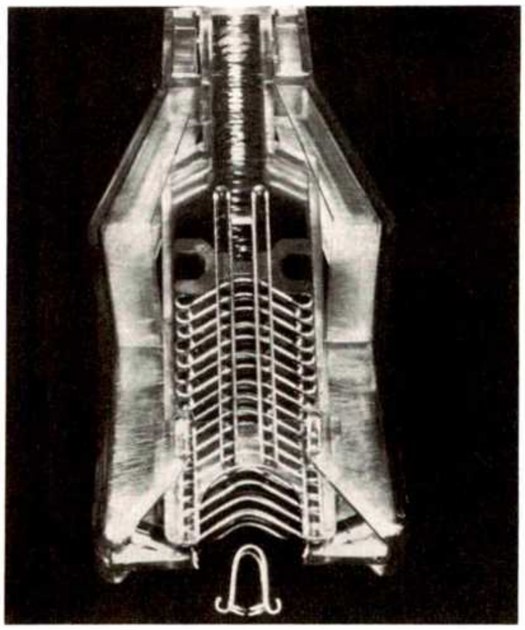

FIG. 2.—The applicator showing the clip after closure.

The technique of application is simple but differs from that usually followed when applying Michel clips. Most, but not all, surgeons apply Michel clips immediately *beyond* the skin-approximating forceps. That is, most right-handed surgeons will move from the left-hand to the right-hand end of the incision, approximating the skin with forceps in the left hand and applying the clip with the right hand.

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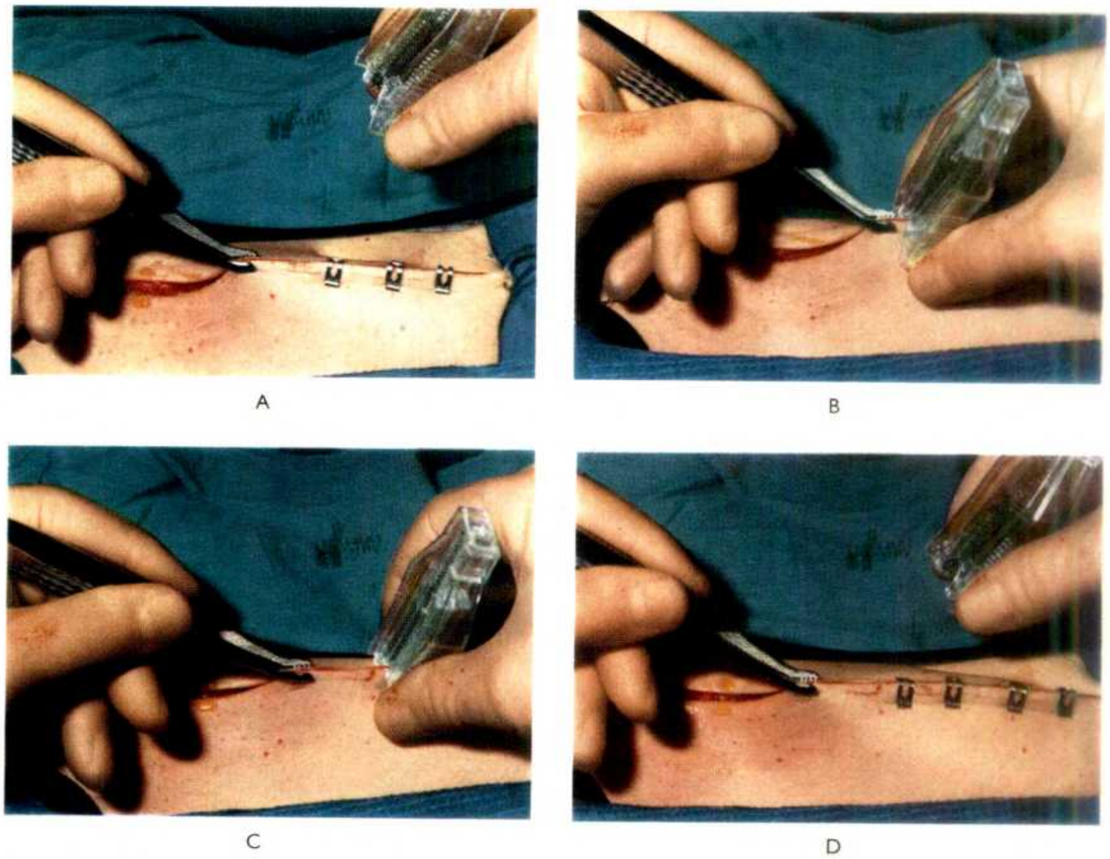
* The device has been developed by the Medical Aids Innovation Unit of I.C.I. Ltd., Runcorn, Cheshire.

Using the Avlox '18' device it has been found better for the right-handed surgeon to begin at the right end of the incision, holding the approximating forceps in the left hand and applying the clips with the Avlox '18' device in his right hand *behind* the approximating forceps. This is illustrated in *Fig*. 3.

It is necessary to take hold of both sides of the skin incision simultaneously in the grasp of a sharp-toothed approximating forceps and to bring the skin edges evenly together, raising them to form a low ridge on to which the clip is closed. A Childe's or Ward's forceps has been found ideal for this purpose (*Fig*. 3A). The clip having been closed on the skin (*Fig*. 3B), pressure is maintained on the device so that the clip is not released until the approximating forceps has been moved on and has grasped the skin edges again about half an inch farther along the incision (*Fig*. 3C). Only then is the clip released from the instrument by relaxing the pressure upon it (*Fig*. 3D). The next clip is then applied behind the approximating forceps and usually about half an inch farther along the wound (*Fig*. 3E). This progression in a two-handed manner is continued until the incision is closed. It can be seen that at all times the skin edges are held together either in the grasp of the approximating forceps or in the Avlox '18' device. This allows the skin edges to be brought neatly together.

The instrument has been used for 117 consecutive skin closures and these have included all the standard incisions in the chest, abdomen, neck, and limbs (*Table I*). Not all patients have sufficiently supple skin to allow a ridge to be made and the clips to be satisfactorily placed. In particular, it has been found difficult to apply the clips in areas where the skin is especially thick and the subcutaneous fat is firmly attached to it, such as at the posterior end of an oblique renal incision and at the posterior ends of thoracotomy incisions.



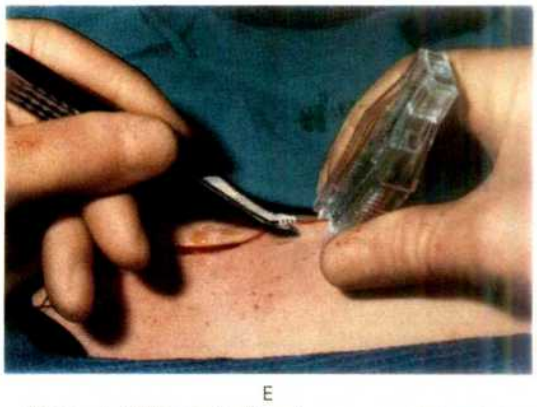


FIG. 3.—A, Taking up the skin edges to receive the fourth clip. B, The fourth clip applied. C, Pressure on the fourth clip is maintained while the approximating forceps is advanced. D, The fourth clip released. E, The fifth clip applied.

Even so, satisfactory skin closure and good skin healing have been achieved in over 95 per cent (113 out of 117 cases) of the incisions closed. It is true that transverse incisions in general are more easily closed with clips than are longitudinal incisions. Nevertheless, the device and the clips that it delivers have been found entirely satisfactory for the closure of all standard longitudinal incisions in the abdomen.

Table I.—SUMMARY OF A SERIES OF CONSECUTIVE OPERATIONS IN WHICH AVLOX '18' CLIPS HAVE BEEN USED

Type of Operation	*No. of Operations*
Head and neck	
Thyroidectomy	7
Parathyroid tumour	3
Branchial cyst	1
Submaxillary gland excision	1
Breast	
Simple excision of cysts, etc.	4
Mastectomy	12
Abdomen	
Cholecystectomy	25
Gastric surgery	13
Cholecystoduodenostomy	1
Pancreaticoduodenectomy	1
Pancreatic insulinoma	1
Resection of colon	8
Colostomy	1
Laparotomy	4
Appendicectomy	1
Adrenalectomy	4
Nephrectomy	3
Oophorectomy	1
Ileal conduit urinary diversion	2
Prostatectomy	3
Hernia	18
Miscellaneous	3
Total	117

Healing has been as good in every way as can be achieved by suturing and there has been a noticeable absence of minor wound infection, probably because the clips do not completely pierce the skin. There is an impression that healing has occurred a little more rapidly than with suturing techniques. The scars are linear and without cross-hatching, the clip marks disappearing entirely within 10 weeks.

The time of removal of the clips has varied and of course depends on the condition of the individual incision, but in the majority of cases it has been found possible to remove alternate clips from thyroidectomy incisions on the second postoperative day and the remaining clips on the third day. In simple abdominal incisions, such as those for hernia repair, the clips have regularly been removed on the fourth postoperative day, and in incisions for major abdominal surgery they have usually been removed on the sixth or seventh day after the operation.

Whilst it is difficult to claim that healing has been more than marginally better with the use of clips, there is no doubt that the application of clips is very much faster than the use of sutures or of individually applied skin clips.

In summary, the application of clips from the device described has proved at least as effective as suturing techniques, and because of the speed with which the clips can be applied has taken much of the tedium out of skin closure. It might be added that the device has been much appreciated by the theatre staff, being presented complete, sterile, and available for immediate use.

THE MANAGEMENT OF VILLOUS TUMOURS OF THE LARGE BOWEL

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SUMMARY

Thirty patients with villous tumours of the rectum are described. With the criterion that invasion of the muscularis mucosae is necessary to make a diagnosis of malignant change the incidence of malignancy was 17 per cent. The technique of local excision per anum using submucosal infiltration is described, and the management of large mucosal defects and of total papillomatosis of the rectum is discussed. Local infection and incontinence have not been features in this series and every patient has had a sphincter-conserving operation. The recurrence rate was 10 per cent and recurrences can be treated by further local excision.

ALTHOUGH villous tumours of the large bowel can be classified histologically into villous papillomas and papillary adenomas, the term 'villous tumour', first used by Holmes in 1861, is a useful one as the features of both types can be found in the same tumour and their behaviour is similar. The pathological and clinical features of these tumours have been described previously and will not be considered here in detail (Ewing, 1950; Harp, Waugh, and Docherty, 1962; Southwood, 1962; Schapiro, 1965). Eighty-five per cent of villous tumours occur in the rectum and sigmoid colon. They are characteristically sessile and papillary, and occur in an older age-group (average age, 65 years) than large-bowel cancer. The most frequent mode of presentation is with diarrhoea, bleeding, and the passage of mucus (Hanley, Hines, Ray, McPherson, and Hibbert, 1962; Nicoloff, Ellis, and Humphrey, 1968). The quantity of mucus produced may be impossible to control and the patient may present with incontinence. As the mucus has a high potassium content, patients occasionally develop severe electrolyte imbalance (Cooling and Marrack, 1957; Case, 1968; Cook, 1969).

Colonic villous tumours rarely constitute a surgical problem as they nearly always require an abdominal resection, although a very small one can be removed with a colonoscope and occasionally sigmoid pedunculated lesions can be intussuscepted into the rectum and removed locally through the anus, or snared through a sigmoidoscope.

PROBLEMS OF MANAGEMENT OF RECTAL VILLOUS TUMOURS

The majority of rectal villous tumours are sessile and can involve a wide area of the rectal mucosa. There is some controversy about the way that these tumours should be treated. Many methods have been described (*Table I*). There are three principal methods: some form of local treatment (excision or diathermy); abdominal resection (segmental excision or colotomy and local excision); abdominoperineal excision of the rectum and permanent colostomy. It will be seen from *Table II* that some surgeons are conservative and others radical in their management of these tumours. There are two principal reasons advanced for radical treatment: first, the tendency of villous tumours to undergo malignant change, and, secondly, the technical problem of treating the extensive rectal villous tumour.

Table I.—METHODS USED IN THE TREATMENT OF VILLOUS TUMOURS

Excision with biopsy forceps
Diathermy snare
Fulguration
Local excision per anum
Posterior proctotomy and excision (Kraske's approach)
Anal sphincter division and excision (Bevan's procedure)
Colotomy and polypectomy
Segmental colonic excision
Anterior resection and anastomosis
Anterior resection and pull-through procedure
Abdominoperineal excision and colostomy
Radon seeds
External radiotherapy

Table II.—MAIN METHODS OF TREATMENT USED IN DIFFERENT SERIES REPORTED IN THE LITERATURE

AUTHOR	NO. OF CASES	PERCENTAGE TREATED LOCALLY (EXCISION OR DIATHERMY)	PERCENTAGE UNDERGOING ABDOMINAL RESECTION	PERCENTAGE UNDERGOING ABDOMINOPERINEAL EXCISION AND COLOSTOMY
Bacon, Lowell, and Trimpi (1954)	28	7·1	71·4	21·5
Freund (1955)	20	85·0	5·0	10·0
Swinton, Meissner, and Soland (1955)	35	62·9	5·8	31·3
Wheat and Ackerman (1958)	50	38·0	24·0	14·0
Southwood (1962)	180	73·3	17·2	7·2
Dreese and others (1962)	41	53·6	29·2	17·2
Hanley and others (1962)	163	60·1	35·0	4·9
Samson and Andarsio (1965)	37	62·1	24·4	10·8
Schapiro (1965)	165	63·0	20·6	16·4
Goligher (1968)	74	46·0	41·9	12·1
Cogan (1968)	163	61·8	22·0	16·2
Nicoloff and others (1968)	40	40·0	57·5	2·5
Boling, Finch, and Nichols (1969)	55	52·7	29·1	10·9
Parks and Stuart (1973)	30	96·7	3·3	0

1. Malignant Potential.—The percentage of villous tumours that have undergone malignant change varies from series to series, largely according to the criteria of malignancy accepted by different pathologists (*Table III*). Focal areas of cellular atypicality are common in these tumours and areas showing hyperchromatism, loss of nuclear polarity, and frequent mitoses may be interpreted as early carcinoma or carcinoma-in-situ. However, if one takes invasion of the muscularis mucosae as the only satisfactory criterion of malignancy (Schapiro, 1965; Ziffren, 1965) invasive carcinoma is found in approximately 1 in 5 cases (*Table IV*). Because malignant change is frequently focal in nature preoperative biopsies may be misleading (Wheat and Ackerman, 1958; Dreese, Gradinger, Hellwig, Welch, and McCusker, 1962). It is only after examination of the whole tumour that the pathologist can be sure that no malignant degeneration has taken place (Birnbaum, 1967), but if the surgeon routinely performs an abdominoperineal excision of the rectum for even extensive lower rectal villous tumours then there is a 60–80 per cent chance that such a radical procedure was unnecessary.

Table III.—PERCENTAGE OF VILLOUS TUMOURS SHOWING MALIGNANT CHANGE IN DIFFERENT SERIES REPORTED IN THE LITERATURE

	NO. OF CASES	TOTAL PERCENTAGE MALIGNANT	PERCENTAGE INVASIVE
Sunderland and Binkley (1948)	48	68	39·5
Bacon and others (1954)	28	35·7	14·3
Swinton and others (1955)	35	31·4	14·3
Freund (1955)	20	30	20
Moran (1957)	32	56·2	?
Wheat and Ackerman (1958)	50	26	16
Hines, Hanley, Ray, and Brallian (1958)	71	27	8·3
Southwood (1962)	180	?	11·6
Hanley and others (1962)	163	19·2	11·6
Dreese and others (1962)	41	31·7	22
Schapiro (1965)	165	42·4	18·7
Cogan (1968)	173	36	?
Nicoloff and others (1968)	55	36·3	?
Porter and Liechty (1968)	108	21	?
Boling and others (1969)	40	?	20

2. Technical Problems.—The second reason sometimes advocated for performing a radical operation is the technical problem encountered in exposing and excising locally a large villous tumour. Pedunculated tumours are easily excised per anum. Small sessile lesions can be excised by raising up an artificial pedicle of the surrounding mucosa by traction on the tumour and then ligating this pseudo-pedicle with a transfixion suture in the same way that pedunculated tumours are removed (Gabriel, 1963; Goligher, 1967). If this technique is attempted with large sessile tumours there is a danger of producing a defect in the rectum owing to the pseudo-pedicle containing the full thickness of the rectal wall. As villous tumours frequently extend microscopically beyond the visible margin of the lesion and only a limited excision can be done in this way, local recurrence is likely. Extensive tumours confined to the

Table IV.—SUMMARY OF DETAILS OF THE PRESENT SERIES

CASE	AGE AND SEX	TUMOUR SIZE (maximum diameter)	TIME AND TYPE OF OPERATION	HISTOLOGY	FOLLOW-UP	COMMENTS
1. C. S.	63 F.	3 cm.	1960. Local excision	Villous papilloma	6 yr.	Small recurrences in 1960 and 1966 (villous papillomas). Died in 1966 from breast cancer
2. C. D.	84 F.	8 cm.	1964. Local excision	Villous papilloma	1 yr.	Died 1965 from 'myocardial degeneration'
3. F. B.	53 M.	8 cm. (height; involving 60 per cent of rectal circumference)	1964. Local excision and imbrication	Villous papilloma	7 yr.	No recurrence
4. J. M.	56 M.	2 cm. (+ polyp 1·5 cm. diameter at 14 cm.)	1964. Local excision (+ snare of polyp)	Papillary adenoma (+ adenomatous polyp)	7 yr.	No recurrence
5. T. M.	78 M.	3 cm.	1965. Local excision	Papillary adenoma	6 yr.	No recurrence
6. F. E.	71 F.	5 cm.	1965. Local excision	Papillary adenoma	6 yr.	Symptom-free (sigmoidoscopy refused)
7. E. K.	57 F.	3 cm. (+ polyp at 14 cm.)	1967. Local excision	Villous papilloma (+ adenomatous polyp)	4 yr.	No recurrence
8. T. H.	31 M.	3 cm.	1967. Local excision	Papillary adenoma	4 yr.	No recurrence
9. A. B.	71 F.	Encircling rectum to 13 cm.	1967. Local excision and pull-through procedure. Mikulicz resection for carcinoma of the transverse colon	Villous and small low-grade A carcinoma. Colonic carcinoma high-grade C1	1 yr.	Died from carcinomatosis
10. F. K.	59 M.	4 cm.	1967. Local excision	Papillary adenoma	5 yr.	No recurrence
11. M. J.	71 F.	Encircling rectum, 7 cm. length (+ polyp transverse colon)	1968. Local excision, pull-through procedure	Villous papilloma (+ adenomatous polyp)	3 yr.	No recurrence
12. J. S.	65 M.	3 cm.	1962. Local excision	Villous papilloma	10 yr.	2 recurrences in 1969, measuring 2 and 4 cm. Larger lesion showed malignant change. Local excision. No recurrence up till 1972
13. H. H.	76 M.	2 cm. (+ 2 small polyps)	1968. Local excision	Villous papilloma + malignant change	1½ yr.	Previous excision of primary hepatoma in 1967. Died in 1970 from unrelated causes
14. J. M.	75 M.	Encircling rectum, 10 cm. length	1969. Local excision and imbrication	Villous papilloma	6 mth.	Recurrence in 1972. Local excision. Histology showed villous papilloma
15. S. G.	63 M.	5 cm.	1969. Local excision and imbrication	Villous papilloma	2 yr.	No recurrence
16. W. P.	57 M.	8 cm.	1969. Local excision	Villous papilloma + malignant change	2 yr.	Proceeded to anterior resection (no residual tumour in specimen). No recurrence
17. N. W.	75 F.	Encircling rectum, 12 cm.	1969. Local excision and imbrication	Villous papilloma	3 yr.	No recurrence
18. K. T.	70 F.	2 tumours both 2 cm.	1969. Local excision	Villous papilloma	2 yr.	No recurrence
19. D. C.	36 F.	3 cm.	1969. Local excision	Sessile adenomatous polyp	2 yr.	No recurrence
20. J. H.	57 M.	5 cm.	1971. Local excision	Villous papilloma	1½ yr.	No recurrence
21. M. S.	63 F.	Encircling 9 cm. length	1971. Local excision and imbrication	Villous papilloma	1 yr.	No recurrence
22. R. C.	60 M.	4 cm.	1971. Local excision	Villous papilloma	1 yr.	No recurrence
23. A. M.	59 F.	5 cm.	1971. Local excision	Papillary adenoma	6 mth.	No recurrence
24. G. T.	82 F.	7 cm.	1971. Local excision	Villous papilloma	6 mth.	No recurrence. Died; road accident
25. L.	80 F.	10 cm.	1971. Local excision	Villous papilloma	1 yr.	No recurrence
26. N. H.	F.	10 cm.	1971. Local excision and imbrication	Villous papilloma	9 mth.	No recurrence
27. M.	64 M.	Almost encircling 9 cm. length	1971. Local excision and pull-through procedure	Villous papilloma	1 yr.	No recurrence
28. J. M.	33 M.	4 tumours, largest 2·5 cm., associated polyposis coli	1971. Local excision, colectomy, caecorectal anastomosis	Papillary adenomata	6 mth.	No recurrence
29. J. M.	73 F.	6 cm.	1971. Local excision	Papillary adenoma + malignant change	15 mth.	Nodule scar 9 mth. later, local excision. Small carcinoma completely removed. Histology showed 'new primary'. No sign of recurrence 4 mth. later
30. H. M.	64 M.	2 polyps 1 cm.	1971. Local excision	Papillary adenomata	1 yr.	Previous pelvic colon carcinoma resected in 1967. 1972, multiple adenomatous polyps of the colon

upper rectum can be managed with an anterior resection. However, many of the extensive lesions also involve the lower rectum.

Several operations have been designed to improve the access to rectal tumours. Lockwood and Taylor (1956) and Wilson and Gordon (1969) recommended the Kraske approach first described in 1885. Through an incision from the fifth sacral vertebra to the anal margin, the coccyx is removed and the levator ani muscles are divided in the midline with conservation of the external anal sphincter. The posterior wall of the rectum is then incised to expose the tumour. The main complication of this approach is the development of a proctocutaneous fistula, occurring in 20 per cent of cases in one series (Wilson and Gordon, 1969).

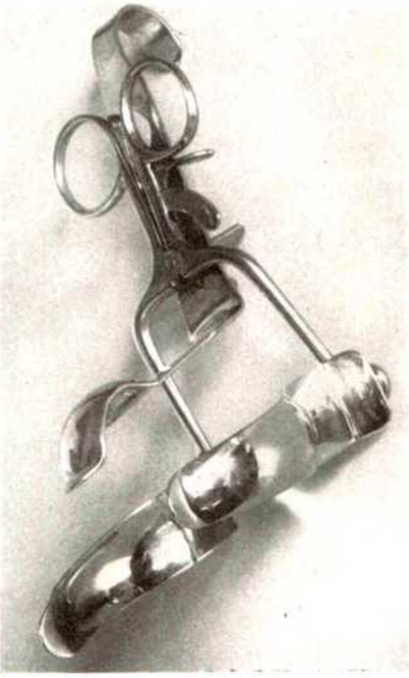
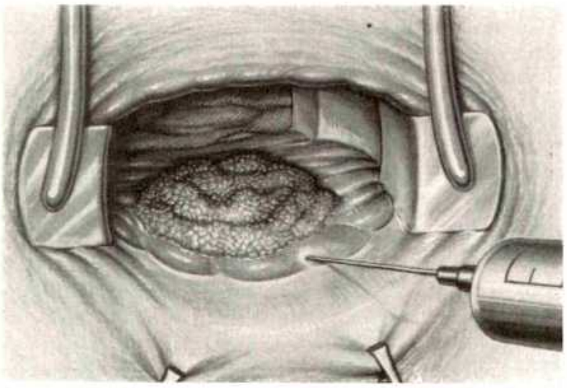


FIG. 1.—Three-bladed self-retaining retractor.



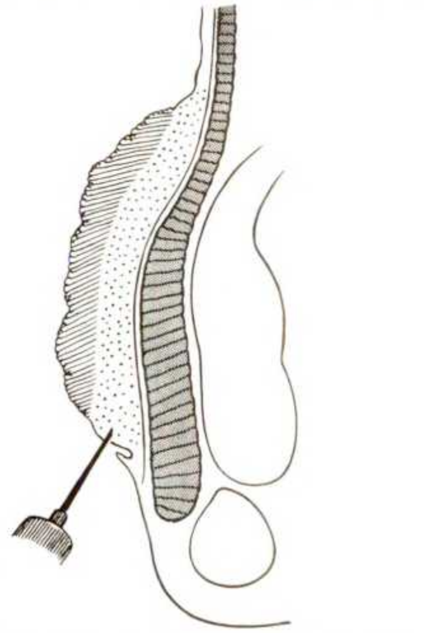


FIG. 2.—Submucosal infiltration with 1 in 300,000 adrenaline in saline. (*Reproduced from Parks, A. G. (1966), in 'Clinical Surgery', Vol. 10 (ed. Rob, C., and Smith, R.), p. 541. London: Butterworths.*)

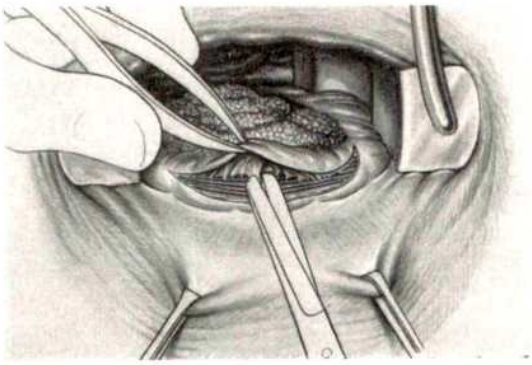
Mason (1970, 1972) has used the Bevan procedure of total sphincter section in the treatment of villous tumours and some carcinomas (Bevan, 1917). The external anal sphincter is completely divided, so laying open the rectum and anal canal. The external anal sphincter is then carefully repaired after excision of the tumour. Mason has had no case of incontinence although over one-third of his cases were complicated by local infection and 1 patient developed a fistula.

PRESENT SERIES

All of the 30 patients in the present series have been treated by per-anal local excision of villous tumours of the rectum. The sex incidence was equal and the average age at operation was 65 years (range, 31–84 years). The average size of the villous tumour was 6 cm. in diameter and 6 cases (20 per cent) were circumferential lesions. Three of these 6 patients had total papillomatosis of the rectum. Three patients had had previous treatment for villous tumours and in 6 cases multiple lesions were present or other polyps were associated with the villous tumour in the rectum. The incidence of malignant change in the series was 17 per cent. A carcinoma elsewhere in the large bowel occurred in 2 cases and has been more frequent in other series (Southwood, 1962; Wilson and Gordon, 1969); hence a barium-enema examination is essential in all cases. An association with malignancy elsewhere in the body has been recorded by other authors (Liechty and Raterman, 1963), and this was found in 2 patients in the present series.

TECHNIQUE OF PER-ANAL EXCISION OF VILLOUS TUMOURS OF THE RECTUM

The technique of local excision (Parks, 1966) depends on two principles. First, that the anal canal is a far more distensible structure than is commonly realized and with a relaxant anaesthetic the anus can be widely opened and exposure maintained with a three-bladed self-retaining anal retractor (*Fig.* 1). The second principle is that the submucosa of the rectum is an easily distensible space. Fluid injected into it spreads rapidly in all directions and distends the space to a thickness of 1–2 cm. This greatly facilitates the dissection of a mucosal lesion from the underlying circular muscle. Submucosal infiltration can also indicate areas of malignant change, as invasion of the submucosa will produce tethering during injection and that area will fail to lift off the muscle. The presence of induration is another guide although previous surgical diathermy and secondary infection can produce both induration and tethering and can make local excision more difficult. It is often helpful to do frozen sections on suspicious areas at operation.



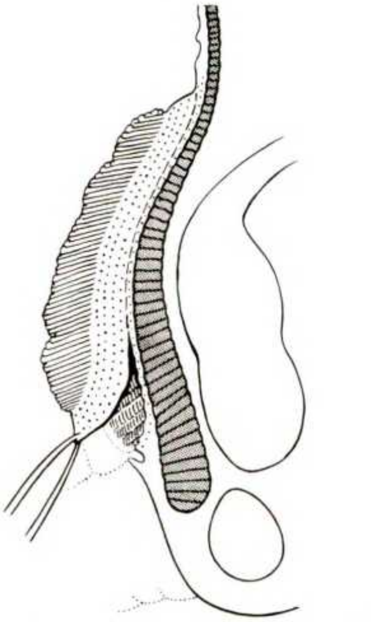


FIG. 3.—Dissection of the tumour off the circular muscle. (*Reproduced from Parks, A. G. (1966), in 'Clinical Surgery', Vol. 10 (ed. Rob, C., and Smith, R.), p. 541. London: Butterworths.*)

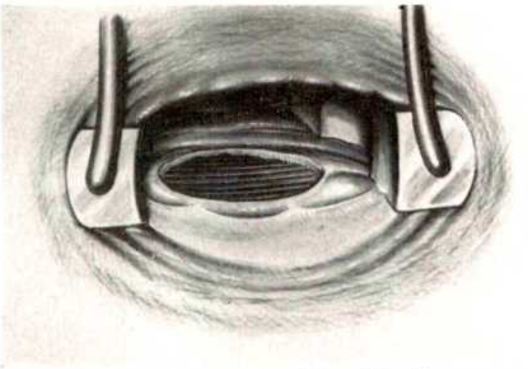


FIG. 4.—Mucosal defect after excision of the villous tumour. (*Reproduced from Parks, A. G. (1966), in 'Clinical Surgery', Vol. 10 (ed. Rob, C., and Smith, R.), p. 541. London: Butterworths.*)

1. Technique for Small Sessile Lesions (2–10 cm., 21 Cases).—After anal dilatation the self-retaining retractor is inserted to expose the tumour, which is carefully palpated for areas of induration. A needle is then inserted into the submucosa of the normal rectal wall adjacent to the tumour and isotonic saline containing adrenaline, 1 part in 300,000, is injected (*Fig.* 2). Sufficient saline is used to lift the whole tumour off the circular muscle of the rectal wall. An incision in the normal mucosa surrounding the tumour is made 1 cm. from the edge of the tumour (*Fig.* 3). The margin is necessary as histology shows that villous tumours can extend beyond the visible margin. Dissection is then carried out with scissors in the submucosal plane close to the circular muscle (*Fig.* 4). After excision all bleeding points are dealt with using diathermy coagulation. Careful haemostasis is necessary in these cases as a large volume of blood can collect in the rectum and lower colon in the postoperative period, without any external evidence of haemorrhage. No suturing of the rectal mucosa is required in most cases as even quite large bare areas of the rectal wall heal with little narrowing of the rectum.

2. Technique for More Extensive Lesions (6 Cases).—In 3 patients in this group the tumour involved the whole circumference of the rectum in a band 9–12 cm. in length (*Fig.* 5). These extensive tumours have to be removed in several pieces but the technique is essentially the same as that for small lesions (*Fig.* 6). When excision of one segment has been completed the retractor is removed and re-inserted to expose a fresh portion of the tumour. The extensive bare area can be reduced by imbricating the rectal wall in a longitudinal plane, approximating the upper mucosal margin to the lower one (*Fig.* 7). This can be done by inserting interrupted 00 chromic catgut sutures through the upper mucosal margin and then inserting the needle several times into the circular muscle before emerging from the lower cut edge of the mucosa. When these interrupted sutures are tied the effect is to concertina the circular muscle, reducing the bare area to a small transverse defect or even closing it altogether (*Fig.* 8).

3. Management of Total Papillomatosis of the Rectum (3 Cases).—Some patients have extensive villous change that can involve the whole of the rectal mucosa. Very frequently an abdominoperineal resection is performed in such cases. However, the whole of the rectal muscosa can be excised in three to four longitudinal strips using a similar technique to that discussed above. Healing would be complicated by a rectal stricture unless the denuded muscle wall can be relined with mucosa. This can be achieved by pulling down a sleeve of sigmoid colon through the denuded rectum and suturing it to the anal canal. Through a left lower paramedian incision the rectum is transected at the level of the mucosal excision. The sigmoid colon is carefully examined for any extension of the villous tumour above the level of excision and the rest of the colon is carefully palpated to exclude further lesions. Any villous change in the sigmoid colon can be treated by partial colectomy. The sigmoid colon is then drawn through the denuded rectum and sutured to the squamous epithelium of the mid-anal canal at the pectinate line (*Fig.* 9). A few sutures are placed between the cut end of the upper rectum and the wall of the colon. A temporary transverse colostomy is then performed which may be closed 3 weeks later.

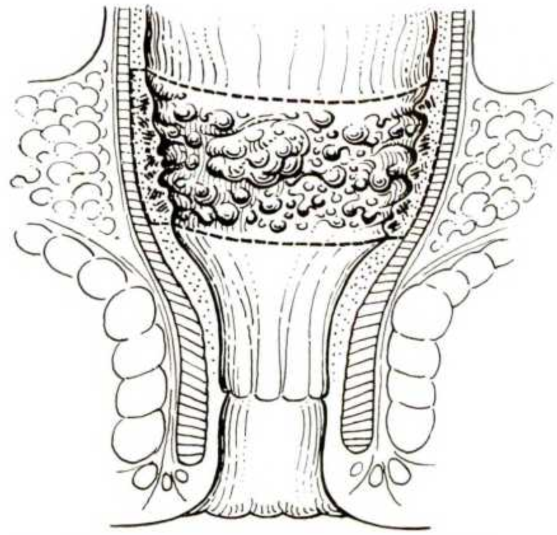


FIG. 5.—Circumferential villous tumour of the rectum.

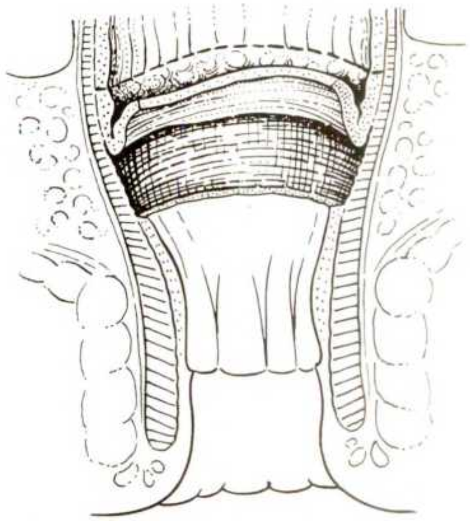


FIG. 6.—Partial excision of a circumferential villous tumour

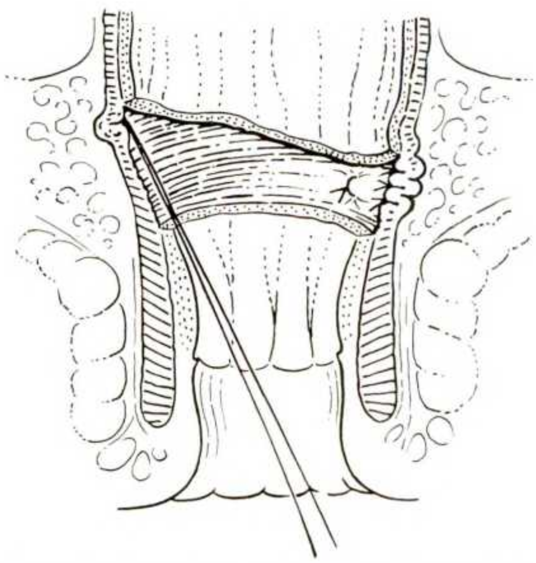


FIG. 7.—Use of interrupted sutures to imbricate circular muscle.

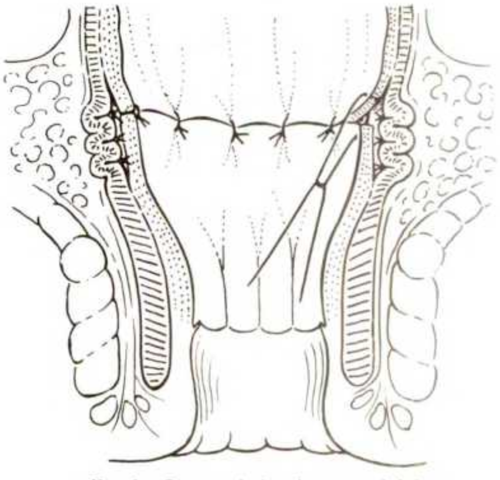


FIG. 8.—Sutures closing the mucosal defect.

The reconstituted rectum now has two muscle coats and an epithelial lining derived from the colon. It is known that rectal sensation depends principally on the tension in the muscle of the rectal wall rather than on nerve-endings in the mucosa (Parks, Porter, and Melzak, 1962), and in the 3 cases in which this more extensive procedure has been performed the functional results have been excellent and the patients are fully continent. This type of procedure is similar to that described by Soave (1964) for the treatment of Hirschsprung's disease.

RESULTS

In this series of 30 cases there has been no operative mortality and no problem with local infection. The average follow-up has been 3 years (range 6 months–10 years). Twenty-one patients had local excision of lesions varying in size from 2 to 10 cm. in diameter. A further 6 patients had imbrication of the circular muscle in addition to local excision for more extensive lesions. Half of these were completely encircling lesions. The remaining 3 patients had marked villous change over most of the rectal mucosa and after a local excision of the rectal mucosa a sigmoid pull-through procedure was performed.

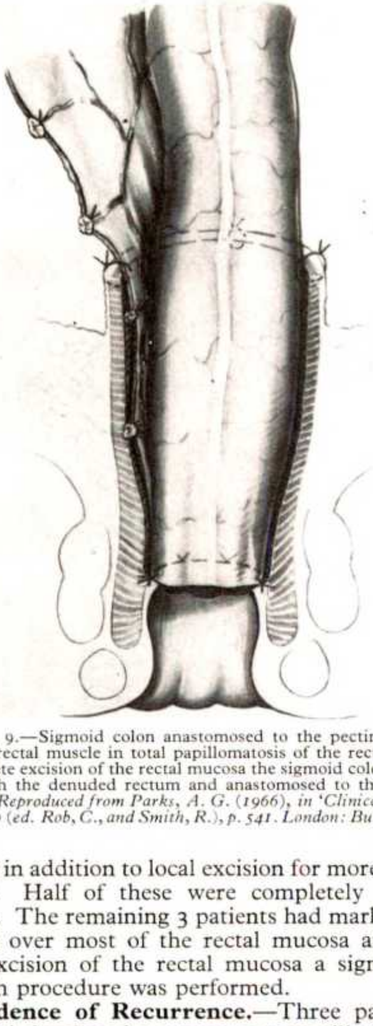


FIG. 9.—Sigmoid colon anastomosed to the pectinate line to reline rectal muscle in total papillomatosis of the rectum. After complete excision of the rectal mucosa the sigmoid colon is pulled through the denuded rectum and anastomosed to the pectinate line. (*Reproduced from Parks, A. G. (1966), in 'Clinical Surgery', Vol. 10 (ed. Rob, C., and Smith, R.), p. 541. London: Butterworths.*)

Incidence of Recurrence.—Three patients (10 per cent) developed recurrent or new villous tumours in the rectum. The recurrences occurred 3, 6, and 7 years after the primary lesions had been excised and were all treated by further local excision. Two of the recurrences were entirely benign. The third recurrence was a 4-cm. tumour with an area of carcinoma invading the submucosa at the apex of the tumour. There has been no further recurrence 3 years later.

Patients with Malignant Change.—The total incidence of malignant change in this series has been 17 per cent (5 cases). It is interesting to note that only 1 of the 6 patients with circumferential lesions in the rectum had malignant change. This patient (*Case* 9) had an extensive circumferential villous tumour of the rectum extending into the sigmoid colon and an associated carcinoma of the transverse colon. The carcinoma was treated with a Mikulicz resection, leaving the two ends of the colon as a transverse colostomy. Three weeks later the whole of the rectal mucosa was excised and a pull-through procedure was performed, anastomosing the sigmoid colon to the dentate line. Examination of the resected sigmoid colon revealed a further carcinoma at the upper end of the extensive villous tumour, and although this proved to be a low-grade A carcinoma the lesion in the transverse colon was a high-grade C1 adenocarcinoma and the patient died a year later with generalized carcinomatosis.

The other 4 cases were found to have early invasive carcinoma on histology after local excision of the villous tumours. One patient had a subsequent anterior resection and no residual tumour was found in the resected specimen. The other 3 patients had no further surgery. One patient died of unrelated causes a year later and another developed a small recurrent carcinoma 9 months later which was again excised locally. Histology suggested that the latter lesion was a new primary tumour and that it had been completely excised. The fourth patient has had no recurrence 3 years later.

DISCUSSION

Although villous tumours are uncommon compared with carcinoma of the rectum they are of surgical importance and interest because of their tendency to undergo malignant change, the severity of the symptoms that they cause, and the large area of the rectal wall that they can involve. A wide difference of opinion has been expressed as to the way that these should be managed (*Tables I, II*). This largely hinges on the pathologist's interpretation of the histological appearance. Although some authors quote a malignancy rate of over 40 per cent (*Table III*), provided that invasion is made the criterion of malignancy, the figure becomes much nearer 20 per cent, even with large tumours. That this criterion is acceptable is supported by the fact that adequate local excision of cases showing carcinoma-in-situ rarely subsequently develop metastatic or recurrent carcinoma (Ziffren, 1965). It is therefore unjustifiable to perform an abdominoperineal excision of the rectum as a routine procedure. The results of this series and others suggest that even if malignant change with early invasion has taken place, radical excision of the rectum may not be necessary as the malignancy is usually confined to the superficial layers and it is rare for there to be metastases to glands or pararectal tissues without an obvious gross carcinoma replacing the villous tumour. In this series of 30 cases, although the incidence of malignant change was 17 per cent, no patient has had a sphincter-destroying operation.

The technique of per-anal local excision using submucosal infiltration has been described and it is emphasized that this technique can be used even with large lesions; indeed, the whole rectal mucosa can be excised in this way. Small bare areas heal without any narrowing of the rectum but larger defects can be reduced in size by the technique of imbrication of the rectal wall. It is of interest that local infection has not been a problem in any of these cases. The Soave

(1964) technique of using a sleeve of sigmoid colon to line the totally denuded rectal wall has been used on three occasions and good faecal control has resulted in each case. Diathermy treatment of villous tumours has a high recurrence rate and makes subsequent local excision very difficult. Diathermy coagulation should be restricted to local recurrences.

Acknowledgements.—We wish to thank Mr. N. Mackie of the Photographic Department, St. Mark's Hospital, and Mr. R. F. Ruddick of the Photographic Department, the London Hospital, for the illustrations, and Mrs. E. S. Whiffin for secretarial assistance.

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MANAGEMENT OF UNCOMPLICATED DIVERTICULAR DISEASE BY COLONIC RESECTION IN PATIENTS AT ST. MARK'S HOSPITAL, 1964–9

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Summary

One-hundred and thirty-nine resections were performed for diverticular disease at St. Mark's Hospital, London, during the period from 1964 to 1969. One hundred and three of the resections were done on selected cases before any of the clinically recognized complications of the disease had occurred. In 46 of the resected specimens no evidence of inflammation could be found despite meticulous examination by the pathologist.

The surgical procedures were accompanied by no mortality, moderate morbidity, and a gratifying relief of symptoms, which are contrary to the generally held belief that surgery for diverticular disease is hazardous.

Over the past decade the understanding of the clinicopathological nature of diverticular disease has changed appreciably. The findings of muscular thickening and the frequent absence of inflammation in the resected specimens have been stressed (Morson, 1963; Arfwidsson, 1964; Fleischner, Ming, and Henken, 1964; Goligher, 1967; Reilly, 1967; Tagart, 1969). With this changing understanding of the disease, a change in the management may be expected.

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In the past surgery has been reserved for the management of complications, e.g., abscess, perforation, fistula, and haemorrhage. More recently surgery has been recommended for certain cases of uncomplicated diverticular disease (Todd, 1955; Colcock, 1958; Thompson, 1959; Reilly, 1964; Wilson, 1965, 1970), although clinically it is often difficult to distinguish the complicated from the uncomplicated type (Fleischner and others, 1964; Tagart, 1969; Parks and Connell, 1970). The medical management of symptomatic uncomplicated diverticular disease is unsatisfactory (Goligher, 1967), but the natural history of the disease is one of spontaneous remissions with few recurrences or complications (Bolt and Hughes, 1966; Parks, 1970). However, if complications do occur they are often serious and unheralded.

Thus, the aim of treatment in future may be to undertake elective surgery before serious complications occur provided that it is accomplished by an acceptable morbidity and mortality. It seemed relevant, therefore, to examine the results of surgical management of uncomplicated diverticular disease at St. Mark's Hospital in order to establish the safety and efficiency of surgery in such cases.

METHODS

The case notes of all the patients who underwent colonic resection for diverticular disease during the years 1964–9 were reviewed. The uncomplicated cases were examined specifically for their clinicopathological features and the nature of the resection, and these findings were correlated with the immediate and late results. In this paper 'uncomplicated' cases are defined by exclusion; by the absence of any recognized preoperative complication, namely paracolic abscess, perforation, fistula, or massive haemorrhage.

PATIENTS

There were 139 cases, of which 36 were complicated, leaving 103 uncomplicated cases for study. These were subdivided according to the indication for operation. Fifty-five patients were operated on for severe symptoms (group I), and 48 cases because cancer of the bowel could not be excluded preoperatively (group II). The colonoscope was not used during this period, but now colonoscopy may be expected to eliminate much of the diagnostic uncertainty in the latter type of case (Williams and Muto, 1972). The average age of the patients was 59 years (range, 48–77 years). There were 67 males and 36 females.

RESULTS

Clinicopathological Features.—

Group I.—Severe recurrent pain was the main symptom in all except 1 patient, who complained of severe mucous diarrhoea. Bleeding per rectum did not occur in this group.

The pain was either colicky or constant but varied considerably in character between patients. The constant pain was described as either nagging or burning and was mostly confined to the left side, although more generalized pain was experienced in several patients (sometimes referred to as reflex dyspepsia (Todd, 1970)). The colic was described as episodic by all the patients and usually as cramping. In many cases it was brought on by eating and was eased by defaecation.

Fifty-two of the 55 specimens resected showed marked muscular thickening and diverticula. The clinicopathological correlation of these cases is shown in *Table I*.

Table I.—CLINICOPATHOLOGICAL CORRELATION IN THE 55 PATIENTS IN GROUP I

SYMPTOMS	NO. OF CASES	PATHOLOGY		
		Diverticula	Muscle Thickening	Inflammation
Constant pain	31	31	29	20
Colicky pain	18	18	18	7
Both	5	5	5	3
Excess mucous diarrhoea	1	1	—	—

Table II.—CLINICAL FEATURES IN THE 48 PATIENTS IN GROUP II

Clinical Features	*No. of Cases*
Recurrent pain	11
Rectal bleeding	7
Both	13
Mass and pain	9
Mass and rectal bleeding	2
Mass, rectal bleeding, and pain	5
Mass and diarrhoea	1

Table III.—CLINICOPATHOLOGICAL CORRELATION IN THE 48 PATIENTS IN GROUP II

SYMPTOMS	NO. OF CASES	PATHOLOGY		
		Diverticula	Muscle Thickening	Inflammation
Constant pain	17	17	17	10
Colicky pain	11	11	11	7
Both	10	10	10	5
No pain	10	10	9	5

Group II.—Thirty-eight of the 48 patients in this group also had troublesome symptoms (*Table II*). Rectal bleeding refers to recurrent macroscopic bleeding, excluding the massive type. The masses which occurred did not have the definite clinical features of an abscess although the clinical differentiation between the complicated and the uncomplicated case becomes difficult here. The masses were felt either rectally or abdominally.

All but one of the specimens showed muscular thickening and diverticula. Seventeen specimens contained polyps. Inflammation was absent in 21 cases. All the specimens containing malignant neoplasms have been excluded. The clinicopathological correlation is shown in *Table III*.

Radiology.—In the symptomatic group barium-enema examinations demonstrated severe disease in 13 patients, moderate disease in 7, and a mild condition in 9 cases. In 7 patients there were strictures. The remaining 19 patients had not had a barium-enema examination in the 12 months preceding surgery.

In group II, barium-enema examinations demonstrated polypoid filling defects in 20 patients and short strictures in 15, both features adding to the clinical suspicion of possible cancer. In the remaining 13 cases diverticula alone were demonstrated.

Operative Procedure.—Eighty-eight of the 103 resections were performed in one stage. In all cases the anastomosis was to the upper rectum; however, the upper extent of the resection was variable (*Table IV*).

Table IV.—TYPE OF OPERATION PERFORMED FOR UNCOMPLICATED DIVERTICULAR DISEASE COMPARED WITH PRESENCE OF INFLAMMATION IN THE OPERATIVE SPECIMEN

OPERATION	NO. OF CASES	NO INFLAMMATION IN SPECIMEN	INFLAMMATION IN SPECIMEN
Sigmoid colectomy			
One-stage	63	32	31
Two-stage	7	1	6
Three-stage	2	0	2
Hartmann's operation	3	0	3
Left hemicolectomy			
One-stage	25	12	13
Two-stage	2	1	1
Three-stage	0	0	0
Synchronous combined excision	1	0	1

Table V.—TYPE OF OPERATION PERFORMED FOR UNCOMPLICATED DIVERTICULAR DISEASE COMPARED WITH OPERATIVE MORBIDITY

OPERATION	NO. OF CASES	COMPLICATIONS			
		Nil	Wound Infection	Surgical	Medical
Sigmoid colectomy					
One-stage	63	49	3	7	4
Two-stage	7	5	1	2	0
Three-stage	2	2	0	0	0
Hartmann's operation	3	2	1	0	1
Left hemicolectomy					
One-stage	25	12	4	6	4
Two-stage	2	2	0	0	0
Synchronous combined excision	1	0	0	1	0

Table VI.—OPERATIVE SEPSIS COMPARED WITH SEPTIC COMPLICATIONS AFTER OPERATION FOR UNCOMPLICATED DIVERTICULAR DISEASE

OPERATIVE SPECIMEN	NO. OF CASES	COMPLICATIONS		
		Wound Infection	Residual Abscess	Faecal Fistula
Inflammation present	57	9	6	0
Inflammation absent	46	4	1	1

One-stage resections were mainly performed in cases where sepsis was not apparent. Twenty-two one-stage resections had concomitant caecostomies performed by surgeons who were interested in this procedure. The three Hartmann's operations were followed later by colonic anastomoses. The synchronous combined excision was for what was considered at operation to be a malignancy. No patients underwent sigmoid myotomy.

Morbidity.—The operative morbidity is shown in *Table V.* The surgical complications were residual abscesses (5), acute retention of urine (3), prolonged ileus probably due to residual abscesses (2), wound dehiscence (2), secondary haemorrhage requiring blood transfusion (2), faecal fistula that closed spontaneously (1), and bowel obstruction (1). The medical complications were chest infections (4), deep-vein thrombosis (3), superficial thrombophlebitis (1), and myocardial infarction (1). A few patients had more than one complication.

Thus of the 103 resections, 72 (71 per cent) had no significant complication, 9 (9 per cent) had wound infections, 16 (16 per cent) had surgical complications, and 9 (9 per cent) had medical complications. The morbidity was almost identical in the two groups studied. *Table VI* demonstrates strikingly that operative sepsis still presents a problem despite newer antibiotics and techniques to combat it.

Mortality.—There were no operative deaths in this series.

Follow-up.—A complete follow-up was performed on all the cases who had troublesome symptoms prior to surgery and in whom the resected specimen had shown no evidence of inflammation, excluding those patients living outside the British Isles. The patients either were examined or replied to a postal questionnaire. The duration of the follow-up from the time of surgery varied from 1½ to 7 years.

Table VII.—RESULTS OBTAINED FROM THE FOLLOW-UP OF 41 PATIENTS WHO HAD HAD TROUBLESOME SYMPTOMS PRIOR TO SURGERY AND IN WHOM THE RESECTED SPECIMEN HAD SHOWN NO EVIDENCE OF INFLAMMATION

Result		*No. of Cases*
Asymptomatic		23
Symptomatic		14
L.I.F.* pain	5	
L.I.F. pain and constipation	3	
L.I.F. pain and diarrhoea	3	
Constipation only	1	
Diarrhoea only	2	
Died from unrelated disease		4
		41

* Left iliac fossa.

The results are shown in *Table VII.* Although 23 of the 41 patients were symptom-free, 14 patients had some residual symptoms. Pain, when it occurred, was always less severe than preoperatively and was located in the left iliac fossa. Constipation was defined as including those patients who required persistent medication. The diarrhoea remained unaltered from its preoperative state in 4 patients. In the fifth patient, who had had a left hemicolectomy, it was a new complaint of frequent bowel actions each day.

Thus, all the patients have improved considerably, but one-third still have residual symptoms of pain, constipation, or diarrhoea, Only 1 patient is dissatisfied and she is suffering from endogenous depression as well.

DISCUSSION

Elective surgery for symptomatic uncomplicated diverticular disease has been performed safely on 103 patients at St. Mark's Hospital in the past 5 years. There have been many advocates for elective surgery for severe recurring symptoms from diverticular disease over the past 20 years (Gilchrist and

Economou, 1955; Todd, 1955; Ransom, 1956; Colcock, 1958; Bacon and McGregor, 1961; Reilly, 1964; Goligher, 1967; Wilson, 1965, 1970). Even in 1953 Lloyd-Davies reported that two-thirds of his elective resections for diverticular disease were for recurrent obstructive symptoms. Arfwidsson (1964) recommended surgery for severe symptoms in patients with the pre-diverticular stage of the disease.

However, opposition to elective surgery in uncomplicated diverticular disease has been great because of the generally benign course of the disease (Bartlett and McDermott, 1953; Greene, 1957; Hughes, 1959; Thompson, 1959; Leigh, Judd, and Waugh, 1962; Bolt and Hughes, 1966; Kyle, 1968). Furthermore, it is clinically difficult to assess the severity of the symptoms (Thompson, 1970), and radiology is of little additional help (Fleischner, Ming, and Henken, 1965; Todd, 1970). However, as diverticular disease is increasing in Britain (Painter, 1969) and the patients are frequently active working people, it is becoming more important to provide relief of symptoms with minimal risk. In our opinion, elective surgery provides such treatment. Possibly a high-bulk diet will be an alternate treatment for these patients but its value has not yet been conclusively shown (Parks, 1970).

The lack of good correlation between resected specimens and preoperative symptoms is confirmed here (Hughes, 1969; Tagart, 1969). The large number of uninflamed specimens examined suggests that the preoperative pain is from the irritability of the thickened sigmoid muscle (Todd, 1965).

The predominant use of one-stage procedures is in keeping with recent surgical trends. However, multi-staged procedures were used when the ideal conditions for one-stage resections were not present.

The excellent immediate results contrast with a much higher incidence of morbidity reported from Belfast recently (Parks, 1970); however, the main indication for surgery in the latter series was the development of complications of the disease. Furthermore, our results demonstrate that elective surgery for symptoms only can be performed with a minimum of risks and thus invalidates such arguments against this type of surgery.

O'Bierne referred to the rectosigmoid sphincter in 1889, and more recently renewed interest has been shown in this region by other workers (Baker, 1970). All the resections in the present series included this region, whereas the proximal extent varied considerably. Including the rectosigmoid region in every resection may prevent anastomotic breakdown postoperatively and also recurrent symptoms later.

Our follow-up confirms that a significant number of patients have persistent symptoms after resection (Parks, 1970). However, in all but one case these were much less severe and the patients were pleased with the relief obtained by surgery. Whether a longer follow-up will demonstrate a recurrence of diverticula and severe symptoms is unknown but it is not suggested from this study.

We conclude that patients with severe persistent symptoms from uncomplicated diverticular disease can be safely treated by colonic resection with complete relief of symptoms in two-thirds of the patients and marked alleviation in the rest.

Acknowledgements.—I would like to thank the staff of St. Mark's Hospital, London, for allowing me to study their records and especially Mr. C. V. Mann for helpful criticism in the preparation of this paper.

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AN EVALUATION OF THE FLUORESCEIN TEST AND PHLEBOGRAPHY IN THE DETECTION OF INCOMPETENT PERFORATING VEINS

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SUMMARY

A study has been made of the accuracy of clinical assessment, the fluorescein test, and phlebography in the localization of incompetent perforating veins using an extensive subfascial exploration as the method of assessing the results. Clinical assessment was found to be 48 per cent accurate, the fluorescein test 39 per cent accurate, and phlebography 69 per cent accurate. Although phlebography is the most useful investigation we do not feel that it can be used to restrict a full surgical exploration of the medial side of the leg. However, it is valuable in drawing attention to the presence of incompetent perforating veins on the lateral aspect of the legs which in this series occurred in 1 of every 2 patients.

THE importance of recognizing and locating incompetent perforating veins in the treatment of patients with varicose veins and venous ulcers is well established (Cockett and Elgan Jones, 1953; Sherman, 1964; Arnoldi, 1967). Their exact localization by clinical examination has proved to be difficult, most series showing an accuracy rate of 50–70 per cent (Townsend, Jones, and Williams, 1967; Beesley and Fegan, 1970; Patil, Williams, and Lloyd Williams, 1970). In view of this, various tests have been devised to localize these veins more accurately. Operative phlebography has been shown to be 92 per cent accurate (Townsend and others, 1967) and preoperative phlebography 81·5 per cent (Lea Thomas, McAllister, Rose, and Tonge, 1972). Thermography has an accuracy rate of between 94 per cent (Patil and others, 1970; Elem, Shorey, and Lloyd Williams, 1971) and 62 per cent (Noble and Gunn, 1972). There have been widely varying claims as to the accuracy of the fluorescein test. Thus, Chilvers and Thomas (1970) found it to be 96 per cent accurate, Elem and others (1971) 16 per cent, and Noble and Gunn (1972) 47 per cent. This paper compares the accuracy in predicting the presence of incompetent perforating veins by clinical assessment, the fluorescein test, and phlebography. The accuracy of the tests was assessed at operation using a long subfascial exploration on the medial side of the leg. This is the most reliable way of locating the maximum number of incompetent perforating veins actually present.

MATERIALS AND METHODS

Patients were selected for this trial when incompetent perforating veins (I.P.V.s) were suspected on clinical examination. The method of clinical examination was a combination of those described by Dodd and Cockett (1956) and Fegan (1967). The technique for the fluorescein test was that described by Chilvers and Thomas (1970). The phlebographic technique has been described in detail elsewhere (Lea Thomas and others, 1972). The operative procedure was to make a long incision on the medial side of the leg, from just above the medial malleolus to approximately the junction of the upper and middle thirds, with an extensive subfascial exploration as described by Dodd and Cockett (1956). In addition, any I.P.V.s indicated by any of our three methods of assessment which could not be reached through this incision were explored through separate 2–5-cm. incisions. This method was used to ligate many of the lateral I.P.V.s. Incompetence of the veins was judged by the Turner Warwick bleed-back test (Warwick, 1931). An I.P.V. was recorded as correctly predicted for any given test if it was located at operation within 2·5 cm. of the predicted site.

Although this was not a blind trial the results of each test and the operative findings were recorded on separate but identical diagram charts without reference to each other as far as possible. To analyse the results the diagrams were superimposed on one another.

RESULTS

The total number of legs operated upon was 45 in 33 patients. Twenty were right legs and 25 left. Twenty-one patients were female and 12 male, with an age range of 22–76 years (average 50·7 years).

There were 106 I.P.V.s found in the 45 legs operated on, an average of 2·4 per leg (1·8 on the medial and 0·5 on the lateral aspect).

The results of each method of detection of I.P.V.s have been expressed in two ways. First, the *detection accuracy* is the total number of correctly predicted I.P.V.s expressed as a percentage of the number of I.P.V.s found at operation. Secondly, the *incorrect prediction rate* is the number of incorrectly predicted I.P.V.s as a percentage of the total number of suspected I.P.V.s for that method of detection. The correctly predicted number of I.P.V.s found by clinical examination, the fluorescein test, and phlebography were 51, 41, and 73 respectively, giving a detection accuracy of 48, 39, and 69 per cent. The number of incorrectly predicted I.P.V.s was 27, 38, and 10 respectively, giving an incorrect prediction rate of 35, 48, and 12 per cent. These results are shown in *Table I*.

Medial and Lateral I.P.V.s.—*Tables II* and *III* show the results for the medial and lateral I.P.V.s. Posterior I.P.V.s have been included in the medial group as these were all ligated through the medial incision. These results suggest that clinical assessment and the fluorescein test are even less accurate on the lateral side of the leg. Phlebography gave consistently better results than either clinical assessment or the fluorescein test. The detection accuracy for phlebography was 68 per cent on the medial side and 74 per cent on the lateral side.

Table I.—OVERALL RESULTS OF METHODS OF DETECTION OF I.P.V.s

TEST	NO. OF PERFORATORS*			DEGREE OF ACCURACY (per cent)	
	Suspected Sites	Correctly Predicted	Incorrectly Predicted	Detection Accuracy	Incorrect Prediction Rate
Clinical	78	51	27	48	35
Fluorescein	79	41	38	39	48
Phlebography	83	73	10	69	12

Total number of I.P.V.s found at operation was 106.

Table II.—RESULTS OF METHODS OF DETECTION OF I.P.V.s ON THE MEDIAL SIDE

TEST	NO OF PERFORATORS			DEGREE OF ACCURACY (per cent)	
	Suspected Sites	Correctly Predicted	Incorrectly Predicted	Detection Accuracy	Incorrect Prediction Rate
Clinical	72	47	25	57	35
Fluorescein	64	34	30	41	47
Phlebography	65	56	9	68	14

Total number of I.P.V.s found at operation was 83.

Table III.—RESULTS OF METHODS OF DETECTION OF I.P.V.s ON THE LATERAL SIDE

TEST	NO. OF PERFORATORS			DEGREE OF ACCURACY (per cent)	
	Suspected Sites	Correctly Predicted	Incorrectly Predicted	Detection Accuracy	Incorrect Prediction Rate
Clinical	6	4	2	17	33
Fluorescein	15	7	8	30	53
Phlebography	18	17	1	74	6

Total number of lateral I.P.V.s found at operation was 23.

Table IV.—EFFECTS OF SKIN HEALTH ON THE DETECTION ACCURACY OF I.P.V.s

TEST	DETECTION ACCURACY (per cent)	
	Healthy Skin	Unhealthy Skin
Clinical	53	61
Fluorescein	40	42
Phlebography	67	68

Effects of Skin Health.—The skin was considered unhealthy if there was induration of the lower half of the leg, combined with pigmentation and/or scarring from previous ulceration. Comparison of the accuracy of each method in patients with healthy or unhealthy skin is shown in *Table IV*. The state of the skin did not appear to affect the accuracy of the tests.

Position of the I.P.V.s.—The distribution of all the I.P.V.s is shown in *Figs.* 1 and 2. On the medial side (*Fig.* 1) the extent of the incision is indicated by the lower two arrows. The level which could be easily inspected subfascially to detect and ligate I.P.V.s above the upper limit of the incision is indicated by the uppermost arrow. Only the two highest I.P.V.s required a separate incision to ligate them.

Wound Healing.—The patients were allowed home as soon as the wounds were soundly healed. The average stay in hospital following operation was 12 days (range, 5–28 days). Only 6 out of the 33 patients were in hospital for longer than 12 days. In 5 of these patients the delay was due to staphylococcal wound infection. The remaining patient's discharge was delayed because of a skin-graft applied at the time of operation. There was only 1 case of superficial necrosis of the skin which did not delay the patient's discharge. No patient had full-thickness skin-loss.

DISCUSSION

In many of the other comparative studies of the accuracy of methods of detecting I.P.V.s only small incisions have been made at the suspected sites (Townsend and others, 1967; Patil and others, 1970; Elem and others, 1971; Noble and Gunn, 1972). We believe that only a long subfascial exploration can provide a really accurate assessment of the presence or absence of I.P.V.s, and all the legs in this series have been explored through such an incision on the medial side.

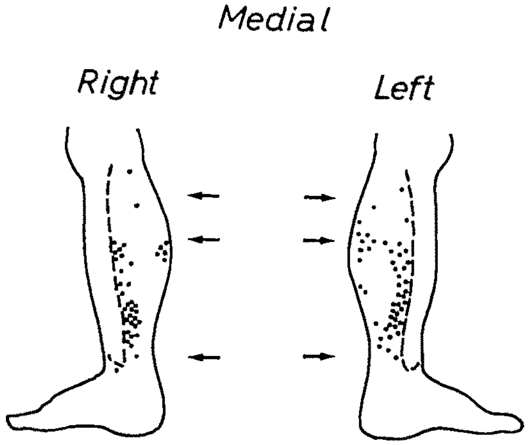

FIG. 1.—Distribution of the I.P.V.s found at operation on the medial side of the leg. The lower two arrows show the extent of the incision, while the upper arrow indicates the level which can be inspected easily.

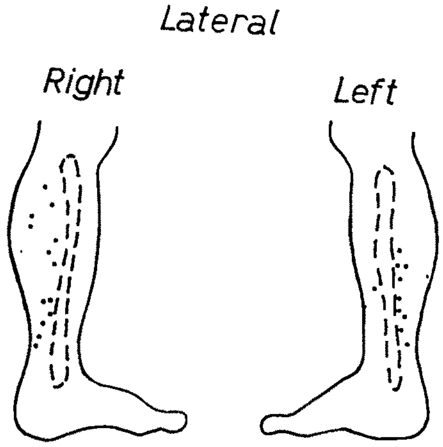

FIG. 2.—Distribution of the I.P.V.s found at operation on the lateral side of the leg.

Clinical assessment of the site of I.P.V.s was accurate in only 48 per cent of cases, a result similar to other reports (Beesley and Fegan, 1970; Noble and Gunn, 1972). However, the decision to explore the perforator region and therefore include a patient in this series was a clinical one and only 1 leg out of the 45 explored was found to have no I.P.V.s at operation. Thus, clinical examination appears to be reliable in indicating the presence of I.P.V.s but is unreliable in showing their exact site.

We had hoped that this series would confirm the good results of the fluorescein test reported by Chilvers and Thomas (1970), as it is simple, safe, and quick to perform. However, our detection accuracy of 39 per cent and the results of Elem and others (1971) and Noble and Gunn (1972) suggest that this method is not sufficiently accurate and that it results in too high an incidence of incorrect predictions (48 per cent). Moreover, it did not show a higher degree of accuracy in legs with healthy skin as was previously suggested.

Phlebography was shown to be the most reliable means of investigation and was particularly useful in demonstrating lateral I.P.V.s. The incidence of incorrect predictions might be expected to be low since in the technique that we use the contrast medium is seen to pass from the deep to the superficial veins on television screening. This contrasts with the fluorescein test which has the inherent inaccuracy of being a blind technique, as the route by which it reaches the skin cannot be directly visualized.

A criticism of phlebography is that the sites of I.P.V.s shown on radiographs are difficult to relate to the patient's leg. In fact, we were able to locate them accurately in 69 per cent of the cases. A further advantage of phlebography over other methods is that it provides additional information about the presence or absence of incompetent valves or obstruction of the deep veins. However, phlebography failed to detect 31 per cent of the I.P.V.s found at operation, so that thorough surgical exploration cannot safely be replaced by multiple small incisions over suspected sites.

Thermography was not used because we did not have access to the necessary equipment. It is not standard equipment in most hospitals and we therefore felt that it was unlikely to become a generally used method.

Using the long medial incision with subfascial exploration (Dodd and Cockett, 1956) we were able to locate and ligate virtually all medial and posterior I.P.V.s (*Fig.* 1). On a number of occasions this incision provided sufficient exposure to ligate lateral I.P.V.s. This operation is often criticized because of the long scar that it leaves and because of the risk of flap necrosis. The latter can be largely avoided by delaying operation until the patient's legs have been properly prepared by a period of using efficient firm supportive bandages and by careful atraumatic technique and suturing the skin without tension. We had no cases of significant flap necrosis and have not found the long scar to be any more unsightly than a number of small scars produced by multiple incisions.

In conclusion we feel that phlebography is the best method of preoperative detection of I.V.P.s but that it is not sufficiently accurate to replace an adequate surgical exploration. It is most useful in assessing people with recurrent varicose veins or venous ulceration, and in cases which are difficult to assess clinically, particularly when it is felt that lateral perforators may be present.

Acknowledgements.—We would like to thank Professor J. B. Kinmonth, Mr. F. B. Cockett, and Professor N. L. Browse for allowing us to study patients who were under their care. We would also like to thank Professor Browse for his valuable advice and criticism.

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GASTRIC SECRETORY RESPONSE TO INSULIN INFUSION IN VAGOTOMIZED SUBJECTS*

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SUMMARY

The results of the insulin-infusion test carried out after vagotomy in 50 patients are presented. In 25 cases a comparison was made between the insulin-infusion test and the conventional Hollander test. A good correlation was observed between the peak acid output induced by insulin infusion and that noted during the Hollander test. It is concluded that with the present criteria for interpretation the insulin-infusion test may be no better than the Hollander technique for defining patients at risk of recurrent dyspepsia. However, the small amounts of insulin used, the gradual lowering of blood-glucose, and the reduced incidence of profound hypoglycaemia which attend the insulin-infusion test suggest that this technique should be adopted for the assessment of vagotomy in preference to the potentially dangerous Hollander test.

THE potentially dangerous Hollander test (Hollander, 1946; Read and Doherty, 1970) has led us to develop an insulin-infusion test aimed at reducing the severity of hypoglycaemic symptoms (Carter, Dozois, and Kirkpatrick, 1972).

The present investigation was designed to study the patterns of the gastric secretory response to an insulin infusion in vagotomized subjects and to compare the acid response to the insulin-infusion test with that produced by the Hollander test. A preliminary report of this work has been presented elsewhere (Dozois, Carter, and Kirkpatrick, 1972).

MATERIAL AND METHODS

The insulin-infusion test was carried out in 50 patients at least 2 months after vagotomy and a drainage procedure. Twenty-five of these 50 patients were also subjected to the Hollander test. The latter test was also conducted at least 2 months after vagotomy and within 2 months of the insulin-infusion test. The subjects ranged in age between 20 and 81 years.

The technique of the insulin-infusion test has previously been reported in detail (Carter and others, 1972). Following a 12-hour overnight fast a nasogastric tube was passed and its ideal gastric position determined by the method of Hassan and Hobsley (1970). Basal gastric secretions were collected for 30 minutes before commencing insulin infusion (0·04 U. per kg. per hr.). Gastric juice was then collected at 15-minute intervals during the 3-hour infusion.

The Hollander test was performed in the usual manner. Following collection of basal secretions a single rapid injection of insulin (0·2 U. per kg.) was given intravenously and gastric juice was collected at 15-minute intervals for 2 hours.

During both tests samples of venous blood were obtained just prior to and every 30 minutes following the start of the infusion (or the injection of insulin). Blood-glucose levels were determined by a glucose-oxidase method using an Autoanalyser.

Each sample of gastric juice was measured in terms of volume (ml.), acid concentration (mEq./l.), and acid output (mEq.). All titrations were made to *p*H 7·0 with 0·1 *N* NaOH solution, using an automatic titrator and a glass electrode (Radiometer, Copenhagen).

DEFINITION OF TERMS

The following parameters of acid secretion were studied:—

1. **Plateau Acid Output (P.$_L$A.O.).**—The sum of the four highest consecutive 15-minute outputs during the infusion, expressed as mEq./hr.

2. **Peak Acid Output (P.A.O.)** (Baron, 1963).—The sum of the two highest consecutive 15-minute outputs during the infusion (or following insulin injection in the Hollander test) multiplied by 2, expressed as mEq./hr.

3. **Mean Plateau Acidity (M.P.$_L$A.).**—The mean concentration of the four highest consecutive

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* Based on a communication to the Surgical Research Society, July, 1972.

15-minute concentrations during the infusion, expressed in mEq./l.

With regard to blood-glucose the parameters studied were:—

1. Plateau Blood-glucose.—The mean of all blood-glucose readings during the second and third hours of insulin infusion, expressed in mg. per 100 ml.

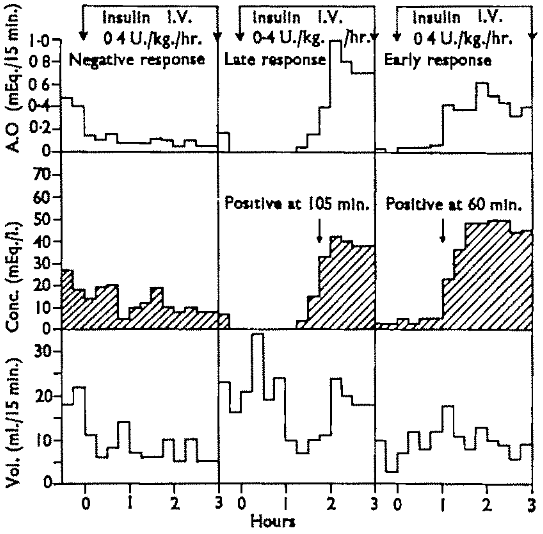

FIG. 1.—Patterns of gastric secretory response to the insulin-infusion test. Positivity of response is based on criterion of mean plateau acidity (*see* text).

2. Lowest Blood-glucose.—The lowest blood-glucose value observed during the insulin infusion (or after insulin injection), expressed in mg. per 100 ml.

Positive Response.—The acid response during the Hollander test was defined as 'positive' when the acid concentration following the injection of insulin was 20 mEq./l. or more in excess of basal values (10 mEq./l. if basal achlorhydria). This positive response was further subdivided into 'early' or 'late' depending on whether it occurred during the first or the second half of the 2-hour test (Burns, Cheng, Cox, Payne, Spencer, and Welbourn, 1969).

With the insulin-infusion test the acid response was considered 'positive' when the mean plateau acidity was at least 20 mEq./l. greater than the mean concentration of basal secretion. This positive response was further subdivided into 'early' or 'late' according to whether it took place during the first or second half of the 3-hour test (*Fig.* 1).

RESULTS

1. Patterns of Gastric Secretory Response to the Insulin-infusion Test.—Twenty-two of the 50 subjects studied had a negative response to the insulin-infusion test, while 15 subjects had an early positive response and 13 subjects a late positive response.

The P.$_{\text{I}}$A.O. of subjects with an early positive response (mean 10·66 mEq. ± S.D. 9·99) and with a late positive response (mean 7·28 mEq. ± S.D. 6·66) did not differ significantly ($P > 0{\cdot}30$, Student's *t*-test for unpaired data), but the mean P.$_{\text{I}}$A.O. of either group differed significantly from that of the negative-response group (mean 0·65 mEq. ± S.D. 0·75, $P < 0{\cdot}001$).

The mean plateau blood-glucose was 26·0 mg. per 100 ml. (± S.D. 11·0) and the mean lowest blood-glucose was 23·3 mg. per 100 ml. (± S.D. 10·6) in the 25 patients also subjected to the Hollander test.

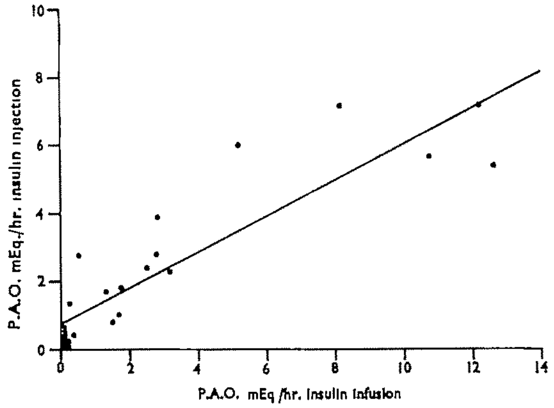

FIG. 2.—Correlation between peak acid output in response to insulin infusion and to the Hollander test in 25 subjects ($r = 0{\cdot}89$; $n = 25$; $P < 0{\cdot}001$; $y = 0{\cdot}53x + 0{\cdot}69$.)

Table I.—PATTERNS OF ACID RESPONSE TO BOTH INSULIN TESTS IN 25 SUBJECTS

INSULIN-INFUSION TEST	HOLLANDER INSULIN TEST		
	Negative	Early Positive	Late Positive
Negative	13	—	3
Early positive	1	2	—
Late positive	—	1	5

Table II.—COMPARISON OF PEAK ACID OUTPUT (P.A.O.) AND LOWEST BLOOD GLUCOSE (L.B.G.) IN 25 SUBJECTS UNDERGOING BOTH INSULIN TESTS

	P.A.O		L.B.G	
	I.I.T	H.T.	I.I.T.	H.T.
Mean	2·73	2·14	23·3	11·4
S.D.	3·9	2·4	10·6	5·3
P*	>0·4		<0·001	

I.I.T., Insulin-infusion test. H.T., Hollander test.
* Student's *t*-test.

2. Comparison between the Insulin-infusion Test and the Hollander Test.—In the 25 subjects where both tests were performed the patterns of acid response were almost identical. Of the 16 patients showing a negative response to insulin infusion, 13 showed a negative response to the Hollander test. Eight of the 9 patients with a positive response to insulin infusion also gave a positive response to the Hollander test. These figures are amplified in *Table I.* In 4 of the 5 cases where a discrepancy was observed between the two tests, both tests had been performed within 6 months of vagotomy. The P.A.O. during infusion correlated significantly ($P < 0{\cdot}001$) with the P.A.O. during the Hollander test (*Fig.* 2) and the magnitude of the acid response was similar in the two tests (*Table II*).

The mean lowest blood-glucose for the 25 Hollander tests was 11·42 mg. per 100 ml. (± S.D. 5·3) which was significantly lower ($P < 0{\cdot}001$, Student's *t*-test for paired data) than the lowest blood-glucose obtained with the insulin-infusion test (23·3 mg. per 100 ml. ± S.D. 10·6).

DISCUSSION

The Hollander insulin test is controversial in its interpretation (Stempien, 1962) but remains the only valuable postoperative means of evaluating the completeness of vagotomy. The potential dangers of extreme hypoglycaemia (i.e., < 15 mg. per 100 ml.) with its associated unpleasant symptoms have recently received attention (Read and Doherty, 1970). A survey of 220 Hollander tests performed in our own gastric secretion laboratory has revealed lowest blood-glucose values of 10 mg. per 100 ml. or less in more than half of the tests. With the object of reducing the severity of hypoglycaemia the continuous insulin-infusion test has been developed. In healthy subjects a dose of 0·04 U. per kg. per hr. of insulin was found to produce the highest acid secretion compatible with an acceptably low level of hypoglycaemic symptoms (Carter and others, 1972).

In vagotomized subjects three types of response to insulin infusion have been observed. The negative response was associated with little or no acid response and probably represents complete gastric vagal denervation. The subdivision of the positive response into early and late categories was suggested by the observation that plateau acid secretion occurred in all subjects with intact vagi within 90 minutes of commencing infusion. However, this division seems unlikely to be of prognostic value in that both groups appeared equally capable of secreting significant amounts of acid. This conclusion has already been reached from the results of the Hollander test because both early and late responses are found in subjects with intact vagi (Burns and others, 1969) and recurrent ulcers occur not infrequently in patients showing a late response (Johnston, Thomas, Checketts, and Duthie, 1967).

The magnitude of the acid response to both types of test proved to be almost identical in individual subjects despite the fact that less profound hypoglycaemia followed insulin infusion. The symptom scoring method (Carter and others, 1972) used routinely to assess the side-effects of the insulin-infusion test could not be applied to the Hollander test so that an objective comparison of the two tests is not possible in this context. However, every patient considered the insulin-infusion technique to be less unpleasant and this is in agreement with the findings of Girvan, Baron, Spencer, and Hansky (1973) in their appraisal of the two techniques. With regard to the interpretation of the two tests, complete agreement was noted in 20 of the 25 subjects (*Table I*). Of the 5 subjects showing differences between the tests, the major discrepancy noted was that 3 subjec showed a negative response to the insulin-infusio test, whereas a subsequent Hollander test w interpreted as positive. None of these patients h experienced recurrent dyspepsia to date. Of t other 2 subjects showing differing responses, o differed merely in the timing of the positive respons whereas the remaining patient exhibited an u equivocally early positive response to insulin infusio while the Hollander test carried out 2 mont previously had been negative. Neither of the patients has recurrent dyspepsia. The cause of the discrepancies is, at present, uncertain but in 4 cas the tests were performed within 6 months of surge and in view of the known lack of stability of t gastric response to insulin within this period (Smit Gillespie, Elder, Gillespie, and Kay, 1972) it will b necessary to repeat the tests at a later date. It mu be borne in mind, however, that the Hollande criterion is *arbitrary* and we are currently attemptin to apply alternative criteria based on changes in aci output to relate the interpretation of the insuli infusion test to the subsequent clinical course of t patient. Even if the insulin-infusion test were t remain equal to the Hollander test in the determin tion of inadequate vagotomy, the minimal side-effec and less profound hypoglycaemia which result fro the small doses of insulin infused justify the routin use of the infusion technique in preference to t potentially dangerous conventional procedure.

Acknowledgements.—The authors gratefull acknowledge the support and advice of Profess A. P. M. Forrest, the assistance of Dr. I. W. Perc Robb and the Biochemistry Department, Roy Infirmary, Edinburgh, in the blood-glucose esti mations, and the invaluable help of Staff Nurse Dale in the performance of the insulin tests. Th assistance of Dr. R. J. Prescott in analysis of the dat was gratefully received.

During the performance of this work R. R. was in receipt of the R. S. McLaughlin Foundatio Fellowship.

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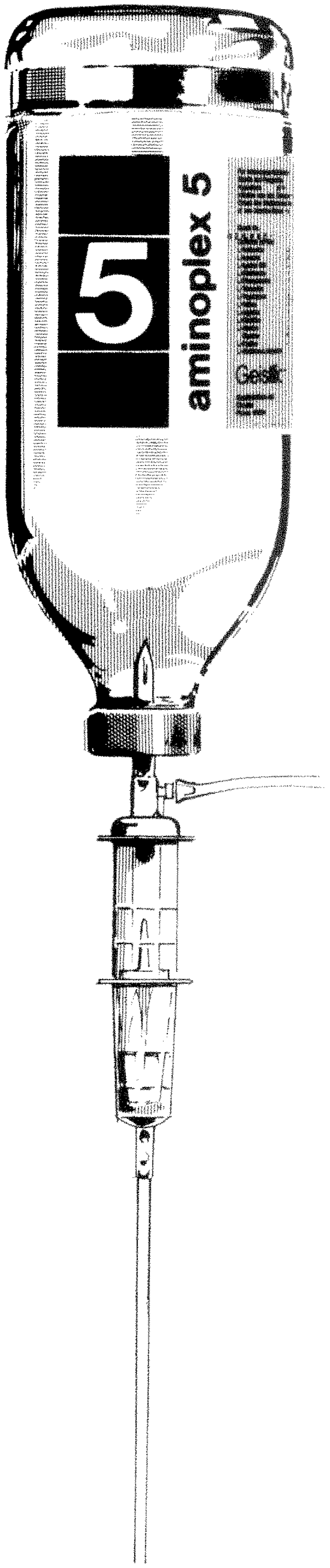

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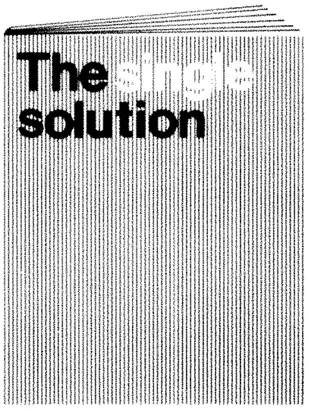

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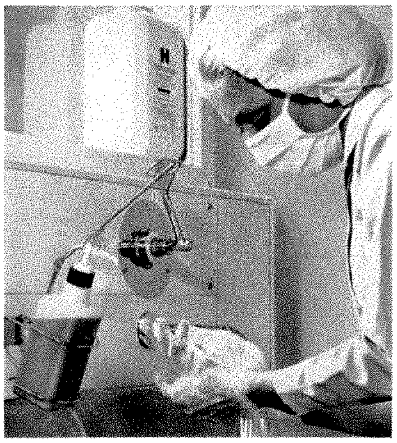

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A NEW METHOD FOR DETECTING CLOTTING IN SHUNTS USED FOR HAEMODIALYSIS

By J. R. SALAMAN, J. CHU, and D. L. CROSBY

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SUMMARY

Thermographic materials were used to monitor the rate of blood-flow through haemodialysis shunts. In an experimental and clinical study it was found that these materials would indicate by a change in colour when blood-flow through a shunt had become diminished or had ceased altogether. As a result clotting episodes were rapidly and easily diagnosed by the patients, and subsequent declotting of the shunts was readily achieved.

THE Silastic arteriovenous shunt has served the needs of chronic haemodialysis for many years. It provides a ready means of access to the patient's circulation whenever dialysis is required but suffers from the disadvantage that it is liable to become thrombosed. For this reason it has been largely replaced by the subcutaneous arteriovenous fistula, which is less liable to develop this complication. Unfortunately it is not possible to establish a fistula in every case and for these patients the shunt is the only alternative. In an attempt to extend the working life of these shunts we have examined possible ways of warning patients when clotting of the shunt is taking place, for early attention to a clotted shunt can usually result in the blood-flow being restored.

A clotted shunt often remains unnoticed by a patient for some hours, although occasionally some pain in the shunted limb may draw his attention to it. Unfortunately this is not a reliable symptom and in most instances clotting is quite painless. Shunt flow rates may be measured with conventional flow meters, but this is not a practical procedure when continuous monitoring is required. The temperature of a well-functioning shunt is very close to that of the blood that is entering it, and since diminished flow or clotting will be accompanied by a fall in shunt temperature we have attempted to use temperature changes as indices of blood-flow. In place of conventional thermometers we have employed thermographic materials to measure shunt temperature since variations in temperature produce an easily recognized change in the colour of the material.

MATERIALS AND METHODS

Samples of thermographic material were obtained from the National Cash Register Corporation. They comprised a layer of micro-encapsulated liquid crystals of a cholesterol derivative applied to a paper or plastic base. Small rectangles of material ('spots') were cut out with scissors and attached to the arterial limb of a shunt with Silastic glue. The material was then protected by covering it with a single layer of cellophane tape (*Fig.* 1). Four types of thermographic material were studied. Each had a defined temperature within which the changes in colour would take place (*Table I*). At the upper end of the range the material would appear blue, and on cooling would then become successively green, red, and black. The materials were first investigated in the laboratory and then the two that had proved most promising were used for a clinical study.

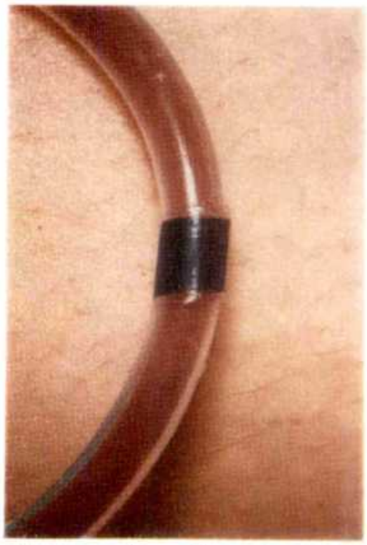


FIG. 1.—A thermographic monitor in place on a haemodialysis shunt. The monitor is registering a blue colour indicating good blood-flow within the shunt.

Table I.—TEMPERATURE RANGE OF THE THERMOGRAPHIC PAPERS USED IN THE PRESENT EXPERIMENTS

Code No.	*Temperature Range* (°C.)
R29	29–33
R33	33–37
R35	35–38
W630	Unspecified

Laboratory Experiment.—Thermographic spots were attached to a segment of shunt tubing which was placed inside a glass condenser. Blood at 37° C. was run through the tubing and the surrounding air temperature was maintained at either 22° C. ('room temperature') or 10° C. ('outside temperature') by pumping water at the correct temperature through the jacket of the condenser. The rate of blood-flow through the shunt was altered by means of a screw-clip on the blood line, and the colour of the thermographic spots was noted at different rates of flow.

Clinical Study.—Twenty-two patients on regular haemodialysis were studied. Thermographic spots of paper R33 were attached to the arterial side of their shunts and the patients were told to observe these spots regularly and to report to the hospital if the colour changed from the normal dark blue to green or black. After 3 months the paper R33 was replaced with paper R35 and the study was continued for a further 3 months.

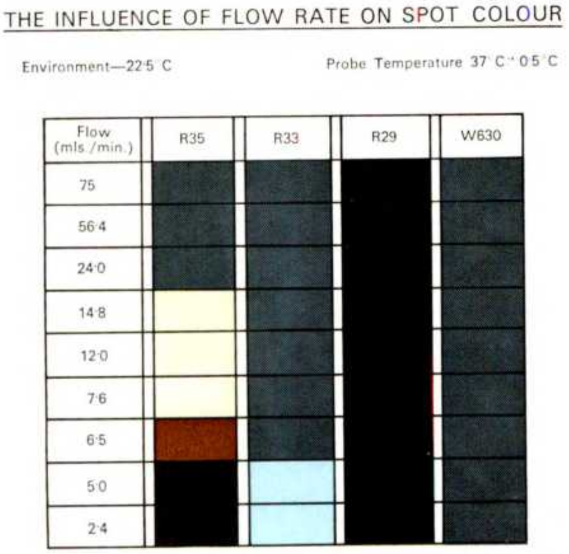
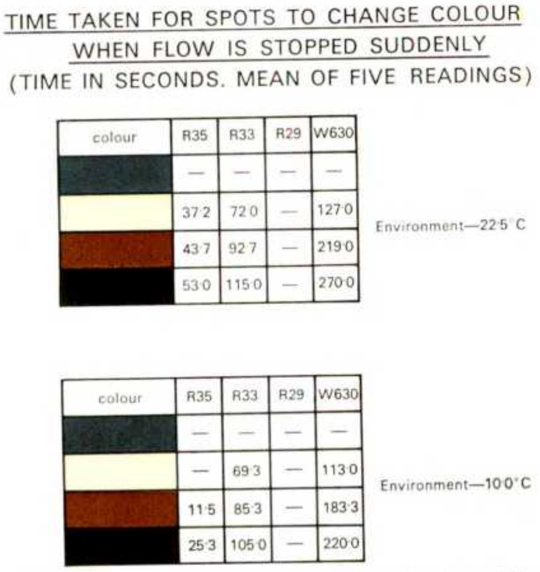


FIG. 2.—The results of *in vitro* experiments in which the colour of four thermographic materials was recorded at different rates of blood-flow. R35 exhibited the greatest change in colour whereas the other materials remained black or blue (reproduced here as a grey).


TIME TAKEN FOR SPOTS TO CHANGE COLOUR WHEN FLOW IS STOPPED SUDDENLY (TIME IN SECONDS. MEAN OF FIVE READINGS)

Environment—22·5 C

colour	R35	R33	R29	W630
🟦	—	—	—	—
⬜	37·2	72·0	—	127·0
🟫	43·7	92·7	—	219·0
⬛	53·0	115·0	—	270·0

Environment—10·0 C

colour	R35	R33	R29	W630
🟦	—	—	—	—
⬜	—	69·3	—	113·0
🟫	11·5	85·3	—	183·3
⬛	25·3	105·0	—	220·0

FIG. 4.—The results of an experiment to determine how quickly after arresting the blood-flow four thermographic materials would change colour.

RESULTS

Experimental.—The results obtained from the laboratory experiments are shown in *Figs.* 2, 3, and 4. It will be seen that at an environmental temperature of 22 or 10° C., R35 registered a change in colour when the blood-flow through the shunt was reduced. It was apparent, however, that in a cool environment R35 never attained a blue coloration even when the blood-flow was in excess of 80 ml. per minute (*Fig.* 3). When the flow of blood was arrested suddenly, a change in colour was noted first in R35 and then later in R33 and W630 (*Fig.* 4). R29 behaved erratically and for the most part remained black. It was clear that R35 and R33 were the most sensitive of the four materials tested and these two were selected for the clinical study.

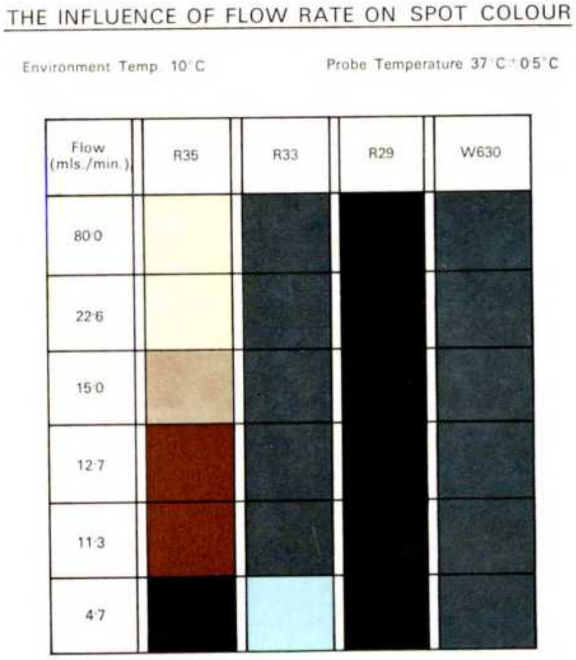


FIG. 3.—The effect of temperature on the performance of four thermographic materials. The experiment was the same as depicted in *Fig.* 2, but the environmental temperature was lowered to 10 C.

Table II.—CLINICAL EXPERIENCE WITH THERMOGRAPHIC MONITORS OF SHUNT FLOW RATES

	TEST MATERIAL	
	R33	R35
No. of shunts studied	20	22
No. of shunts which clotted	10	9
No. of clotting episodes	20	16
No. of clotting episodes detected by the material	20	16
No. of clotting episodes treated successfully	18	14

Clinical.—During the clinical study 19 patients had a total of 36 clotting episodes (*Table II*). In each instance clotting was accompanied by the appropriate change in colour of the shunt spot, and to most of the patients this was the first indication that clotting had occurred. Materials R33 and R35 seemed to be equally effective in registering this event, and in most cases subsequent declotting of the shunt was accomplished without difficulty. When functioning shunts were examined in a cool environment it was frequently noted that the spots of R35 had become green. This was to be expected (*see above*) and the patients were advised to re-examine their shunts in warmer surroundings. Two patients (one with R35 and the other with R33) noted a change in the spot colour before clotting had occurred. These changes were indicative of a poor blood-flow, and by the time the patients had arrived in hospital, clotting had taken place. As a result of this timely action, declotting of these shunts was easily achieved.

DISCUSSION AND CONCLUSION

The thermographic spot provides the dialysis patient with a useful guide as to the rate of blood-flow within his shunt. Not only does it inform him when clotting has occurred, but it can also indicate when flow rates have fallen to levels at which clotting has become imminent. By taking appropriate action at this early stage it should prove possible to extend considerably the working life of many haemodialysis shunts.

THE USE OF GASTROGRAFIN IN THE RELIEF OF RESIDUAL AND LATE BOWEL OBSTRUCTION IN CYSTIC FIBROSIS

By J. F. McPARTLIN, J. A. S. DICKSON,* and V. A. J. SWAIN
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SUMMARY

The incidence, pathology, and standard surgical management of meconium ileus are described. In uncomplicated cases an 80 per cent survival rate can be expected. The indications for instillation of Gastrografin into the bowel as an alternative to operation, either as an enema or through an ileostomy, are discussed. Three instances of its successful use to relieve late obstruction are reported. The probable method of action of Gastrografin is suggested, and the precautions to be observed in its use are listed. By avoiding the pulmonary and surgical problems associated with laparotomy the use of Gastrografin should decrease morbidity and mortality.

MECONIUM obstruction in the ileum occurs in between 10 and 15 per cent of children with fibrocystic disease (Di Sant'Agnese, 1956; Santulli, 1969; McPartlin, Dickson, and Swain, 1972). The excessively tenacious meconium produced as a result of the defective pancreatic and intestinal secretions accumulates in and obstructs the mid-ileum, which is dilated and hypertrophied; the distal ileum is firmly contracted on small plugs of grey mucus; the colon is empty. The dilatation of loops of proximal bowel is the cause of complications, ranging from simple volvulus to atresia, gangrene, and peritonitis, in up to 50 per cent of cases.

Table I.—RESULTS OF SURGICAL TREATMENT FOR MECONIUM ILEUS REPORTED IN THE LITERATURE

AUTHOR	HOSPITAL	NO. OF CASES	SURVIVAL FROM SURGERY	OPERATIVE MORTALITY (Per cent)	LATE DEATHS	LONG-TERM SURVIVAL	
						No.	Per cent
McDonald and Trusler (1960)	Hospital for Sick Children, Toronto, Canada	27	9	67	4	5	19
Holsclaw, Eckstein, and Nixon (1965)	The Hospital for Sick Children, Great Ormond Street, London	109	45	58	27	18	17
Donnison, Schwachman, and Gross (1966)	Children's Hospital, Boston, Mass.	127	51	60	24	27	21
Santulli (1969)	Babies Hospital, New York, U.S.A.	68	35	49	22	13	19
Rickham (1969)	Alder Hey Hospital, Liverpool	52	24	54	17	7	13
O'Neill, Grosfeld, Boles, and Clatworthy (1970)	Children's Hospital, Columbus, Ohio, U.S.A.	33	13	60	5	8	24
Kalayoglu, Sieber, Rodnan, and Kiesewetter (1971)	Children's Hospital, Pittsburgh, Pennsylvania, U.S.A.	46	23	50	9	14	30
Present series (1962–70)	Queen Elizabeth Hospital, London	24	17	30	2	15	63

Until recently the only hope of relief in established obstruction was operation combined with intensive care to prevent associated respiratory problems. In most published series not more than 50 per cent of children survived the initial surgical treatment and only 30 per cent at best survived for 1 year (*Table I*). Recent results have been more encouraging, with a long-term survival of 62·5 per cent (80 per cent in uncomplicated cases) (McPartlin and others, 1972). Unpublished information from other centres suggests that this figure may be more representative of contemporary experience. These relatively good results are probably due to improvements in surgical technique and the recognition of the importance of intensive medical care. The most important improvement in surgical management appears to have been the adoption of the Bishop-Koop resection with Roux-en-Y anastomosis (Bishop and Koop, 1957; *Fig.* 1). In this technique the dilated obstructed ileum is resected and the end of the proximal segment is anastomosed to the side of the distal segment, the open end of which is brought to the surface of the abdomen as an ileostomy. Clearing the bowel can be helped by washing out the meconium and mucus plugs with the detergent Tween 80, 1 per cent in tyrode solution. The stoma acts as a safety valve through which the proximal bowel may decompress itself while the inspissated meconium and mucus plugs are digested and the unexpanded distal bowel assumes its normal size and function. By reducing the copious loss of fluid and electrolytes and the digestion of the abdominal wall seen in other forms of ileostomy this technique reduces morbidity and mortality.

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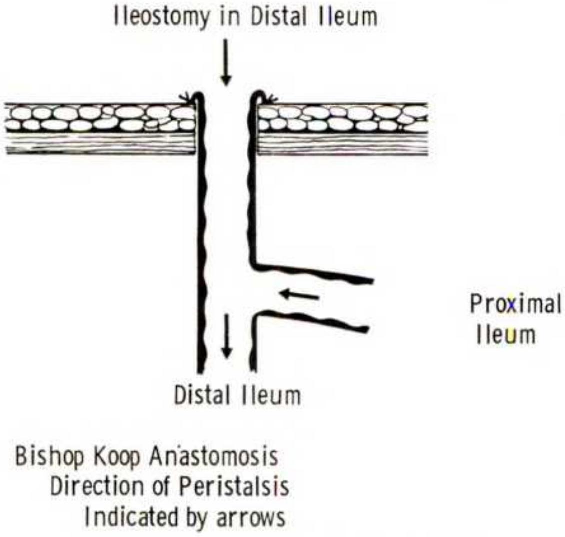


FIG. 1.—Diagram of Bishop-Koop anastomosis.

Noblett (1969), while investigating a patient with uncomplicated meconium ileus, observed relief of the obstruction from a diagnostic Gastrografin (Schering) enema. In this child and 3 subsequent children with meconium ileus the obstruction was relieved and operation avoided by the use of Gastrografin enemas. Similar results have been reported from other centres (Wagget, Bishop, and Koop, 1970; Lillie and Chrispin, 1972) and suggest that the use of Gastrografin or a similar substance (Frech, McAlister, Ternberg, and Strominger, 1970) should have a place in the primary management of meconium ileus.

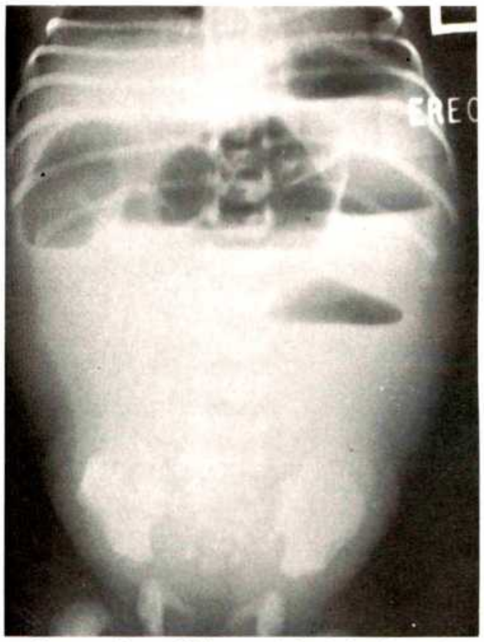
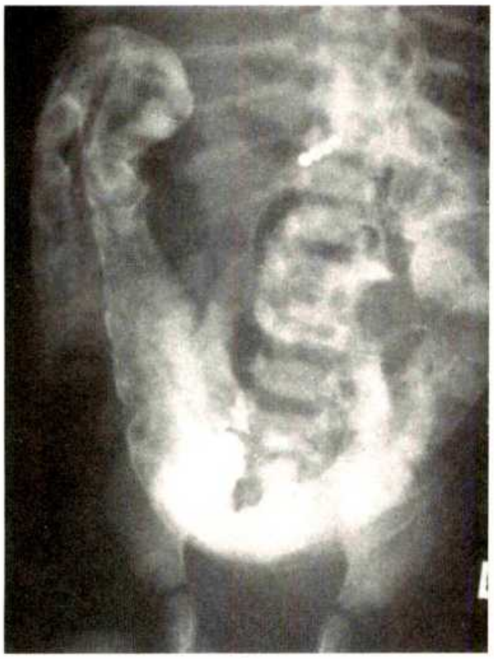


FIG. 2.—*Case* 1. Plain erect abdominal radiograph.



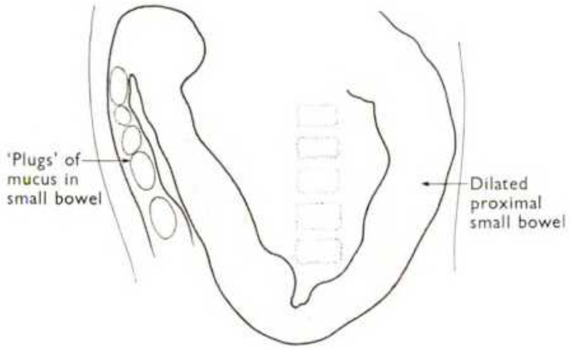


FIG. 3.—*Case* 1. A, Supine radiograph after instillation of Gastrografin. B, Explanatory diagram.

In a number of cases successful relief of meconium ileus is followed later by a recurrent intestinal obstruction due to inspissated faeces (Nixon, 1955; Cordonnier and Izant, 1963). The management of this is often difficult and the use of Gastrografin appears to offer a simple alternative to operation.

CASE REPORTS

Case 1.—A full-term male infant of birth weight 3·15 kg. developed abdominal distension and bilious vomiting shortly after birth. A radiograph (*Fig.* 2) showed a high intestinal obstruction. Laparotomy on the day of birth revealed an ileal obstruction due to an adhesion band with an underlying atresia with incipient gangrene at this level, and a meconium obstruction distally. The atretic and distended loop of bowel was excised and a Bishop-Koop anastomosis was performed. Although a little fluid was passed from the ileostomy there was no action per rectum. By the fourth postoperative day the abdomen was distended and he began to vomit again. A radiograph showed a high small-bowel obstruction.

On the fifth day 5 ml. of Gastrografin were instilled into the ileostomy. On the radiographs this outlined a distal blockage with meconium plugs (*Fig.* 3). A few hours later the patient began to pass meconium per rectum for the first time. He has had no further obstructive episodes and remains well.

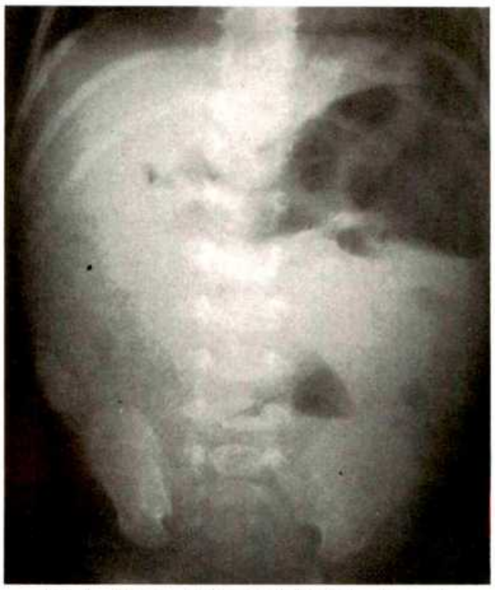


FIG. 4.—*Case* 2. Plain erect abdominal radiograph.

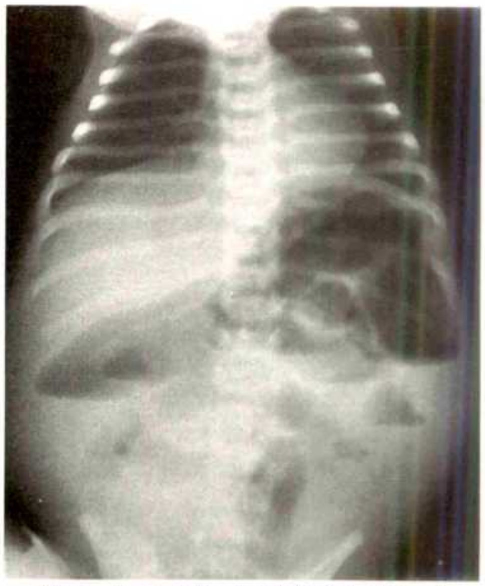


FIG. 5.—*Case* 3. Plain erect abdominal radiograph.

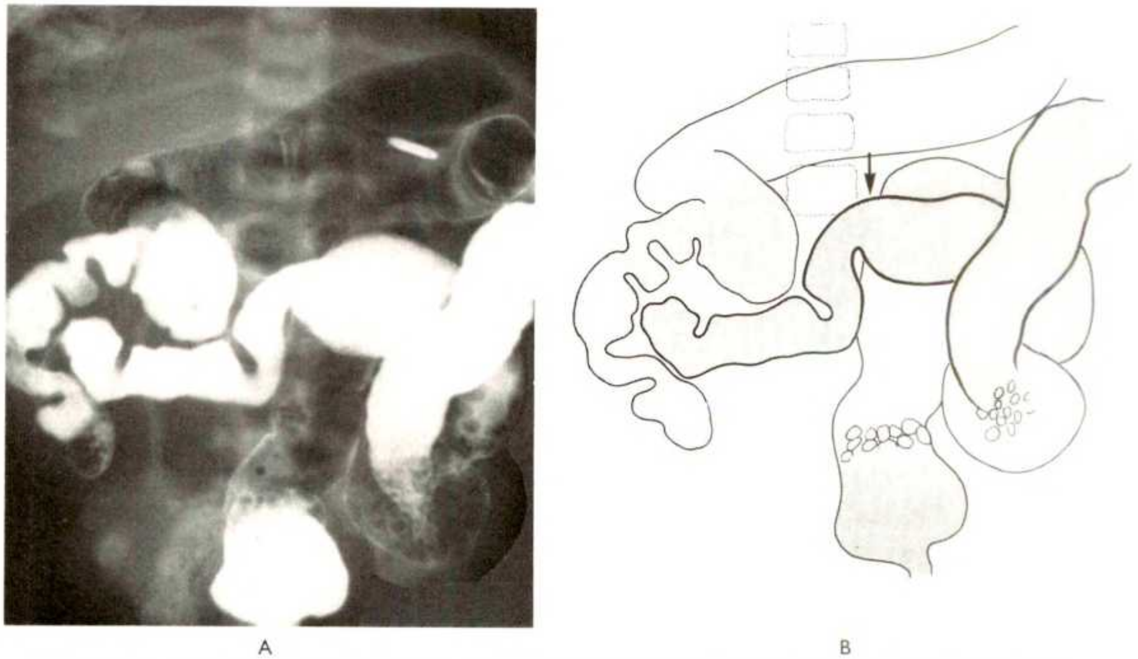


FIG. 6.—*Case* 3. A, Gastrografin-enema film. Arrow indicates site of change in diameter of the bowel. B, Explanatory diagram.

Case 2.—A male of birth weight 2·32 kg. was admitted at the age of 48 hours with abdominal distension and bilious vomiting. A laparotomy performed the same day revealed a meconium obstruction. Thirteen cm. of dilated ileum were excised, meconium plugs were milked out of the bowel, and a Bishop-Koop anastomosis was made. His postoperative course was complicated by several episodes of severe pulmonary infection. The ileostomy worked satisfactorily for a few days, after which he started to pass faeces per rectum. When aged 3 months, in spite of being maintained on the normal medical régime with oral pancreatic enzymes, he began to vomit, his abdomen became distended, and a radiograph showed small-bowel distension with fluid levels. Instillation of Gastrografin into the ileostomy was followed by the passage of a large quantity of faeces, and his abdomen became less distended. Intermittent vomiting continued, and at the age of 4 months a pyloric tumour became palpable. Following a Ramstedt's operation the vomiting ceased. Six weeks later he had a further episode of vomiting and abdominal distension. A radiograph (*Fig.* 4) showed small-bowel distension with faeces in the ascending colon. Gastrografin was injected into the ileostomy. A further radiograph showed the Gastrografin flooding back into normal bowel on the left and some passing on to the right. A few hours later he passed large quantities of faeces. His abdominal distension subsided rapidly and he has had no further obstructive trouble.

Case 3.—A female of birth weight 3·8 kg. was operated on at another hospital in the second day of life for meconium ileus. No resection was performed. She was not given any pancreatic supplements postoperatively.

She was fairly well until a month later when she developed further abdominal distension with vomiting and constipation. A radiograph (*Fig.* 5) showed a small-bowel obstruction and faeces in the descending colon. A Gastrografin enema with radiographic screening control (*Fig.* 6) showed filling of the colon with reflux into the terminal ileum extending back into the distended bowel. A few hours later she began to pass faeces and decompressed herself. She has had no further trouble.

DISCUSSION

The efficacy of Gastrografin in the relief of uncomplicated meconium ileus and faecal obstructions appears to be due to its physical properties. Gastrografin is an aqueous solution containing 10 per cent sodium diatrizoate and 66 per cent meglumine diatrizoate with 1·0 per cent Tween 80, as a wetting agent, and flavouring. This radio-opaque solution is hypertonic and hygroscopic. The presence of the detergent Tween 80 enables the fluid to pass easily around and into masses of inspissated meconium or faeces. The hypertonicity draws fluid into the bowel lumen with softening of the faeces and produces an osmotic diarrhoea aided by the peristalsis induced by the irritant nature of the solution.

The process should be followed with close radiographic supervision, preferably screening, so that leakage into the peritoneal cavity from a perforation or errors in the clinical diagnosis can be immediately recognized. Escape of the contrast medium has been reported in primary meconium obstruction even with very low-pressure injection (Wagget and others, 1970), presumably through a pre-existing perforation. If this is seen early operation is essential.

The successful use of Gastrografin to relieve the obstruction in the event of failure of primary surgery (*Case* 1) and late faecal plugging (*Cases* 2 and 3) suggests that the method has a place in the postoperative as well as in the primary management of meconium ileus.

The following safety precautions are recommended:

1. The procedure must be treated with the gravity of an operation and should be carried out under the supervision of the surgeon in charge, with the child prepared for immediate transfer to the operating theatre.
2. The instillation should be under radiographic control.
3. In view of the loss of fluid into the bowel during the examination, the state of the child's hydration must be watched, and it may be wise to have an intravenous infusion running.

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PEROPERATIVE CHOLANGIOGRAPHY

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SUMMARY

Operative cholangiography was performed in 30 patients by a technique using a modified Foley catheter introduced into the common bile-duct after exploration. The visualization was satisfactory with flow into the duodenum, and additional stones, strictures, and congenital abnormalities were detected. This procedure is likely to reduce the incidence of residual stones following choledochotomy.

OPERATIVE cholangiography is an accepted technique for the detection of any abnormality in the biliary tree and has been shown to reduce the need for choledochotomy—a procedure associated with an increased morbidity and mortality. However, there remains the problem of establishing the normality of the duct system after the removal of any stones. T-tube cholangiography has been used for this purpose and although good pictures can be obtained of the proximal ducts the distal common bile-duct is often poorly shown and the dye frequently fails to pass into the duodenum (Griffin and Wild, 1967; Lawson and Gunn, 1970). Serial films and cine-radiology can improve the results but the former is time-consuming and the latter not always available. Furthermore, the presence of the T-tube distorts the duct and can permit the introduction of air-bubbles.

It has been suggested (Lawson and Gunn, 1970) that satisfactory visualization of the ducts can be obtained by the use of a Foley catheter passed into the common duct after the exploration. This paper reports the results achieved by this method.

MATERIAL

Two hundred and fifty-five patients were admitted for surgical treatment of benign biliary-tract disease in the 3-year period between 1969 and 1972 and operative cholangiography was a routine procedure. Choledochotomy was indicated in 57 patients on the basis of the clinical features modified by the operative cholangiography (*Table I*).

Table I.—RESULTS OF EXPLORATION OF THE COMMON BILE-DUCT IN 57 PATIENTS UNDERGOING CHOLEDOCHOTOMY

Findings	*No. of Cases*
Stones	40
Stones and stricture	8
Stricture	5
Acute pancreatitis	2
No abnormality	2

Stones were found in 40 patients, stones and strictures in 8, and stricture alone in 5 patients. Two patients had acute pancreatitis associated with cholelithiasis and the common bile-duct was drained to relieve pressure in the pancreaticobiliary system. Two patients had the duct explored and no abnormality was found.

Thirty patients had Foley cholangiography by the method described here; of the remaining 27 patients, 21 were treated before the method was standard practice, and 2 had choledochoduodenostomy and 3 had sphincterotomy as additional procedures and Foley cholangiograms were not attempted. In 1 patient the procedure was omitted.

METHODS

A 10 FG female Foley catheter was modified by cutting off the end distal to the balloon (*Fig.* 1), and was then tested for any damage to the balloon. The proximal end was shortened to take a 10-ml. syringe.

After exploration of the duct the catheter was introduced into the common bile-duct just distal to the choledochotomy and the balloon was inflated. Water was injected down the catheter to test that satisfactory occlusion of the common duct had been obtained. All foreign bodies such as swabs and packs were removed, and films were taken during the injection of 25 per cent Hypaque. One film was usually sufficient.

The balloon was deflated, the catheter was moved into the common hepatic duct, and the procedure was repeated. In the absence of a choledochoduodenostomy the choledochotomy was closed around a T-tube and thereby postoperative cholangiography was possible at 10 days.

RESULTS

All the patients had films that showed satisfactory filling of both the hepatic ducts and the common bile-duct (*Table II*); in 28 patients the films revealed good flow into the duodenum and in 2 patients there was a stricture that was causing obstruction.

Table II.—RESULTS OF FOLEY CHOLANGIOGRAPHY IN 30 PATIENTS

Findings	*No. of Cases*
Visualization of hepatic ducts	30
Visualization of common bile-duct	30
Flow into duodenum	28
Additional stone	3
Stricture	5
Tumour of common bile-duct	1

Additional stones were discovered in 3 patients (*Fig.* 2), and after removal of these stones further films using the same technique showed that the duct had been cleared. Ten-day postoperative films through the T-tube revealed no other stones and no patient has developed further symptoms in the short follow-up period (3–33 months).

DISCUSSION

Modification of the Catheter.—The standard Foley catheter has an end that projects more than 1 cm. beyond the balloon with a subterminal opening, and if not removed this can simulate a stone. This modification can damage the balloon which must be tested before introduction. The proximal end of the catheter requires trimming of the connexion so that an accurate fit is obtained with the syringe and air-bubbles are avoided.

Position of the Balloon.—The balloon should be inflated as close to the opening in the common duct as possible so that maximal filling of the lower part of the duct with flow into the duodenum can be obtained. Inflation of the balloon must occlude the duct to prevent extravasation by back-flow through the opening in the duct. The balloon gives a round filling defect which can be recognized and is usually seen as a convex indentation into the column of radio-opaque medium.

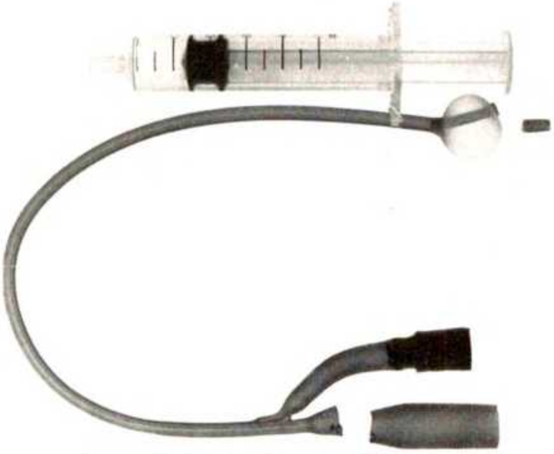

FIG. 1.—Modification of a 10 FG Foley catheter.

Table III.—COMPARISON OF THE MEAN OF THE DIAMETER OF THE COMMON BILE-DUCT BY DIFFERENT TECHNIQUES

TECHNIQUE	DIAMETER (cm.)		
	Maximum	Minimum	Lower End
Operative cholangiogram	1·41	0·56	0·68
Foley cholangiogram	1·27	0·49	0·59
T-tube cholangiogram	1·27	0·41	0·48

Volume of Hypaque.—The volume of Hypaque injected distally varied from 5 to 10 ml. and is not critical in that any excess passes into the duodenum while the film is taken. In the presence of obstruction resistance is felt and further injection results in backflow around the balloon of the Foley catheter.

The volume injected into the hepatic ducts depends on the size of the duct and is continued until resistance is felt. Excessive amount results in over-opacification and stones may be hidden.

Pancreatic Duct Filling.—Eleven patients showed filling of the pancreatic duct on the Foley cholangiogram compared with 3 patients showing filling on the initial operative films and 2 on the 10-day T-tube cholangiogram. The reflux of medium into the pancreatic duct under pressure could be potentially dangerous with damage to the pancreas but this has not been detected.

Interpretation of the Films.—It is appreciated that these films were taken under pressure and that this might lead to distortion of the duct system with the risk of misinterpretation of the findings. Comparison of the appearance of the duct in the initial, Foley, and T-tube films shows little difference and this was confirmed by the mean of the diameter of the duct at different points (*Table III*).

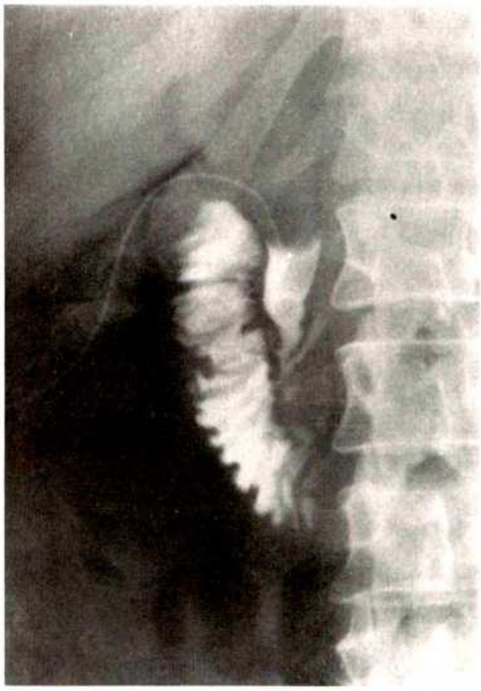

FIG. 2.—Foley cholangiogram showing residual stones and reflux into the pancreatic duct.

Indications.—In this series this technique was only used when choledochotomy was not followed by choledochoduodenostomy or sphincterotomy. However, this restriction was probably unwise in that more detail could be obtained of the abnormality and of the appearance of the sphincterotomy.

CONCLUSION

The Foley cholangiogram has been shown to be an easy and useful technique after operations on the common bile-duct and should limit the number of residual stones after choledochotomy for choledocholithiasis.

This procedure will also reveal stricture deformity at the lower end of the common bile-duct.

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VAGOTOMY AND PYLOROPLASTY IN THE ELECTIVE TREATMENT OF GASTRIC ULCER

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SUMMARY

Vagotomy and pyloroplasty have been used in the elective treatment of gastric ulcer in 72 patients. In 33 patients there was associated duodenal ulcer (G.D.U.). In the other 39 patients (G.U.) there was no evidence of duodenal ulcer. Patients with pre-pyloric gastric ulcer were excluded. The operative mortality was nil.

At an average follow-up of 3½ years the functional results in the G.U. group were good for 89 per cent of the cases, satisfactory for 5·5 per cent, and poor for 5·5 per cent compared with 73, 10, and 17 per cent respectively in the G.D.U. group. Two patients in each group showed recurrent ulcer, an incidence of 5·4 per cent in the G.U. group and 6·7 per cent in the G.D.U. group. There is no statistically significant difference in these results.

Vagotomy and pyloroplasty appear to comprise a satisfactory treatment for gastric ulcer whether or not the ulcer is associated with duodenal ulcer. The present findings do not support the view that the good results previously reported were due to the inclusion of patients with pre-pyloric gastric ulcer or with associated duodenal ulcer.

Three patients showed malignancy in the ulcer and a further case has been recorded in the total of 102 patients undergoing surgery during the period of the review (an incidence of 4 per cent), underlining the need for biopsy of the ulcer in all cases.

IN the treatment of benign gastric ulcer good results following vagotomy and pyloroplasty have been reported by Hendry and Bahrani (1965), Farris and Smith (1966), McNeill, McAdam, and Hutchison (1969), Burge, Gill, Maclean, and Stedeford (1970), de Miguel (1970), and Kraft, Myers, Overton, and Fry (1971).

Only Duthie and his co-workers have presented a statistical evaluation of the results of vagotomy and pyloroplasty for gastric ulcer. Duthie, Moore, Bardsley, and Clark (1970) suggested that previously reported good results might be due to the inclusion of patients who would be expected to do very well following such a procedure, namely, those with associated duodenal ulceration and those with pre-pyloric gastric ulcers.

Douglas and Duthie (1971) examined their results with reference to the site of the gastric ulcer and the coexistence of a duodenal ulcer and found that the functional results were better when the gastric ulcer was associated with a duodenal ulcer. Kennedy, Kelly, and George (1972) reported similar findings, although others (Clarke, Lewis, and Williams, 1972) considered that vagotomy and pyloroplasty were not a satisfactory treatment for gastric ulcer associated with duodenal ulcer.

The present paper reviews the results of vagotomy and pyloroplasty in the elective treatment of gastric ulcer. The patients have been assessed in two groups: those with chronic gastric ulcer alone (G.U.) and those with chronic gastric ulcer associated with duodenal ulcer (G.D.U.). The two groups are compared on the basis of (1) operative morbidity, (2) functional after-effects of surgery, and (3) recurrent ulceration. The incidence of malignancy has been assessed. The results have been submitted to statistical analysis.

MATERIALS AND METHODS

During the 5-year period from January, 1966, to December, 1970, the total number of patients undergoing surgery for chronic gastric ulcer was 102. Thirty patients have been excluded from this review for the following reasons: 6 patients had pre-pyloric gastric ulcer, 8 patients had vagotomy and pyloroplasty as an emergency procedure for bleeding, 3 patients had only vagotomy or pyloroplasty alone, 4 patients had vagotomy and gastro-enterostomy, 6 patients had gastrectomy, and only 3 patients have been lost to follow-up. The remaining 72 patients who were treated electively by vagotomy and pyloroplasty were studied.

At operation the ulcer edge was biopsied in four quadrants or the ulcer was excised completely and the material was submitted for immediate histological examination by a frozen-section technique. The drainage procedure was a Heineke-Mikulicz pyloroplasty with a one-layer closure. The type of vagotomy varied, being truncal in 16 cases (9 G.U., 7 G.D.U.), bilateral selective in 26 cases (11 G.U., 15 G.D.U.), and anterior selective in 30 cases (19 G.U., 11 G.D.U.).

Five of the 72 patients have died since the time of surgery and the remaining 67 patients have been traced and interviewed. Each patient was allocated to one of four grades using a modification of the classification of gastric symptoms introduced by Visick (1948). Patients in grade I are those with no gastric symptoms; those in grade II have minor gastric symptoms readily controlled by slight modification of diet or habit; those in grade III have moderate symptoms which are not simply controlled by minor adjustments but which do not interfere with work or social life; grade IV includes patients with symptoms which interfere with work or social life, and which are as bad or worse than before surgery, those with recurrent ulcer, and those who have required a second operation for suspected recurrence.

Barium-meal examination was carried out in 61 patients during review in 1971–2, but 6 patients who were totally symptom free refused barium-meal examination. Patients with symptoms or radiological signs suggestive of recurrent ulceration were investigated further by gastroscopy, insulin test, and repeat barium meal.

RESULTS

Data from all 72 patients have been used in calculating the average age, length of history, length of follow-up, and operative morbidity. Figures relating to postoperative assessment are based on the results in the 67 surviving patients.

Of the 72 patients, 33 had a gastric ulcer associated with active or healed duodenal ulceration. In the other 39 patients there was no evidence of duodenal ulceration either on barium-meal examination or at the time of operation. The average age at operation and duration of follow-up were similar in both groups, but symptoms had been present for a longer period in the G.D.U. group (*Table I*). The minimum period of follow-up was 1 year and 48 patients were followed up for more than 3 years.

Table I.—DETAILS OF THE GROUPS STUDIED IN THE PRESENT SERIES

	G.U. GROUP			G.D.U. GROUP		
	Male	Female	Both	Male	Female	Both
Age at operation (yr.)	52·1	46·6	48·3	56·0	50·7	53·4
Duration of symptoms (yr.)	3·8	7·4	5·8	12·6	9·3	11·0
Duration of follow-up (yr.)	3·4	3·8	3·7	3·1	3·5	3·3
No. of patients	12	27	39	17	16	33

Table II.—INCIDENCE OF POSTOPERATIVE COMPLICATIONS

COMPLICATIONS	G.U. GROUP	G.D.U. GROUP
Wound	5	6
Chest	6	4
Renal	2	—
Deep-vein thrombosis	1	—
Splenectomy	—	1
Patients with complications*	12	11
Total No. of patients	39	33

* Two patients in the G.U. group each suffered two complications.

Operative Morbidity.—All 72 patients survived operation. One patient in the G.D.U. group required splenectomy at the time of operation because the splenic capsule was inadvertently stripped but her convalescence was uneventful. None of the patients developed breakdown of the pyloroplasty suture line or any other intra-abdominal complication. *Table II* shows the complications which arose. In the G.U. group 12 patients showed complications and in the G.D.U. group 11 patients were affected. The commonest complications were wound haematomas or infections and chest infections.

Late Deaths.—Five patients out of the 72 died between operation and the most recent follow-up. *Table III* shows the details in these cases. One patient died of gastric carcinoma more than 5 years after the initial surgery. The biopsy at the initial operation was reported as simple and the tumour did not present until 3 years later. Another patient died 4 months after operation from pulmonary tuberculosis. She had suffered from this condition for many years and the disease was known to be active at the time of her operation. The other deaths were due to myocardial infarction (2) and congestive cardiac failure associated with bronchitis (1).

Functional Results of Surgery.—Of the 67 surviving patients, 37 were in the G.U. group and 30 were in the G.D.U. group. The symptomatic grading at follow-up is shown in *Table IV*. Patients in both grades I and II (no gastric symptoms or mild symptoms readily controlled) can be considered as having good results. In the G.U. group 33 out of 37 patients (89 per cent) are in those grades and in the G.D.U. group 22 out of 30 patients (73 per cent) are in grades I and II. Those in grade III can still be regarded as satisfactory results. Patients who have had recurrent ulcer or a second operation for suspected recurrence have been graded IV although following further surgery only 1 patient now falls into grade IV with symptoms worse than before the initial surgery. The reasons for the poor functional results are shown in *Table V*.

Table III.—DETAILS OF THE LATE DEATHS

PATIENT	AGE AT OPERATION (yr.)	SURVIVAL (yr.)	CAUSE OF DEATH	GASTRIC GRADE	ULCER TYPE
C. McF.	67	2·6	Congestive cardiac failure. Bronchitis*	I	G.D.U.
J. C.	65	0·6	Coronary	I	G.D.U.
J. McC.	47	4·3	Coronary	I	G.D.U.
J. N.	55	0·3	Pulmonary tubercle	I	G.U.
E. M.	46	5·3	Gastric carcinoma	IV	G.U.

* Ulcer healed at post-mortem examination.

Table IV.—COMPARISON OF THE RESULTS ACCORDING TO VISICK GRADING

VISICK GRADE	G.U. GROUP		G.D.U. GROUP	
	No.	Per cent	No.	Per cent
I	21	56·6	15	50·0
II	12	32·4	7	23·4
III	2	5·5	3	9·9
IV	2	5·5	5	16·7
Total No. of patients	37		30	

Table V.—ANALYSIS OF THE POOR RESULTS

	G.U. GROUP	G.D.U. GROUP
Recurrent ulcer	2	2
Reoperation for suspected recurrence	—	2
Reoperation for carcinoma	—	1

There is no significant difference in the functional results between the G.U. group and the G.D.U. group either when the four grades are examined separately ($\chi^2 = 3·024$, d.f. 3, $P < 0·5 > 0·1$) or when grades I and II are combined ($\chi^2 = 2·902$, d.f. 2, $P < 0·5 > 0·1$).

Recurrent Gastric Ulcer.—Four patients have shown a definite recurrent gastric ulcer. There have been 2 recurrences in each group, producing recurrence rates of 5·4 per cent in the G.U. group and 6·7 per cent in the G.D.U. group. There is no significant difference in the recurrence rate between the two groups ($\chi^2=0{\cdot}0469$, d.f. 1, $P<0{\cdot}9>0{\cdot}5$). Two patients with recurrent ulcer had positive insulin tests, and in the other 2 patients details of the insulin response before the second operation are missing from the case records.

No other patients in this series have shown recurrence of either the gastric ulcer or a duodenal ulcer. Two patients have, however, had further surgery on account of recurrent symptoms. In both cases there was no sign of ulcer recurrence either at gastroscopy or laparotomy, and insulin tests were negative.

Malignancy.—In this series of 72 patients 3 cases of gastric carcinoma associated with chronic gastric ulcer have been noted (4·2 per cent). Two of these cases were diagnosed histologically at operation, but the third had a negative initial biopsy and presented 3 years later. Sixty-six of the patients had frozen-section examination of the biopsy or excised ulcer so that the likelihood of the ulcer being shown to be malignant at the time of surgery is 3 per cent (2 out of 66 cases).

A fourth case of malignancy was noted in the other 30 patients not included in this review, giving an overall incidence of malignancy of 3·9 per cent (4 out of 102 cases).

DISCUSSION

The incidence of combined duodenal and gastric ulceration in the present series is 46 per cent. If all the cases of benign gastric ulcer submitted to surgery during the 5 years of the review are considered then the incidence of combined ulcer is 40 per cent. This is somewhat higher than that noted by Douglas and Duthie (1971) but is similar to that found by Rumball (1971).

There was no mortality in the group of 72 patients undergoing vagotomy and pyloroplasty electively for benign gastric ulcer. Postoperative morbidity was noted in about one-third of the patients in each group. It is noteworthy that there were no postoperative bowel complications. This is in contrast to the incidence of gastric fistula (6 per cent) and paralytic ileus (6 per cent) reported following Billroth-I gastrectomy by Duthie and others (1970). The complications occurring in the present review were mainly chest and wound infections.

The functional results of surgery were essentially the same in both groups of patients. In the G.U. group there were 89 per cent good results (grades I and II), 5·5 per cent satisfactory results (grade III), and 5·5 per cent poor results (grade IV). In the G.D.U. group there were 73·4 per cent good, 9·9 per cent satisfactory, and 16·7 per cent poor results. There is no statistically significant difference in these results ($\chi^2=2{\cdot}902$, d.f. 2, $P<0{\cdot}5>0{\cdot}1$). Other workers have recorded good functional results similar to the present ones following vagotomy and pyloroplasty in patients with gastric ulcer not associated with duodenal disease. De Miguel (1970), reporting on 38 patients, found 84 per cent to be in grades I and II with a follow-up of up to 4½ years, and Sawyers, Scott, and Graham (1971) found 77 per cent of 22 patients to be in these grades with a follow-up of up to 6 years. This is in contrast to the findings of Douglas and Duthie (1971), who found similar good results with the G.D.U. group but their G.U. group had significantly poorer results ($\chi^2=8{\cdot}1989$, d.f. 2, $P<0{\cdot}02$).

The reason for the difference in functional results between the present series and that of Douglas and Duthie (1971) is not immediately clear. The number of patients in the two series is similar. However, the proportion of male and female patients in the two series differs. In the groups of Douglas and Duthie there was a preponderance of male patients, the male : female ratios being 1·7 : 1 in the G.U. group and 4·3 : 1 in the G.D.U. group. In the present series, while the numbers of males and females were about equal in the G.D.U. group, the G.U. group contained more than twice as many females as males. This does not appear to be the explanation of the different functional results obtained here as there is no significant difference on χ^2 testing when the present groups are broken down on the basis of sex (males, $P<0{\cdot}5>0{\cdot}1$; females, $P<0{\cdot}975>0{\cdot}9$).

In the present series about one-third of the patients had the ulcer completely excised in a wedge of stomach, but there is no significant difference in the functional results between the G.U. and G.D.U. groups when examined by χ^2 testing on the basis of excision or no excision ($P<0{\cdot}5>0{\cdot}1$).

Another difference between the two series is in the proportion of patients undergoing truncal or selective vagotomy. In the series of Douglas and Duthie (1971) most patients had truncal vagotomy but 7 patients in each group had selective vagotomy. In the present series χ^2 testing showed no difference in the functional results between the G.U. and G.D.U. groups on the basis of the type of vagotomy employed (truncal, $P<0{\cdot}99$; anterior selective, $P<0{\cdot}9>0{\cdot}5$; bilateral selective, $P<0{\cdot}5>0{\cdot}1$).

The difference between the functional results in the present report and those noted by Douglas and Duthie (1971) is probably more apparent than real. While recurrence in the present series occurred in equal numbers in both the G.U. and G.D.U. patients, Douglas and Duthie had 5 recurrent ulcers in the G.U. group and none in the G.D.U. group. Commenting on this difference in recurrence they point out, 'although not by itself significant ($P<0{\cdot}1>0{\cdot}05$) it accounts to a large extent for the differences [in functional results] between the two groups'. The other 3 patients in the G.U. group of Douglas and Duthie included in the poor functional results could equally well occur by chance in either group (1 patient had postoperative haemorrhage requiring gastrectomy and the other 2 had diarrhoea), and taken on their own they do not represent statistically significant occurrences.

It would appear then that there might be no real difference in the poor results between the G.U. and G.D.U. groups reported by Douglas and Duthie, as significance has only been produced by the accumulation of several chance occurrences each of which by itself is not statistically significant. Our present finding that there is no statistically significant difference in functional results between patients with G.U. and those with G.D.U. undergoing vagotomy and pyloroplasty has been made in a group of patients separated on the basis of associated duodenal ulceration and where patients with pre-pyloric ulceration have been excluded from the G.U. group. The functional results grading was similar to that used by Duthie and his co-workers.

This present finding does not support the suggestion of Duthie and others (1970) that earlier favourable reports on the results of vagotomy and pyloroplasty for gastric ulcer have been simply due to the inclusion of patients with associated duodenal ulceration or pre-pyloric gastric ulceration. It would appear, therefore, that the procedure of vagotomy and pyloroplasty is equally effective, as far as functional results are concerned, whether used for isolated gastric ulcer or that associated with duodenal ulceration.

In the present series recurrent ulceration was noted in 2 patients with G.U. and in 2 patients with G.D.U., the incidence in each group being 5·4 and 6·7 per cent respectively. Reports on the incidence of recurrent gastric ulcer following vagotomy and pyloroplasty appear at a casual glance to show higher recurrent ulcer rates when the operation is used in the case of isolated gastric ulcer (Lewis and Qvist, 1971; Sawyers and others, 1971) and lower recurrence rates when used in the treatment of combined gastric and duodenal ulceration (Burge and others, 1970; Wasunna, Kennedy, Gillespie, and Kay, 1971). However, Douglas and Duthie (1971) have shown that there was no statistically significant difference in the ulcer recurrence rate between G.U. and G.D.U. groups and the present findings support this view. It is also interesting to note that contrary to popular belief there was no statistically significant difference in recurrent ulcer rates when the results of vagotomy and pyloroplasty were compared with those of Billroth-I gastrectomy in a controlled trial (Duthie and others, 1970).

Four patients out of the grand total of 102 were found to have malignant ulcers. This incidence (4 per cent) is similar to that reported by others (Duthie and others, 1970; de Miguel, 1970). Three of the tumours noted in the present series appeared to be undoubtedly localized areas of change within the peptic ulcer. In the fourth patient the initial biopsy was negative and the tumour did not present until 3 years later.

Duthie and Smith (1968) have advocated biopsy of all the edges of the ulcers and our experience supports this view. In one of the present cases limited biopsy was reported as benign on frozen-section examination but when the locally excised ulcer was submitted for routine histology a localized area of malignant change was found. In another case localized biopsy was reported on frozen section as showing an aplastic carcinoma and led to the patient having total gastrectomy. However, none of the other blocks taken from the whole specimen in that case showed malignant change. Biopsy of the ulcer should be carried out even when the ulcer appears at operation to be healing. Biopsy should also be done routinely in the patients with associated duodenal ulceration as the coexistence of the two ulcers does not exclude malignancy in the gastric one. Indeed, one of our cases of gastric carcinoma had a duodenal ulcer and at operation the gastric ulcer appeared to be healing. With adequate routine biopsy malignancy should not be missed when the ulcer is left behind.

CONCLUSION

Vagotomy and pyloroplasty appear to comprise a satisfactory treatment for gastric ulcer whether or not the ulcer is associated with duodenal ulcer, giving good functional results in more than 80 per cent of patients. The present findings do not support the suggestion of Duthie and others (1970) that the good results previously reported have been due to the inclusion of patients with pre-pyloric gastric ulcer or with associated duodenal ulcer.

The risk of missing malignancy is not a problem, provided that adequate biopsy or local excision of the ulcer is undertaken at the same time.

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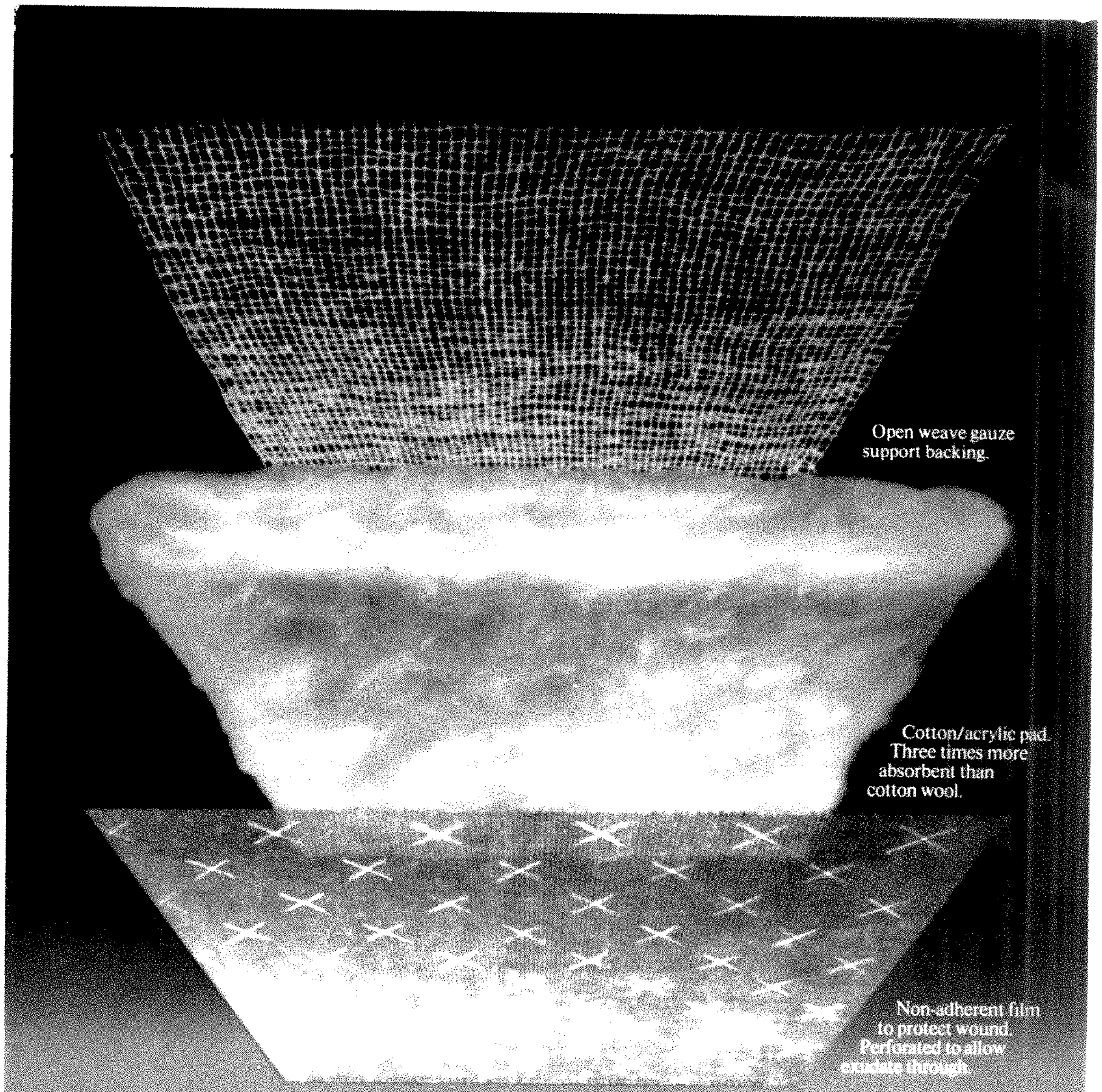
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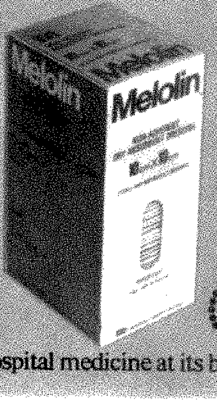

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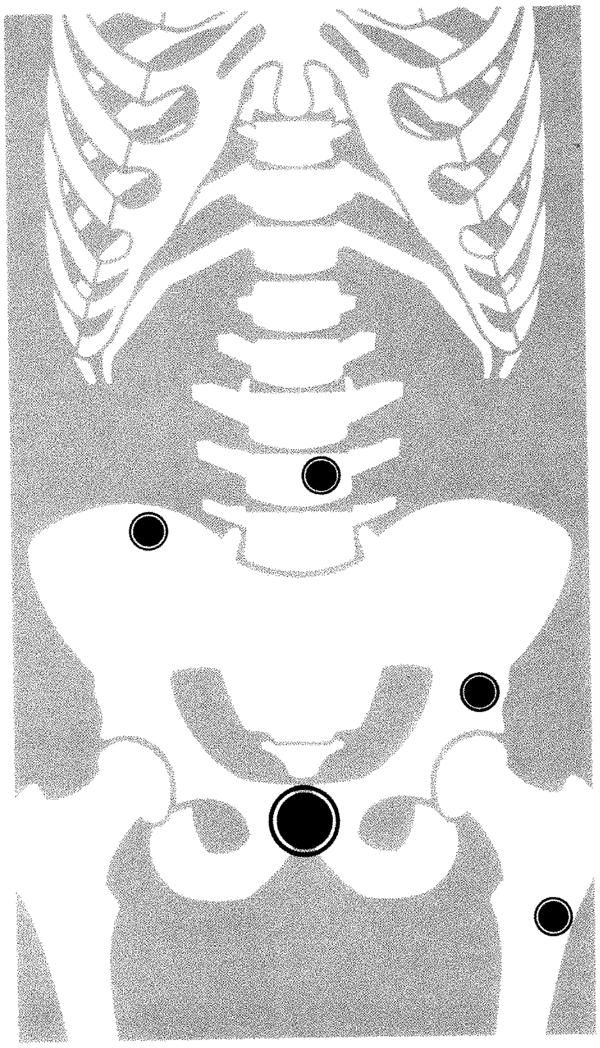

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THE GASTRO-OESOPHAGEAL JUNCTION BEFORE AND AFTER OPERATIONS FOR DUODENAL ULCER

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SUMMARY

Thirty-seven patients with duodenal ulceration were studied with oesophageal manometry pre-operatively and then again 6–12 months after operation. In 28 patients who had been treated by truncal vagotomy and either a pyloroplasty or a gastro-enterostomy the length of the zone of elevated pressure at the gastro-oesophageal junction was reduced, although the maximum pressure was unchanged. In 9 patients who had had a Polya partial gastrectomy the zone was also shortened, but there was a significant fall in the maximum pressure as well. It is suggested that this reduction of the resting pressure in the sphincter may account for the gastro-oesophageal reflux which is frequently seen after a Polya partial gastrectomy, and may be caused by low circulating gastrin levels since the antrum has been removed.

GASTRO-OESOPHAGEAL reflux is known to occur after a partial gastrectomy and there have been several reports of oesophagitis and oesophageal stricture after such operations (Bingham, 1958; McKeown, 1958; Benedict, 1960; Cox, 1961). It has been suggested that reflux occurs because the gastro-oesophageal angle is altered by these procedures. There is said to be more reflux after a Billroth-I operation than after a Polya partial gastrectomy (Windsor, 1964), and this is cited as evidence for the loss of this angle since the alleged longitudinal tension after a Billroth-I operation could be expected to eliminate the angle of His. There is, however, no real proof that the gastro-oesophageal angle is different after these two types of partial gastrectomy. Reflux is also present after vagotomy and drainage for a duodenal ulcer (Clarke, Penry, and Ward, 1965) and the loss of the gastro-oesophageal angle cannot be invoked as the cause, so factors other than the loss of a mechanical flap valve may be responsible for reflux. Recent work on the hormonal influences on the sphincter has demonstrated that gastrin increases resting pressures (Giles, Mason, Humphries, and Clark, 1969; Cohen and Lipshutz, 1971; Rosenberg and Harris, 1971), and these hormonal levels are reduced when the antrum is removed (Trudeau and McGuigan, 1971). The present study was undertaken to investigate the gastro-oesophageal sphincter using manometry before and after operations for duodenal ulceration in order to find out whether reflux occurred because the resting pressures were reduced.

PATIENTS AND METHODS

Thirty-seven patients who required surgical treatment for a duodenal ulcer were divided into two groups depending on the type of operation that they underwent. Twenty-eight patients were treated by a truncal vagotomy and either pyloroplasty or gastro-enterostomy. Nine patients were treated by a Polya partial gastrectomy with or without a vagotomy. The choice of operation was usually determined by the maximal acid output as determined by the standard pentagastrin test. If more than 40 mEq. H^+ were secreted in an hour after pentagastrin a partial gastrectomy was performed, but this was often done with levels lower than this.

Pressure measurements at the gastro-oesophageal junction were made with techniques which have previously been described (Earlam, 1970). The recording units were passed through the mouth into the patient's stomach. Pressure measurements were made with three water-filled polythene tubes (external diameter 1·65 mm., internal diameter 1·12 mm.). The distal tube was covered with a 0·5-cm.-diameter balloon and the remaining two tubes had lateral openings 3 and 6 cm. from the balloon. SE 4–8 MK 2 transducers converted pressures to electrical activity which was recorded by an SE 2005 6-channel ultra-violet recorder on 15-cm. paper. The units were drawn slowly through the gastro-oesophageal junction at 0·5-cm. intervals to obtain values for the sphincteric pressure in the resting state. Two resting pressure profiles were obtained in each test.

End-expiratory and end-inspiratory pressures were measured throughout the zone of elevated pressure at the gastro-oesophageal junction. From these, mean pressures were calculated for each patient from open-tip and two balloon recordings. The three parameters used were the length of the zone of elevated pressure, the intragastric pressure, and the difference between the mean maximal sphincteric pressure and the mean intragastric pressure which for the purposes of this study has been called the 'barrier pressure'.

Tests were performed in the week prior to surgery and then between 6 months and 1 year after operation. At the time of the postoperative test all the patients were interviewed and assessed clinically with regard to symptoms of gastro-oesophageal reflux. It was not thought justifiable to perform an oesophagoscopy, a Hollander insulin test, or a further pentagastrin test on any of the postoperative patients in the absence of severe symptoms.

RESULTS

The zone of elevated pressure at the gastro-oesophageal junction (*Table I*) measured 4·4 ± 1·1 cm. (mean ± S.D.) in length in the 37 patients taken as a whole group. Following a vagotomy and drainage operation the length measured by open tip was reduced to 3·5 ± 1·0 cm. and after a Polya gastrectomy to 2·9 ± 0·8 cm. A reduction in length was also demonstrated by balloon measurement. The levels of significance according to Student's *t*-test are shown in *Table I*.

The barrier was not significantly reduced after a vagotomy and drainage operation (*Table I*). Patients who had had a pyloroplasty did not differ from those who had had a gastro-enterostomy. After a Polya partial gastrectomy the barrier pressure was reduced to 3·2 ± 2·5 cm. H_2O by open-tip measurement and to 16·3 ± 8·0 cm. H_2O by balloon recording.

The intragastric pressure was increased after both types of operation (*Table II*).

Of the 37 patients, only 3 had postoperative heartburn, and all of these had had a vagotomy and pyloroplasty. There was neither a hiatus hernia nor a low pressure demonstrated by manometry at the gastro-oesophageal junction in these 3 patients.

Table I.—PRESSURES MEASURED AT THE OESOPHAGEAL JUNCTION BEFORE AND AFTER OPERATION FOR DUODENAL ULCER

TYPE OF OPERATION AND PRESSURE MEASURED	OPEN-TIP RECORDING		BALLOON RECORDING	
	Pre	Post	Pre	Post
Total ($n = 37$)				
Zone of elevated pressure (cm.)	4·4 ± 1·1	3·4 ± 0·9	5·4 ± 1·5	4·3 ± 1·3
	$P < 0\cdot001$		$P < 0\cdot001$	
Barrier (cm. H_2O)	9·8 ± 6·4	7·5 ± 5·1	27·1 ± 13·9	20·8 ± 12·0
	$P = 0\cdot1$		$P = 0\cdot04$	
Truncal vagotomy and drainage ($n = 28$)				
Zone of elevated pressure (cm.)	4·1 ± 0·8	3·5 ± 1·0	5·2 ± 1·3	4·4 ± 1·4
	$P = 0\cdot015$		$P = 0\cdot03$	
Barrier (cm. H_2O)	10·3 ± 7·1	8·8 ± 4·9	28·8 ± 14·9	22·4 ± 12·8
	$P = 0\cdot35$		$P = 0\cdot07$	
Polya partial gastrectomy ($n = 9$)				
Zone of elevated pressure (cm.)	5·2 ± 1·5	2·9 ± 0·8	6·6 ± 1·4	3·9 ± 1·1
	$P < 0\cdot001$		$P < 0\cdot001$	
Barrier (cm. H_2O)	8·0 ± 3·3	3·2 ± 2·5	24·8 ± 10·3	16·3 ± 8·0
	$P < 0\cdot005$		$P < 0\cdot01$	

Table II.—INTRAGASTRIC PRESSURE BEFORE AND AFTER OPERATION FOR DUODENAL ULCER

TYPE OF OPERATION AND PRESSURE MEASURED	OPEN-TIP RECORDING	
	Pre	Post
Total ($n = 37$)	17·9 ± 5·0	22·6 ± 4·7
	$P < 0\cdot001$	
Truncal vagotomy ($n = 28$)	18·6 ± 5·1	22·8 ± 4·8
	$P < 0\cdot001$	
Polya partial gastrectomy ($n = 9$)	15·4 ± 4·3	21·6 ± 4·7
	$P < 0\cdot01$	

DISCUSSION

The most significant finding in this study is that the zone of elevated pressure at the gastro-oesophageal junction is shortened and reduced in height after a Polya gastrectomy. This finding is compatible with the clinical impression that reflux does occur after such an operation, although in this small series there were no such symptoms. It is suggested that the fall in sphincteric pressure is due to the decrease in circulating gastrin which occurs when the antrum is removed (Trudeau and McGuigan, 1971). Gastrin has been shown to increase the sphincteric tone (Giles and others, 1969; Cohen and Lipshutz, 1971; Rosenberg and Harris, 1971). In patients with the Zollinger-Ellison syndrome, where there is a high circulating gastrin level, sphincter pressures are higher than normal (Isenberg, Csendes, and Walsh, 1971). The reduction in the length of the zone of elevated pressure demonstrates that the sphincter remains at the hiatus and has not been displaced. There is no way of demonstrating by manometry whether a gastro-oesophageal angle exists or not, so that the results of this study cannot settle this particular point.

The pressure characteristics of the gastro-oesophageal junction in duodenal ulceration have already been described in a larger series of patients (Earlam, 1972). The height of the barrier pressure is within normal limits but the length is increased. It was suggested in that study that this increased length in the whole group was due to an increased number of cases with proximally displaced sphincters which allowed reflux. Since none of these patients had a radiologically demonstrable hiatus hernia the displaced sphincter should be considered as a small hiatus hernia which can only be demonstrated by manometry.

Both before and after a vagotomy and drainage operation the resting pressure at the gastro-oesophageal junction is normal. This pressure is produced by a combination of gastro-oesophageal sphincteric squeeze and the superimposed effect of the crura, and it is known that displacement of the sphincter alone may reduce the pressure by eliminating the diaphragmatic component. In the present study the effect of reducing a hiatus hernia would be expected to increase the pressure, just by combining the effect of the sphincter and the diaphragm, but there are obviously other factors which are involved which would counterbalance this effect. Gastrin is well known to have an effect on the gastro-oesophageal sphincter and the resting level of gastrin may be different after a vagotomy (Korman, Hansky, and Scott, 1972), but other gastro-intestinal hormones, such as secretin, cholecystokinin, and pancreozymin (Thomas and Earlam, 1973), also have an effect on the sphincter and the level of these hormones may be altered. There are also other factors, such as acid in the fundus which increases sphincteric pressure (Giles, Humphries, Mason, and Clark, 1969) whereas acid in the antrum reduces the pressure, presumably by the gastrin mechanism. In the presence of so many factors which could be altered by a vagotomy and drainage procedure no conclusion can be drawn from this study as to which reflexes or what hormonal levels have been altered by the operation. More dynamic tests of sphincteric function are obviously needed to test the altered reflexes. This study demonstrates only that the resting sphincteric pressure is unaltered by a truncal vagotomy.

This study has demonstrated that the zone of elevated pressure at the gastro-oesophageal junction is reduced in length after a truncal vagotomy and drainage operation. Any decrease in length can either be an artefact due to the overall reduction in pressure or be caused by the superimposition of sphincteric and diaphragmatic pressures by reduction of a hiatus hernia. Since the barrier pressure was not significantly reduced after a truncal vagotomy the reduction in the length of the zone of elevated pressure is most likely due to the correction of a hiatus hernia. In a truncal vagotomy the oesophagus is usually reduced well below the hiatus so that the main trunks of the vagus can be divided as they lie near the oesophagus and the oesophageal wall cleared of small fibres. The resulting fibrosis probably prevents the gastro-oesophageal junction from slipping back too far into the chest and it remains reduced. In none of the present series was any stitches inserted into the crura to tighten the hiatus.

These results differ from two previous studies comparing the gastro-oesophageal pressure profiles before and after truncal vagotomy and a drainage operation, which both found that there was a significant fall in pressure (Williams and Woodward, 1967; Mann and Hardcastle, 1968), but these studies were done within a few weeks of the operation. The results of the present study are not incompatible with these earlier findings since the pressures have been measured 6–12 months after truncal vagotomy, when full recovery of the sphincter would be expected.

There is considerable controversy over the technicalities of oesophageal manometry as to whether perfused or non-perfused open-tip tubes should be used. The method used in this study was to fill the small polythene tubes with water without continuous perfusion. Since perfusion always increases the pressures recorded and accentuates differences, the addition of perfusion would have not altered the results. Perfusion techniques differ according to the size and length of the tubing used as well as the rates of perfusion, and therefore have the additional difficulty of standardization. The advantage of the present system is that the technique is exactly the same as that used by many other workers so the results can be compared.

The effect of gastro-oesophageal reflux depends on the nature of the substance being refluxed as well as on the ability of the sphincter to prevent reflux. If the acid and pepsin levels in the stomach have been satisfactorily reduced by removing the antrum and part of the body of the stomach, gastro-oesophageal reflux of the gastrin contents is unlikely to cause symptoms arising from the lower oesophagus, even though some reflux may occur through a weak sphincter. After a vagotomy and drainage operation the level of acid produced by the stomach is not reduced to such a low level and the acidity may be still high owing to an incomplete vagotomy so that there remains enough noxious material capable of being refluxed. Since after such an operation there is no evidence that the sphincter is weakened, the resistance to reflux is usually capable of preventing symptoms even though the gastric contents are more acid than after a partial gastrectomy.

The clinical implications of this study are related to surgical techniques. Since there is evidence that the sphincter is reduced into the abdomen after a truncal vagotomy and drainage operation, there appears to be no rationale for inserting stitches into the crura or maintaining the position of the cardia as a routine, unless the hiatus is known to be wide and flaccid. This study provides no information as to the position of the gastro-oesophageal sphincter after a selective or highly selective vagotomy, in which procedures the lower oesophagus is not so thoroughly mobilized.

Acknowledgements—We would like to thank the physicians and surgeons in charge of the patients at the London Hospital and the patients themselves for allowing these studies to be performed.

Part of this work was carried out while one of the authors (P. A. T.) held a Wellcome Surgical Research Fellowship.

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MUCOUS EXTRAVASATION THEORY AS A CAUSE OF PLUNGING RANULAS

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SUMMARY

The theory that plunging ranulas arise as a result of mucous extravasation from the sublingual salivary gland is investigated.

Biochemical, histochemical, and histological results support the view that plunging ranulas are salivary gland extravasations, which most probably arise from the sublingual gland.

Two cases of plunging ranula were treated by primary excision of the sublingual gland through the mouth.

The successful results support the view that the extravasating source is the sublingual gland.

THE pathogenesis and treatment of plunging (cervical, burrowing) ranula, in contradistinction to those of non-plunging (oral) ranula, have been the subject of conflicting opinion.

The experimental study of Bhaskar, Bolden, and Weinmann (1956b) in animals has shown that ranulas may be due to mucous extravasation from the salivary glands. Killey, Seward, and Kay (1971) suggested that plunging ranulas appear as a result of mucous extravasation from the posterior portion of the sublingual gland but they do not give proof of this theory.

Usually a plunging ranula is approached through a suitably placed cervical incision and the cyst is excised (Gardham and Suggit, 1969). This approach is technically difficult because the extensions of the ranula are too wide for complete and effectual excision. The recurrence rate is high. An alternate method, that of removing the sublingual gland, was undertaken by Crile (1957) for recurrent plunging ranulas, and thereafter employed for oral ranulas with considerable success by Catone, Merrill, and Henney (1969).

Two patients with plunging ranula were studied in order to examine the validity of the mucous extravasation theory and to establish the source of the secretions. Both patients were treated by primary excision of the sublingual gland through the mouth without any cervical approach.

PATIENTS AND METHODS

The patients were 2 African females aged 14 and 29 years respectively (*Cases* 1 and 2). Both had a typical plunging ranula, which in *Case* 1 had marked retropharyngeal extensions (*Fig.* 1). The following procedures were undertaken:—

1. Aspiration and biochemical analyses of the ranula contents for amylase and protein were done and these were compared with the serum amylase and protein levels.

2. Histological amylase estimation of the sublingual gland was undertaken. One anterior and one posterior portion of the second gland (*Case* 2) were quenched in liquid nitrogen and suitable cryostat sections were analysed both quantitatively and qualitatively for amylase activity according to the method of Shear (1972).

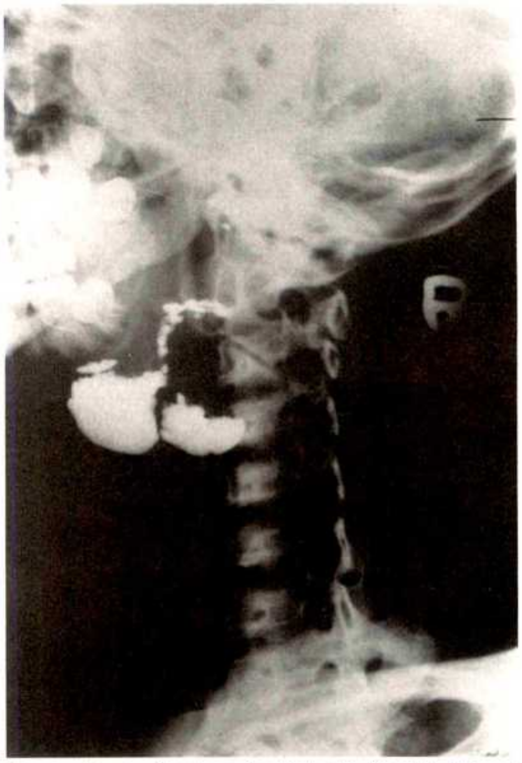

FIG. 1.—*Case* 1. Ranula partly filled with Lipiodol. There is marked retropharyngeal and cervical extension of the cyst.

3. The histological nature of the cyst wall was carefully studied.

4. A dissection of three cadaver sublingual glands was undertaken in order to assess the anatomy of this gland.

RESULTS

The aspirates from both ranulas were mucoid and although one was blood-stained no inflammatory cells were detected. The total protein and amylase levels are shown in *Table I*. The amylase levels of the aspirate were, respectively, four and six times higher than the prevailing serum level and almost twice as high as the normal upper limit of the serum amylase.

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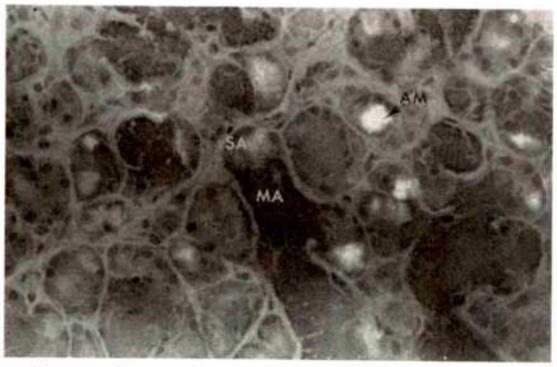

FIG. 2.—*Case* 2. Cryostat section of the sublingual gland mounted on starch films. Clear areas, showing complete starch digestion, indicate amylase activity (AM). Serous (SA) and mucous (MA) acini are distinguishable. Starch-PAS. (× 96.)

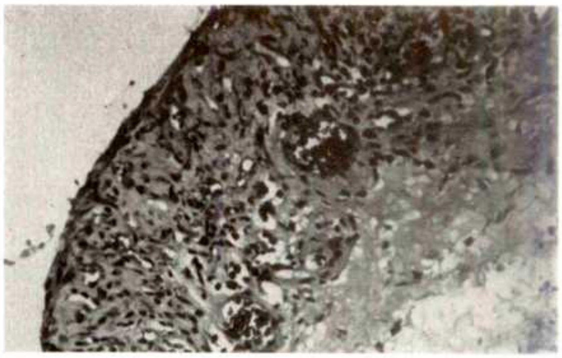

FIG. 3.—*Case* 1. Ranula lining of fibrous tissue with an outer more vascular layer. H. and E. (× 64.)

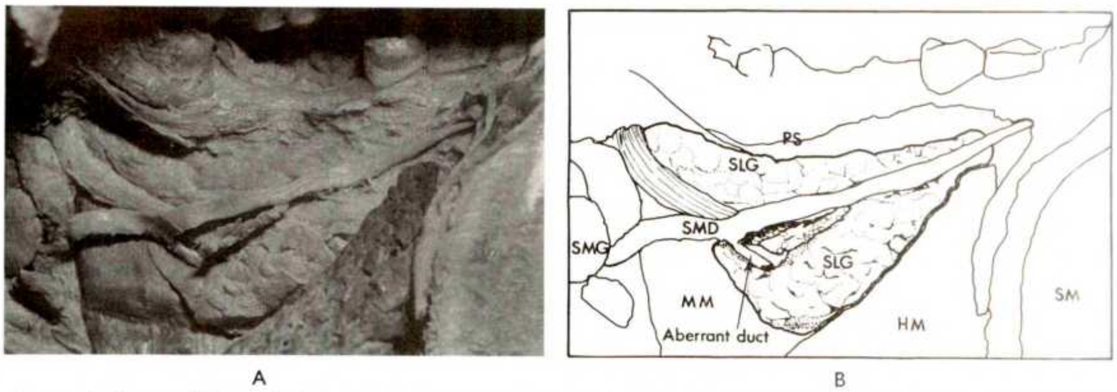

FIG. 4.—A, Human sublingual gland (left) showing anomalous drainage of the deep portion into the submandibular duct. B, Explanatory line drawing. HM, Hyoglossus muscle. MM, Mylohyoid muscle. PS, Plica sublingualis. SLG, Sublingual gland. SMG, Submandibular gland. SMD, Submandibular duct. SM, Symphysis menti.

Table I.—AMYLASE AND PROTEIN LEVELS OF THE RANULA CONTENTS COMPARED WITH THOSE OF THE SERUM

	CASE 1		CASE 2	
	Serum	Cyst Fluid	Serum	Cyst Fluid
Volume	—	5. ml, blood-stained, no inflammatory cells	—	4 ml., clear, mucoid, amorphous
Amylase (Street-Close units)*	17	60	10	60
Total protein (g. per cent)	8·4	4·5	10·1	2·8

* Normal serum amylase is 9–35 Street-Close units.

Histochemically, amylase activity was detected only in the posterior portion of the sublingual gland and was localized to the serous acini which were associated with numerous mucous acini (*Fig.* 2). Amylase activity was found in the cyst and in between the lobules of the gland. The quantitative amylase activity of cryostat sections of the sublingual gland was 0·00028 mg. maltose production per μg. of protein.

In both cases portions of the ranula wall contained no epithelial lining in any of the sections studied. The lining consisted of two layers; an inner layer of chronic fibrous tissue rich in macrophages and an outer loose vascular fibrous tissue layer (*Fig.* 3). Foci of sialo-adenitis were seen but no gland atrophy was observed.

In none of the dissections of the three cadaver sublingual glands was a distinct superficial and deep lobe of the sublingual noted as is sometimes described. Drainage of the gland was usually by small ductules to the plica sublingualis, but in 1 case a large aberrant ductule, draining into the submandibular duct, was found (*Fig.* 4).

Postoperative follow-up of both patients revealed no recurrence after 8 months.

DISCUSSION

In the pathogenesis of oral ranulas an extravasation or retention of salivary gland secretions is implied. The gland of origin is variably given as minor salivary glands, the sublingual gland, or the submandibular gland (Thoma, 1970; Lucas, 1972).

Extravasation of Secretions.—The diffuse ramification of the ranula shown in *Case* 1 strongly suggests diffusion of an extravasating fluid, and the fibrous lining, with no surface epithelial cells, probably reflects a tissue response to the extravasated fluid. Experimentally it is possible to produce similar fibrous-lined cysts by dividing salivary gland ducts, thereby letting the secretions escape into the tissue spaces (Bhaskar and others, 1956b). Standish and Shafer (1959) showed that 93 out of 97 oral ranulas had a fibrous lining not unlike those observed in the present 2 cases. These points support the view that extravasation causes plunging ranulas.

Retention and Duct Obstruction.—Clinically, total duct obstruction of the salivary glands leads to the depression of secretions. Experimentally, Bhaskar and others (1956a) demonstrated that mouse submandibular duct ligation led to gland atrophy. On the other hand, it has been shown clinically that partial duct obstruction does not lead to gland atrophy (Patey, 1971). No gland atrophy was noted in either of our cases.

An anatomical abnormality of the draining ducts, as is shown in one of the dissections, may, following obstruction, predispose to extravasation of salivary secretions.

Source of Extravasation.—The sublingual gland, owing to its numerous mucous acini, produces secretions which have a higher protein content than those of the submandibular gland which has seromucous acini. Jenkins (1966) states that whereas the protein level of normal submandibular secretion is 0·10 g. per cent and of normal parotid secretion 0·21 g. per cent the protein level of the sublingual gland secretions is considerably higher. The high protein content of the ranula fluid suggests a sublingual gland origin (*Table I*).

The amylase concentration gradient between the cyst fluid and the serum implies that there is an active secreting source though the gland of origin is not thereby established. The human submandibular gland produces a considerable amount of amylase (Shear, 1972). Amylase measurements from cryostat sections of human submandibular gland show 0·048 mg. maltose production per μg. of protein (unpublished data), which is an amylase activity 170 times higher than that found in the sublingual gland above. The quantitative differences of submandibular and sublingual tissue amylase may be significant. The extravasated fluid in the 2 cases presented here showed only moderately raised levels which may be more in keeping with a sublingual gland origin. Further quantitative correlation between normal and pathological tissue amylase in sublingual and submandibular glands needs to be undertaken.

Sublingual Gland Removal.—Removal of the sublingual gland is based on the inference that plunging ranulas are extravasation phenomena from this gland. Excision of the salivary gland removes the secreting source, thereby preventing recurrences, and also avoids the problem of a difficult neck dissection.

As far as the authors were able to ascertain, excision of the sublingual gland has been undertaken for recurrent plunging ranulas (Crile, 1957; Whitlock and Summersgill, 1962) but has not been employed as the initial form of treatment. In the 3 recurrent ranulas of Crile and Whitlock and Summersgill several attempts were made at removal through an external cervical incision. Recurrence of the ranulas occurred in their cases after the submandibular but not the sublingual gland had been removed, presumably because the sublingual gland was still present.

Catone and others (1969) described 9 cases of non-plunging ranula which were treated successfully by sublingual gland excision.

By excising the sublingual gland a technical marsupialization is achieved. In addition, gland removal safeguards against possible recurrence by effectively removing the secreting source.

Acknowledgements.—The cases are reported with the kind permission of the Superintendent, Baragwanath Hospital, Johannesburg. The authors are indebted to Professor M. Shear, Department of Oral Pathology, for undertaking the qualitative and quantitative histochemical amylase estimation, to Mr. G. Decker for allowing us to study *Case* 2, and to Professor P. V. Tobias for permission to dissect cadaver specimens of sublingual glands.

This work was supported by a grant from the South African Medical Research Council (No. M14/73/S1).

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AN INVESTIGATION INTO THE SPREAD OF BACTERIAL INFECTION IN LOWER-LIMB AMPUTATIONS

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SUMMARY

An investigation into the spread of bacterial infection in lower-limb amputations carried out for ischaemia and terminal gangrene of the limb is reported. Under the conditions described in the study the spread of infection through the deep tissues of the leg does not appear to be as important as external infection which occurs following contamination in the operating theatre or in the ward when the wound remains unhealed. In many cases where bacterial contamination or infection of the amputation site occurred the organisms responsible had also been isolated from the gangrenous lesions in the limb. Thus documentation of the bacterial flora at the gangrenous site should not be ignored.

DEGENERATIVE vascular disease is today the commonest cause of amputation of the lower limb (Vitali, Harris, and Redhead, 1967). In the ischaemic limb where reconstructive vascular surgery is not possible gangrene or severe rest pain makes amputation necessary. There are many factors concerned in the successful healing of an amputation stump. Breakdown of the wound may occur because of ischaemia, haematoma, infection, and other general conditions, such as malnutrition and uraemia. It was decided to carry out a bacteriological investigation on amputees to try to assess the part played by infection. The stimulus for this survey resulted from an amputation survey with immediate postoperative fitting of a prosthesis carried out at five London teaching hospitals, the initial results of which were reported by Vitali and Redhead in 1967. Although Vitali and Redhead did not record any delay in wound healing, they and the surgeons concerned were unhappy with the way that some subsequent patients developed infection under their plaster dressing which resulted in wound breakdown with delayed healing or amputation to a higher level. This raised the question of how the infection had occurred. The possibilities were: lymphatic or vascular spread from the already infected gangrenous area of the foot, cross-infection of the wound during the operation, either autogenous or from some other operating-theatre source, or, finally, by secondary infection after amputation. Vitali and Redhead (1967) stated that in women the plaster socket easily becomes contaminated with urine and this may have an adverse effect on healing of the stump and may increase the risk of infection.

This bacteriological survey was carried out on patients who had severe ischaemia of a lower limb with established gangrene of the toes or foot who were unsuitable for direct arterial surgery and on whom it had been agreed that amputation was necessary. Blocks of tissue were excised at predetermined levels from the neurovascular bundles of the amputated limbs, under sterile conditions, to ascertain whether or not existing infection in a gangrenous lesion could be tracked up the limb to the site of amputation. Theatre swabs were also cultured and plates of culture medium were left exposed to the operating-theatre atmosphere. We have attempted to correlate these results with the subsequent progress of the wound.

MATERIAL

Twenty-eight patients (21 males and 7 females) requiring lower-limb amputation were investigated in 1970 and 1971. They were selected for this survey where there was distal gangrene of the toes or foot but no extensive gangrene of the limb or generalized cellulitis. Twenty-four of the patients had had arteriography to exclude the possibility of direct arterial surgery, 4 of the patients had had a recent sympathectomy, but none had had recent surgery on the affected limb. Of the 28 cases, 14 had right below-knee amputation (12 men and 2 women), 7 had left below-knee amputation (4 men and 3 women), and 7 had right above-knee amputation (5 men and 2 women). Of this last group, 2 cases were reamputations because the below-knee stump had developed gangrene. The remaining 5 cases were primary planned above-knee amputations. The youngest patient in the series was 45 years old and the eldest 86 years old. The mean age was 71·8 years. Three of the patients were diabetic.

METHODS

On the day prior to amputation swabs were taken from the nose, perineum, and gangrenous lesion. The leg was shaved, where necessary, and prepared with povidone-iodine (Lowbury, Lilly, and Bull, 1964; Ayliffe and Lowbury, 1969). It was again treated with povidone-iodine and covered with gauze before the patient was taken to the operating theatre. A sterile polythene bag was tied over the foot so as to exclude the gangrenous area. As premedication each patient was given 1 MU. of benzylpenicillin intramuscularly and the penicillin was continued in this dosage 6-hourly for 3 days. This was the surgical unit's routine prophylaxis against gas gangrene (Taylor, 1960; Johnstone, 1963; Johnstone and Cockcroft, 1968).

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Two blood-agar plates were exposed to the atmosphere of the operating theatre during the period of the operation to measure the degree of possible contamination (Williams, Blowers, Garrod, and Shooter, 1966). At intervals of 15, 35, and 45 minutes after the commencement of the operation, blood-stained theatre swabs were taken for culture. The amputated limb was laid on a separate sterile trolley with its own set of sterile instruments. One of us then rescrubbed wearing a gown, gloves, and mask to take specimens of tissue from the amputated leg at predetermined sites and levels in order to trace the possible spread of infection along the deep lymphatics and vascular channels.

Tissue was removed from the neurovascular bundle immediately adjacent to the gangrenous area of the foot. Next a block of tissue was removed to include the posterior tibial vessels behind the medial malleolus at the ankle. In below-knee amputations a further block of tissue was taken to include the major vessels in the mid-calf region, while in above-knee amputations a block of tissue was taken from the vessels in the popliteal fossa. In all the amputations a final block of vascular tissue was taken from the main neurovascular bundle at the site of amputation. In order to exclude external contamination the skin surface was seared before it was incised by a sterile knife prior to removing the block of tissue for culture. The specimens of tissues from different sites were inoculated on two blood-agar plates, one MacConkey's medium, and one Robertson's cooked-meat medium, and incubated at 37° C. overnight. Of the two blood-agar plates, one was incubated anaerobically. When there was no growth after primary culture, subcultures were made from the cooked-meat medium. The amount of bacterial growth was classified, depending on the number of colonies, as follows: >300 colonies; $+++$; >200 <300 colonies, $++$; >50 <200 colonies, $+$. When the number of colonies was less than 50 or when the growth was obtained only after subculture it was classed as scanty growth ($\pm$). The scale was also used to assess the heaviness of growth of different types of bacteria that were present at any one site. The final identification of organisms was carried out according to the method described by Cowan and Steel (1965).

In order to determine whether different types of organisms isolated from various sites were the same or similar, a range of tests was employed. For *Staphylococcus aureus* phage typing was carried out. For *Pseudomonas aeruginosa* pyocine typing was performed. With *Proteus* species the antibiotic-sensitivity pattern was studied and Diene's method was applied to differentiate between any two strains. Lastly, for *Escherichia coli* and *Streptococcus faecalis* the sensitivity pattern was taken into account to classify them (serological typing of *E. coli* was not available.)

At the termination of the operation, but before skin closure, the wound was dusted with bacitracin and polymyxin powder and a Redivac suction drain was placed in the wound in order to drain any possible haematoma in the amputation stump. The wound was dressed with sterile gauze, wool, and crêpe bandage. The drain was removed after 48 hours. At this time culture swabs were taken from the wound and from any fluid in the drain. The stump was rebandaged with sterile dressings and crêpe bandage. The sutures were removed 21 days after operation. All the skin sutures were nylon.

RESULTS

Twelve of the amputations healed without trouble. In 8 cases some breakdown of the skin suture line occurred after removal of sutures which was attributed to subjecting the stumps to rather more stress than they were capable of taking during the fitting and use of artificial limbs. In these cases only skin breakdown occurred and eventual healing took place without surgical intervention. In 2 cases it was necessary to trim the wound but the amputation healed at the same level. In 5 cases it was necessary to reamputate at a higher level. The remaining patient died before healing was complete but his amputation wound remained sterile. Five of the group died before rehabilitation could be completed.

Of the main groups of pathogenic bacteria isolated, there were five phage types of *Staph. aureus* (types 29/52/52A/80/81, 80/81, 47/53/75/77, 75/77, and 52A/79), three species of *Proteus* (*mirabilis*, *vulgaris*, and *morganii*), and two strains of *Ps. aeruginosa* (types 10 and 30).

In the nasal and perineal swabs pathogens occurred in 5 cases. *Staph. aureus* was found in the nasal swab of 3 patients, *Str. pyogenes* in the nasal swab of 1 patient, and *Clostridium welchii* was grown from the perineal swab of 1 patient (*Tables I*, *II*, and *III*). In *Case* 6 *Staph. aureus* which was cultured from the postoperative nasal swab subsequently infected a wound which initially healed satisfactorily and later broke down because of trauma. No other pathogens obtained from these cultures gave rise to subsequent infection. In most cases the gangrenous lesion of the toes or foot was infected as was the adjacent tissue of the foot. The incidence of organisms isolated from the gangrenous areas is as follows: *Staph. aureus*, 12; *Proteus* spp., 6; *Str. faecalis*, 5; *E. coli*, 4; *Str. pyogenes*, 2; *Ps. aeruginosa*, 2. In 2 cases the culture proved sterile. In 9 cases either the same organism (e.g., *Staph. aureus*) or a similar species of organism (e.g., *E. coli*, *Proteus*) was isolated from the culture of the vascular tissue at the ankle to that obtained from the culture of tissue adjacent to the gangrenous area of the foot. It was rare to find organisms in the tissue cultures from higher levels and in only 3 cases were similar organisms found at the amputation site. In 15 cases one or more of the cultured gauze operation swabs was found to be contaminated. There was contamination of the wound in 8 cases and in 7 of these the same organism was found in the gangrenous area. There were only 3 cases of primary wound infection resulting in breakdown of the wound and this occurred in *Cases* 4, 13, and 27.

In the plates exposed to the atmosphere of the operating theatre 21 were contaminated; 9 with micrococci, 5 with *Staph. albus*, and 4 with *Staph. aureus*. In *Case* 4 a penicillin- and tetracyline-resistent *Staph. aureus* was cultured from the exposed theatre plate (an organism not previously cultured from this

Table I.—THE ORGANISMS CULTURED AND RESULTS FOR 14 PATIENTS UNDERGOING RIGHT BELOW-KNEE AMPUTATION

CASE	AGE AND SEX	NOSE	PERINEUM	FOOT	ANKLE	LEG	AMPUTATION SITE	SWABS	THEATRE PLATES	DRAIN/WOUND	RESULTS
1	73 M.	NP	NP	*Staph. aureus* ± (Pen. R, Tet. R)	Sterile	Sterile	Sterile	Sterile	Micrococci +	Sterile	Stump breakdown, initially sterile then infected with *Proteus*. Converted to above-knee amputation
2	68 M.	NP	NP	*Staph. aureus* + + (Pen. R, Tet. R) *Str. faecalis* + +	*Staph. aureus* + + (Pen. R, Tet. R) *Str. faecalis* + +	*Str. faecalis* +	*Str. faecalis* +	*Str. faecalis* +	Sterile	Sterile	Healed well
3	83 M.	NP	NP	*Staph. aureus* + + (Pen.R, Tet.R)	Sterile	Sterile	Sterile	Sterile	Sterile	Sterile	Delayed healing. Sterile but became infected with *Staph. aureus* (Pen. R, Tet. R)
4	66 M.	β-Haemolytic streptococci	NP	*Proteus* +	Sterile	Sterile	Sterile	*E. coli* + *Staph. albus* +	*Staph. aureus* ± (Pen. R, Tet. R)	*E. coli* β-Haemolytic streptococci + *Staph. aureus* + (Pen. R, Tet. R)	Infected wound. *Staph. aureus* (Pen. R, Tet. R). Above-knee amputation, which became infected with *Staph. aureus*. Patient later died
5	63 M.	NP	NP	Sterile	Sterile	Sterile	Sterile	Sterile	*Staph. albus* +	Sterile	Wound breakdown. Sterile, later infected with *Staph. aureus* (Pen. R, Tet. R)
6	70 M.	*Staph. aureus* + + (Pen. R, Tet. R)	*Cl. welchii* ±	*Proteus* +	*Staph. albus* +	Sterile	Sterile	Sterile	*Staph. albus* +	Sterile	Wound breakdown. Sterile at first, later infected with *Staph. aureus* (Pen.R, Tet.R). Reamputation above-knee
7	70 M.	NP	NP	*Staph. aureus* + + + (Pen. R, Tet. R)	*Staph. aureus* + (Pen. R, Tet. R)	Sterile	Sterile	Sterile	*Staph. albus* + + +	Sterile	Clean and sterile for 3 weeks then infected with *Staph. aureus* (Pen. R, Tet. R) with wound breakdown. Later above-knee amputation
8	74 M.	NP	NP	*Proteus* + + + *Staph. aureus* + + (Pen.R, Tet.R) *Paracolon bactrium* +	*Staph. aureus* (Pen. R, Tet. R) *Paracolon bactrium* +	Sterile	Sterile	*Proteus*	*Staph. aureus* (Pen. R, Tet. R)	Sterile	Wound breakdown at first, later infected with *Staph. aureus* (Pen. R, Tet. R). Healed later after trim
9	71 F.*	NP	*Proteus* + *Str. faecalis* + + *E. coli* +	*Proteus* + *Str. faecalis* + *E. coli* ±	*Staph. albus* ±	*Proteus* +	*Proteus* +	*B. subtilis* +	*Staph. albus* +	Sterile	Slight wound breakdown Sterile at first, some infection later with *Proteus* and *E. coli*, healed
10	66 M.	NP	NP	*Staph. aureus* + (Pen.R, Tet.R)	Sterile	Sterile	Sterile	Sterile	Micrococci ±	Sterile	Healed well
11	80 F.*	NP	NP	*Staph. albus* ±	*Staph. albus* ±	Sterile	Sterile	*Staph. albus* ±	Micrococci ±	Sterile	Healed well
12	77 M.	NP	NP	*Staph. aureus* + + + (Pen.S, Tet.S)	Sterile	Sterile	Sterile	Sterile	Sterile	Sterile	Healed well
13	84 M.	NP	NP	*Str. faecalis* + +	Sterile	Sterile	Sterile	Sterile	Micrococci +	*Staph. aureus* + (Pen.R, Tet.R)	Healed slowly, *Str. faecalis* infection from 10 days
14	73 M.	NP	NP	*Staph. aureus* + (Pen.S, Tet.S)	Sterile	Sterile	Sterile	*Staph. aureus* + (Pen.S, Tet.S)	Micrococci	Sterile	Died from a coronary 4 days later

* Diabetic.

NP, No pathogens. Pen. penicillin. Tet., Tetracycline. R, Resistant. S, Sensitive.

Table II.—The Organisms cultured and Results for 7 Patients undergoing Left Below-knee Amputation

Case	Age and Sex	Nose	Perineum	Foot	Ankle	Leg	Amputation Site	Swabs	Theatre Plates	Drain/Wound	Results
15	75 F.	NP	NP	*B. aerogenes*+	*E aerogenes*	Sterile	Sterile	*Paracolon bactrum*+	Diphtheroids+ and micrococci ±	Sterile	Slight skin breakdown. Remained sterile. Healed
16	68 M	NP	NP	*Staph. aureus*+++ (Pen. R, Tet. R)	Sterile	Sterile	Sterile	*Staph. aureus*+ (Pen. R, Tet R)	*Staph aureus*+ (Pen. R, Tet. R) Micrococci ±	Sterile	Healed well
17	65 M	NP	NP	*E. coli*+	Sterile	Sterile	Sterile	Scanty diphtheroids ±	Sterile	Sterile	Healed well
18	85 F.	*Staph aureus*+++ (Pen R, Tet. R)	NP	*Proteus*+++	Sterile	Sterile	Sterile	*Paracolon bactrum* ++ *Staph. albus* ++	*B. subtilis*+ Micrococci ±	Sterile	Breakdown of wound at 3 weeks, sterile, became infected with *Proteus*. Eventually healed
19	78 F *	*Staph. aureus*+++ (Pen S, Tet. S)	NP	*Str. faecalis*+	Sterile	Sterile	Sterile	Sterile	Micrococci+	Sterile	Healed well
20	70 M	NP	NP	*Proteus*+ *Str. faecalis* ±	Sterile	Sterile	Sterile	Sterile	Micrococci+	Sterile	Healed. Died from infected aortic graft (*Staph aureus*). Ruptured false aneurysm
21	45 M.	NP	NP	*Staph aureus*++ (Pen. R, Tet. R)	Sterile	Sterile	Sterile	*Staph. albus*	Micrococci ±	Sterile	Healed well

* Diabetic. *See Table I* for key to abbreviations

Table III.—THE ORGANISMS CULTURED AND RESULTS FOR 7 PATIENTS UNDERGOING RIGHT ABOVE-KNEE AMPUTATION

CASE	AGE AND SEX	NOSE	PERINEUM	FOOT	ANKLE	LEG	AMPUTATION SITE	SWABS	THEATRE PLATES	DRAIN/WOUND	RESULTS
22	62 M.	NP	NP	*Staph. albus* +	*Staph. albus* +	Sterile	Sterile	Sterile	Sterile	Sterile	Healed well
23	77 M.	NP	NP	*Str. pyogenes* + +	*Str. pyogenes* +	*Proteus* +	Sterile	Sterile	Sterile	Sterile	Wound breakdown at 3 weeks. Sterile for 2 weeks then infected. *Staph. aureus* and *Proteus*. Healed slowly
24	73 F.	NP	NP	*Staph. aureus* + + + (Pen. R, Tet. R) *Proteus* ± *E. aerogenes*	Sterile	Sterile	Sterile	*Proteus* ±	*Staph. aureus* +	Sterile	Healed well. Died 14 days later
25	58 F.	NP	NP	*Ps. aeruginosa* + *B. subtilis* + *Staph. albus* +	*Ps. aeruginosa* + +	*Cl. welchii* ±	Sterile	*B. subtilis* *Paracolon bactrium*	Micrococci ±	Sterile	Breakdown of wound at 3 weeks. Sterile then became infected with *Staph. aureus* 12 days later. Healed after trim
26	86 M.	NP	NP	Sterile	Sterile	Sterile	Sterile	Sterile	Micrococci	Sterile	Failed to heal. Hip amputation. Died 10 days later
27	68 M.	NP	NP	β-Haemolytic streptococci + *Proteus* + *E. coli* +	*Proteus* + + *E. coli* + +	*Proteus* + *E. coli* +	*Proteus* + *E. coli* +	*Proteus* ± *E. coli* ±	Sterile	*Proteus* + + + *E. coli* +	Wound breakdown, *Proteus*. Healed later
28	70 M.	NP	NP	(Below-knee stump) *Staph. aureus* + + (Pen. R, Tet. R) *E. coli* + *Ps. aeruginosa* +	—	Sterile	Sterile	*Staph. albus*	*Staph. albus*	Sterile	Healed well

See *Table I* for key to abbreviations.

patient). An organism of the same phage type was again cultured from the wound and drain, and it subsequently produced a wound infection necessitating a higher amputation which also failed as a result of infection. The patient died from a cerebrovascular accident and bronchopneumonia following the second amputation.

From the results in *Tables I*, *II*, and *III* it can be seen that where wound breakdown occurred, apart from the 3 cases of primary infection already mentioned, the wounds remained sterile for several days according to routine culture. These wounds later became infected with organisms found either on the patient or within the general ward in which recovery was taking place. An analysis of the primary and secondary stump infection is shown in *Table IV*.

Table IV.—ANALYSIS OF THE PRIMARY AND SECONDARY INFECTION IN 13 CASES

PATHOGENS	NO. OF CASES	OTHER SITES WHERE PATHOGENS FOUND
Staph. aureus only	7	Foot 3, nowhere else 2, theatre plates 2, nose 1
Proteus only	3	Foot 2, nowhere else 1
Str. faecalis only	1	Foot
Proteus + *E. coli*	1	Both organisms found in foot
Staph. aureus + *Proteus*	1	Nowhere else

Of the 13 amputation stumps that suffered from primary or secondary infection, 10 healed satisfactorily initially but broke down after removal of the sutures. The reason for this was excessive use and perhaps trauma in teaching the patients to use an artificial limb. In the remaining 3 cases the presence of wound infection was a major contributing factor to the failure of wound healing and breakdown of the stump. It must also be noted that in these 3 cases there was considered to be some degree of residual haematoma following inadequate wound drainage (*Case* 4, 13, and 27).

DISCUSSION

A trial of immediate postoperative fitting of prostheses to lower-limb amputees was carried out at six London teaching hospitals by Vitali and Redhead in 1966 and 1967 in order to achieve early rehabilitation. A few distressing cases of stump infection and breakdown raised the questions of the source and spread of such infections, and the present work has been carried out to try to ascertain whether or not infection present in a gangrenous segment of the distal limb could be traced through the deep lymphatic and vascular channels to the site of amputation. A great many factors play their part in wound healing; possible wound infection is clearly an important one, particularly when faced with ischaemic tissue in elderly patients who are frequently further debilitated because of pain and other metabolic disorders such as diabetes and uraemia. Operative factors that are difficult to standardize are the careful and gentle handling of tissues and possible residual haematoma formation. Infection of the amputation wound is possible through intrinsic spread from an already established infected lesion on the ischaemic limb or by autogenous spread from the patient's skin, nose, perineum (Parker, 1969), or gangrenous foot. Cross-infection is also possible from other patients or from medical and nursing staff who may be pathogen carriers. Cross-infection may take place in the operating theatre or during subsequent wound dressing.

A search was made for the patient's own pathogens by culturing swabs taken from the ischaemic lesion of the foot, from the perineum, and from the nasal space. Possible sources of extrinsic contamination were assessed by repeated culture of operation swabs, and the operating-theatre atmosphere was checked with culture plates exposed to the atmosphere during the amputations. At the time of the removal of the first dressing the end of the drain and any fluid within it were cultured together with culture of the swab taken from the wound surface. Where primary wound healing did not occur or where there was subsequent wound breakdown repeated swabs were taken from the wound site.

Tissue cultures were taken from the amputated limb in order to try to assess the possible spread of pathogens from the gangrenous area along the deep vessels and deep lymphatics of the limb. It is appreciated that much lymph drainage is superficial, but cultures of tissues along the course of the long saphenous vein were not taken because of possible direct skin contamination of very superficial structures.

The gangrenous lesions on the feet harboured pathogens on culture in all but 2 cases. In 9 cases organisms similar to those cultured from the gangrenous area were also cultured from the posterior tibial tissue block. In only 3 cases could organisms be traced to lymphovascular tissue blocks taken from the leg and amputation site. In 2 cases (*Cases* 9 and 27) there were wound infection and wound breakdown but with eventual satisfactory healing. Out of the 13 primary or secondary stump infections, in only 2 cases could spread of the organisms be traced to the tissues of the limb. Extrinsic infections in the operating theatre or in the postoperative course form the majority of pathogenic infections occurring in this series. It must again be stressed at this point that these patients were given adequate preoperative intramuscular penicillin cover and that topical antibiotics were used in the wound before suture. This practice might easily have had a bearing upon the results obtained. It is thus more accurate to state that under the conditions in which the amputations in the present series were carried out spread of the infection through the tissues did not appear to be important, but that it is important to take greater steps to protect the amputations from contamination in the operating theatre and in the postoperative period. The results do underline the fact that apparently healed amputation stumps may require only slight trauma to produce wound breakdown, making subsequent infection of the broken-down wound likely when it is nursed in the open ward. Greater care must be taken for a longer period of time with ischaemic amputation stumps. Where wound breakdown does occur, the wound must be protected from infection and preferably isolated, either by isolating the patient or better still by isolating the stump in a controlled environmental chamber of its own, such as the one now under development and trial in the Biomechanical Research and Development

Unit, Department of Health and Social Security, Roehampton.

CONCLUSIONS

Twenty-eight patients undergoing lower-limb amputation were the subjects of a bacteriological study to investigate the possible spread of bacteria present in the gangrenous areas of the feet or toes. Patients were nursed in an open general surgical ward and operation was carried out in a general surgical operating theatre under antibiotic cover. In 16 cases some degree of bacterial contamination was observed. In only 2 cases could bacteria be traced through the tissues of the limb to the amputation site. Other infections suggested extraneous contamination either at the time of the operation or following later traumatic breakdown of a supposedly healed wound. Under the conditions of surgery described external bacterial contamination appears to be more important than the spread of bacteria through the deep lymphatics or deep vessels of the limb.

The study does underline how easily a freshly healed stump may be injured, resulting in wound dehiscence and secondary bacterial infection before healing of the ischaemic tissue occurs by secondary intention.

Acknowledgements.—We would like to express our gratitude to Dr. J. Kohn, Consultant Bacteriologist, and Mr. K. P. Robinson, Consultant Surgeon, for their encouragement, help, and criticism of this study; to the nursing staff of the surgical wards and operating theatres of Queen Mary's Hospital, Roehampton, for their understanding co-operation; and to Miss R. Kitson for the preparation of the manuscript.

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A METHOD OF SUPPORTIVE BANDAGING FOR AMPUTATION STUMPS

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SUMMARY

A supportive dressing for amputation stumps as an alternative to conventional bandaging is described. This dressing is effective in controlling oedema and satisfactory healing occurs. It is easily applied by both staff and the patient, and is comfortable to wear.

ONE of the first essentials following amputation is to produce a well-healed non-oedematous stump in order that prosthetic rehabilitation may begin in the shortest possible time. Adequate supportive bandaging is an important contributory factor in achieving this during the postoperative period. The unsatisfactory stumps resulting from poor application of present methods of bandaging have given rise to a stimulus to look for an improved technique. As a result a foam bandage dressing has been developed at the Limb Fitting Centre, Roehampton, and used on lower-limb amputees in the Surgical Unit of Queen Mary's Hospital, London.

MATERIALS

The materials required are: (1) a cotton stump sock* (*Fig.* 1A); (2) two strips of 1·3-cm.-thick polyurethane foam† (*Fig.* 1B and C); (3) a length of Tubigrip sewn up at one end‡ (*Fig.* 1D); (4) a suspender belt for through-knee and above-knee stumps (*Fig.* 1E). The first three items can be sterilized in an autoclave.

METHODS

Below-knee Amputation Stumps.—After positioning any necessary dressing (we are currently using Furacin gauze and dry gauze postoperatively), the cotton sock is pulled on to the stump (*Fig.* 2). We have used a sock 40 cm. in length for all amputations at this level. Two strips of foam 60 cm. long are cut to a suitable width according to the diameter of the stump. One is placed over the stump in an anteroposterior direction, covering the knee-joint; the second is cut to fill the gaps between the sides of the first strip without overlapping, and is shaped in its centre portion where it covers the tapering end of the stump as shown in *Fig.* 1C. It is then placed in position on the stump (*Fig.* 3). A sleeve of Tubigrip, approximately 45 cm. long, of a size which will apply medium tension to the stump is selected. We have used either G5 or G4X Tubigrip. To facilitate application the sleeve is rolled down with the seam on the outside (*Fig.* 4). It can then be stretched over the stump and pulled on firmly to hold the foam in contact with the distal end of the stump. The Tubigrip is unrolled to cover the foam strips and its upper end is trimmed to ensure that it does not extend beyond the edges of the foam and cause constriction around the thigh (*Fig.* 5).

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* C. and H. Coverdale, Mountsorrel, Leicestershire.

† Price Bros., Staplegrove Mills, Wellington, Somerset.

‡ Seton Products Ltd., Tubiton House, Oldham, Lancashire.

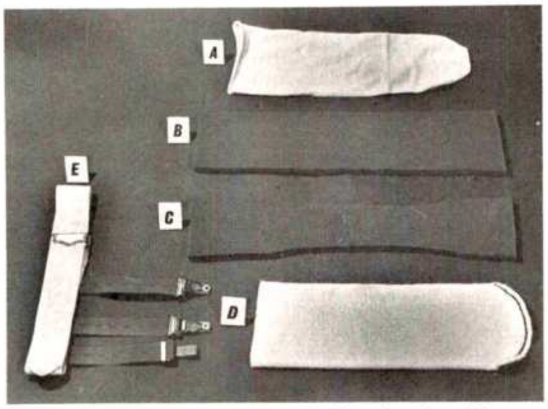

FIG. 1.—A, Cotton stump sock. B, Straight strip of foam. C, Shaped strip of foam. D, Tubigrip sleeve. E, Waist belt.

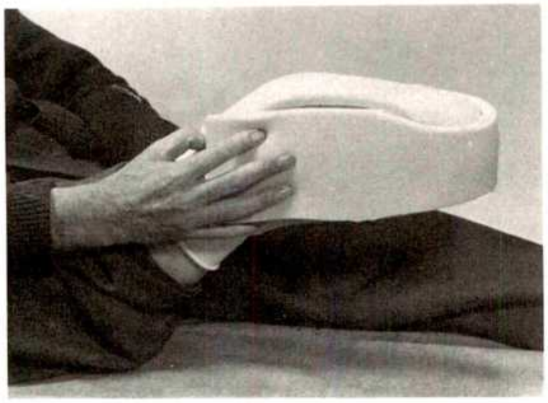

FIG. 3.—The two strips of foam in position.

Through-knee and Above-knee Amputation Stumps.—The method of application is similar to that described for below-knee amputation stumps. To maintain the dressing a waist belt with two or three suspenders is used to which the cotton and Tubigrip socks are attached. To obtain a comfortable fit in the groin the socks may be cut down on the medial side. It may be necessary to use different sizes of all the materials to fit the stump. We have used G5, G6, and G7 Tubigrip on stumps at these levels. The completed dressing is shown in position on an above-knee stump in *Fig.* 6.

RESULTS

The foam bandage dressing has been used on 23 amputation stumps in 19 patients, all of whom had had lower-limb amputations as a result of peripheral vascular disease. The ages of the patients ranged from 62 to 85 years.

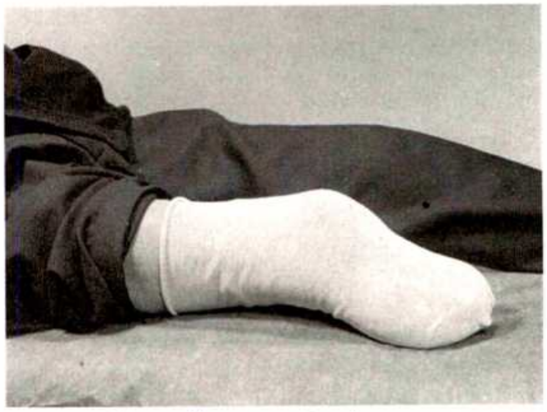

FIG. 2.—The cotton sock on the stump.

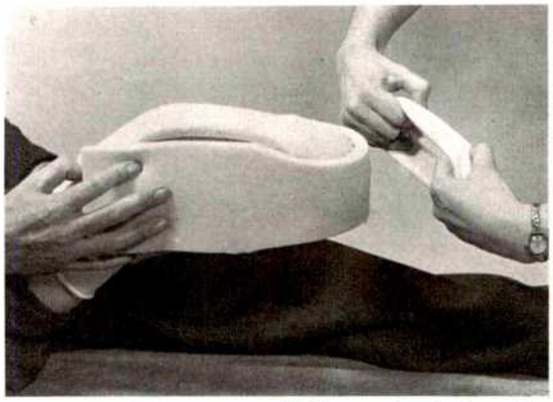

FIG. 4.—The Tubigrip sleeve rolled down and ready for application.

In 4 cases the dressing was applied immediately following amputation, in 7 cases 48 hours after amputation, and in 12 cases after initial wound healing.

In 11 cases where the dressing was applied immediately or soon after amputation satisfactory healing occurred although in 2 cases healing was delayed by superficial wound infection. In the other 12 cases the dressing was used where late ulceration developed or oedema had persisted in the stump. In all cases satisfactory healing took place, oedema was controlled, and the stumps were well shaped.

DISCUSSION

For many years elasticated bandages have been used on amputation stumps (Humm, 1969). In order to be effective these bandages must be expertly applied and constant practice is necessary to acquire the expertise. A bandage incorrectly applied can cause considerable damage to the stump. If circular turns are used instead of figure-of-eight turns the bandage will cause constriction in the middle of the stump. Venous and lymph return is thus restricted and terminal oedema soon develops. Dehiscence of the suture line may then occur, leaving the stump prone to infection. Skin necrosis may occur under a tight fold of bandage ('bandage burn'). Today the majority of lower-limb amputations are carried out on the elderly patient who is suffering from vascular insufficiency (Annual Report of the Chief Medical Officer of the Department of Health and Social Security, 1970) and in whom the healing process is slow. Any breakdown of the stump will therefore delay prosthetic rehabilitation and the patient must remain in hospital for a considerably longer period of time.

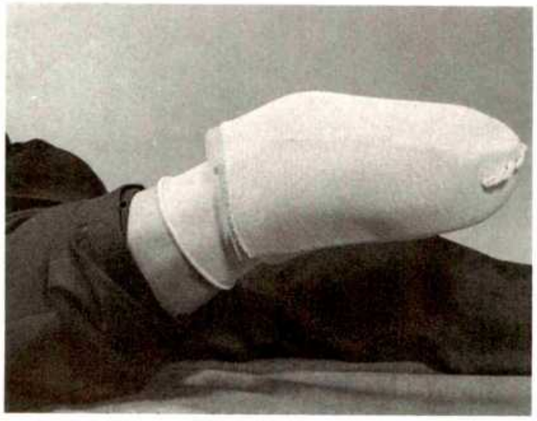

FIG. 5.—The completed dressing on a below-knee stump.

Tubular elastic bandages have often been used on stumps but have not proved satisfactory owing to their tendency to roll down, causing constriction and losing their terminal pressure. The placing of a layer of foam over the area to be covered by the Tubigrip has eliminated this problem. Foam applied directly to the skin causes discomfort, and the cotton sock prevents this. This sock also supports dressings and absorbs perspiration. It should be replaced if it becomes wet or soiled. It is recommended that the Tubigrip be reapplied every 24 hours initially, and then as the patient becomes more active and the stump less painful at least twice a day. It is unnecessary to remove the foam and the cotton sock in the postoperative period. In many patients this dressing will remain in position for at least 3 days. Evidence of the maintenance of terminal pressure can be seen by the impression of the cotton sock on the skin. In only one below-knee amputee did the dressing repeatedly come off during the night, and this patient was disorientated and extremely restless.

The foam dressing is quicker and simpler to apply than a bandage, thus reducing the amount of time required to do dressings in the ward. It can be done by an inexperienced person without the attendant hazards of a badly applied bandage. No serious harm has so far come to any stump when this simple technique has been followed.

Every patient has found this dressing very comfortable to wear, and some have reported an easing of existing stump pain as compared with the conventional stump bandaging.

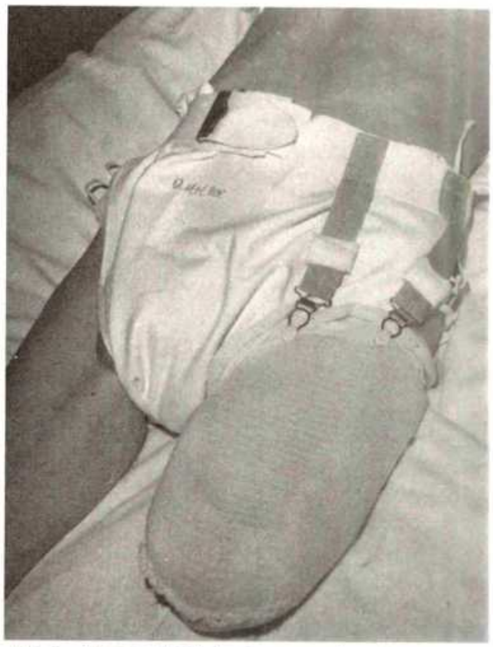

FIG. 6.—The completed dressing on an above-knee stump.

The foam strips can be sealed along their edges with adhesive plaster to form a cap. The patient is then able to apply the dressing himself. Very few elderly amputees are able to bandage their own stumps adequately, but our patients quickly learnt to manage this procedure.

Acknowledgements.—We should like to express our gratitude to Mr. K. P. Robinson and Dr. M. Vitali for their encouragement and permission to use their cases; to the nursing staff of the Surgical Unit of Queen Mary's Hospital for their co-operation and criticism in the trial of this new dressing; to the staff of the Biomechanical Research and Development Unit, Roehampton, for their assistance, and to the Department of Health and Social Security for permission to publish this article.

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A FUNCTIONAL AND SOCIAL REVIEW OF LOWER-LIMB AMPUTEES

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SUMMARY

The results of 119 lower-limb amputations for ischaemic disease in 105 patients over a 6-year period are reviewed to assess their progress and rehabilitation. The patients had an average age of 69·84 years at the time of the first amputation. The hospital mortality was 18·1 per cent. Life expectancy after amputation was seldom more than 3 years. A long period of hospitalization was accepted in order to achieve a high proportion of rehabilitated patients. Of those discharged, only 6 who came from their own homes had to be sent to an institution.

A study was made of the 52 surviving amputees. Forty-six patients were visited in their homes. The remaining 6 patients were traced and followed up by letter. A high standard of rehabilitation was maintained once amputees had been satisfactorily settled into the community, even though 11 out of 44 ambulant patients discontinued walking in favour of a wheelchair life.

MANY studies have been carried out on the merits of different levels of lower-limb amputation and various methods of rehabilitation and returning the patient to an environment. The amputee requires considerable in-patient and out-patient hospital care and frequently makes heavy demands upon the social services and welfare workers of the hospital and the community. Every attempt is made to return the patient to his original environment or to an improved environment where previous living conditions were poor. Where patients are unable to achieve sufficient independence to live alone and where there are no relatives to help, other permanent-care homes have to be found.

Little has been written about the continuing welfare of the patient once the hospital treatment has been completed. The Tunbridge Report (Rehabilitation, 1972) emphasizes the need for more research and knowledge about the rehabilitation of the disabled, particularly in the geriatric age range. The major group of amputees is comprised of elderly atherosclerotics.

The Department of Health statistics for 1970 show that of 4559 new patients who attended limb-fitting centres in England, 3176 were suffering from vascular disease (including diabetes). Of this latter group, 84 per cent were over 60 years of age; 87·4 per cent were single-leg amputees and 12·6 per cent were double-leg amputees. There were 2190 males (69 per cent) and 986 females (31 per cent).

In the following study patients who had had lower-limb amputations for peripheral vascular disease in the Westminster Hospital Teaching Group under the care of two consultant surgeons over a 6-year period were reviewed. The review was instigated to determine the needs of the elderly amputee and to assess the degree of rehabilitation maintained by the patients who were still living. This assessment was carried out by visiting the amputees in their home environment and determining their functional ability.

Details are given of all our amputations for vascular disease over the 6-year period. It will be seen that there is a bias towards the below-knee as opposed to higher levels of amputation. No attempt at a trial, controlled or otherwise, has been carried out, and although the surgical staff concerned believe that the below-knee amputee fares better than the above- or through-knee amputee, it is not intended to try to use the results of this work to make a plea for one amputation site over another. It is intended to show how this group of patients fare following amputation surgery and to look at ways of improving the service.

PATIENTS AND METHODS

During the period from December, 1965, to December, 1971, 105 patients with peripheral vascular disease required major amputation of one or both lower limbs. One hundred and nineteen amputations were carried out in the Westminster Hospital Group under the care of two consultant surgeons; 15 of the bilateral amputees had one leg amputated at another hospital.

When the survey was started in 1971, 51 patients (48·6 per cent) were already deceased and 2 patients (1·9 per cent) could not be traced. The remaining 52 patients (49·5 per cent) were made the subject of a separate study which involved visiting the patients at home.

The following aspects were considered. What was the state of rehabilitation? Was the patient wearing his prostheses (if supplied), and how did he function on them? How did wheelchair patients function? Was the patient independent? Were living conditions suitable?

We visited 46 patients in their own environment. We did not give them any warning of our intention to call on them. Six patients were not visited; 5 who lived more than a hundred miles away and 1 who had been admitted to hospital with advanced Parkinson's disease. In these cases information was obtained by postal communication from the patients and their relatives, or by personal interview with the patient at the Limb Fitting Centre or hospital. By the time that the data had been assembled 3 of the patients who had been visited had died.

RESULTS AND DISCUSSION

The Patients.—A series of elderly atherosclerotic amputees is presented (*Table I*). They were treated mainly at Queen Mary's Hospital, Roehampton, though a few were initially treated at the Westminster Hospital and later transferred to Queen Mary's Hospital. Some of the patients had had amputations carried out at other hospitals and were admitted under surgeons in the Westminster Group for amputation surgery to the other leg. The surgeons responsible held views expressed by Romano and Burgess (1971) and Robinson (1972), and adhered to a policy of treating lower-limb ischaemia which was not amenable to arterial surgery by below-knee amputation whenever possible. Amputation at a higher level was performed only when it was thought that a below-knee amputation would fail, or when it had already failed.

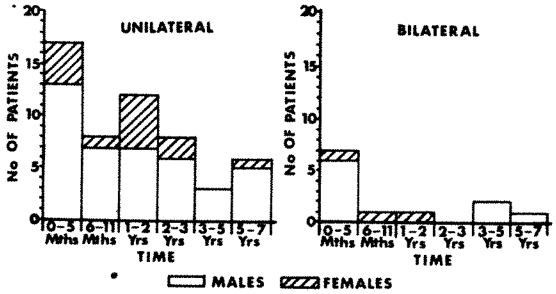

FIG. 1.—Survival times of deceased patients (54) after unilateral or bilateral amputation.

Table I.—REVIEW OF THE ORIGINAL 105 AMPUTEES WHO HAD 134 LOWER-LIMB AMPUTATIONS CARRIED OUT BETWEEN DECEMBER, 1965, AND DECEMBER, 1971

	No. of Cases
Single amputees	76
Double amputees	28
Triple amputees	1
Males	78 (98 amputations)
Females	27 (36 amputations)
Amputations carried out in the Westminster Hospital Group	119
Amputations carried out in other hospitals	15
Patients living in London	56
Patients living elsewhere	49

	Males	*Females*	*Total*
Patients still alive	35	14	49
Patients untraced	2	0	2
Patients dead	41	13	54
Patients who died in hospital	14	5	19
Patients who died after discharge	24	8	32
Patients who died after visit	3	0	3

Additional existing disabilities	*Males*	*Females*	*Total*
Diabetes mellitus	18	15	33
Ischaemic heart disease	20	5	25
Cerebrovascular accident + hemiplegia	7	3	10

Average ages (yr.)	
At first amputation	69·84
At second amputation	71·00
Diabetics (at first amputation)	69·85
Non-diabetics (at first amputation)	69·83

A review of the 105 patients shows an 18·1 per cent hospital mortality. This takes into account mortality during the convalescent and rehabilitation period in addition to the operative mortality occurring within the first 28 days (the operative mortality was 10·5 per cent). Of the patients who were discharged from hospital, only 52 were alive at the commencement of this study. Of those who had died, few had survived for more than 3 years (*Fig.* 1). Only 2 of the survivors had lived for more than 5 years (*Fig.* 2).

Additional existing disabilities in the patients treated are shown in *Table I*; 31·4 per cent of the patients were diabetic. This compares with approximately 25 per cent of all amputees being diagnosed as diabetic in the Annual Report of the Chief Medical Officer of the Department of Health and Social Security for 1970. There was a 23·8 per cent incidence of symptomatic ischaemic heart disease, and 9·5 per cent of the patients had had a cerebrovascular accident resulting in disability which interfered with rehabilitation.

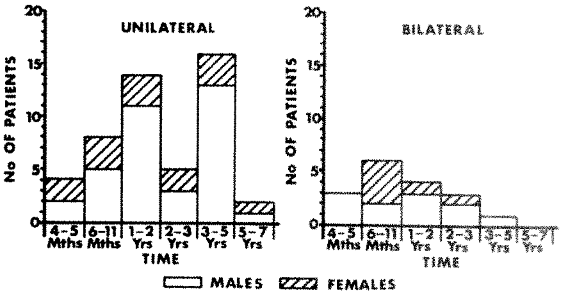

FIG. 2.—Survival times of living patients (49) from unilateral or bilateral amputation to date of visit.

Table II.—AGES OF THE 105 PATIENTS AT THE TIME OF THEIR FIRST AMPUTATION

SEX	AGE (yr.)			
	Under 40	40–59	60–79	Over 80
Males	2	6	61	9
Females	0	2	19	6
Total	2	8	80	15

The average age of the patients in this series at the time of the first amputation was almost 70 years, which is 7 years older than the patients presented by Burgess, Romano, Zettl, and Schrock (1971). The average age of patients requiring amputation of the second leg was 71 years. There was an average time interval of 14 months between amputation of the first and second legs. There was no significant difference in the average age of diabetic patients requiring amputation as compared with non-diabetics. Department of Health statistics for 1970 showed that 84 per cent of primary amputees suffering from vascular disease were over 60 years of age. In this series 91·5 per cent of the patients were over the age of 60 (*Table II*).

Period of Hospitalization.—In a group of patients with a short life expectancy it is important to take into account the length of time spent in hospital following amputation (*Table III*). The single primary below-knee amputee spent an average of 83 days in hospital and only 3 of the 40 successes in this group failed to walk. In the single primary above-knee amputation group the average time spent in hospital was 56 days, but 8 of the 16 successes did not walk. There were only 5 single primary through-knee amputees who all walked and they spent a comparable time in hospital to the above-knee patients.

There were 9 patients admitted with an existing single below-knee amputation who required below-knee

Table III.—MAIN GROUPS OF AMPUTATIONS RELATING MORTALITY, PATIENTS DISCHARGED WALKING, AND TIME SPENT IN HOSPITAL FOLLOWING AMPUTATION

TYPE OF AMPUTATION	NO. HEALED	TIME IN HOSPITAL (d.)		DISCHARGED WALKING	DIED BEFORE REHABILITATION
		Min./Max.	Average		
Single primary below-knee amputation (60 patients)					
Healed at B.K. level	39	36/171	83	36	7
	1†	492		1	
B.K. failed; healed at A.K. level	10	52/141	108	10	3
Single primary through-knee amputation (8 patients)					
Healed at T.K. level	5	27/97	58	5	1
T.K. failed; healed at A.K. level	2	57/71	64	2	0
Single primary above-knee amputation (23 patients)					
Healed at A.K. level	16	11/51	56	8	5
A.K. failed; healed at T.H. level	1	58	58	1‡	1
Bilateral amputees (26 patients)					
B.K.; B.K. other leg	10	49/210	110	10	0
A.K.; A.K. other leg	2	88/135	111	0	2
Other amputations (A.K./B.K ; A K./T.K.; T K /B.K.)					
Healed	8	24/162	86	4	0
Failed; healed at higher level	4	85/239	148	1	0
Total	98			77	19

A.K., Above knee. B.K., Below knee. T.K., Through knee. T.H., Through hip.
* Separate figures are not given for males and females because there was no significant difference.
† This patient was blind and deaf and although she could walk accommodation proved difficult to find.
‡ Discharged on crutches.

amputation of the other leg, and 1 patient had bilateral below-knee amputations on the same day. The average time spent in hospital was 110 days and all 10 patients were discharged walking. There were 4 single above-knee amputees who were admitted for above-knee amputation of the other leg; 2 died and the other 2 were discharged in wheelchairs. There were 11 single amputees who had amputation of the second leg at a different level from their original amputation, and 1 patient had bilateral amputations during a single admission. Only 5 of these 12 patients became ambulant. The number of days spent in hospital by the patients whose stumps healed satisfactorily (average 86 days) is influenced by 2 patients who were able to return to geriatric accommodation shortly after surgery.

In commenting on these figures it must be remembered that almost half our patients came from outside the London area, and many of the patients who lived within the London area had unsuitable homes or could not return to their previous accommodation. To obtain a high proportion of rehabilitated patients the necessity of retaining them in hospital until they were capable of an independent existence was accepted (Robinson, 1971). The reduced average time spent in hospital by the single above-knee as compared with the single below-knee amputee was in part due to a difference in wound healing. Of the 40 below-knee amputees whose stumps healed, there was delayed healing in 13 cases (32·5 per cent). Of the 16 above-knee amputees whose stumps healed, there was delayed healing in 3 (18·7 per cent). Another factor was the reduced period of hospitalization of the non-ambulant above-knee amputees.

Rehabilitation.—There are two main aspects to be considered in the postoperative rehabilitation of the amputee.

First, there is physical rehabilitation, which includes training the patient to walk on an artificial limb, and teaching him to use a wheelchair and other ancillary aids. Implicit in this training is the necessity to regain independence. Patients must accept the loss of their limb and the necessity to replace it with an artificial one. In the elderly it is difficult to overcome reduced learning capacity and poor memory. Deafness and impaired vision may be significant handicaps, and corrective measures, where possible, are very important. Other disabilities resulting from cardiovascular disease frequently impose extra problems in locomotion and mental function.

Secondly, there is social rehabilitation, which incorporates the return of the patient to suitable accommodation. Even when the patient returned to his original accommodation it had to be modified with handrails, bath and toilet aids, and to take a wheelchair. Where modifications had to be carried out by local councils long delays were sometimes experienced. Where the patient could not return to his own home or to the home of relatives there were occasionally long delays in obtaining accommodation. The longest delay in our experience was for a female patient who had to stay in hospital for 492 days before accommodation could be found.

A further aspect for the younger amputee is resettlement, to which early consideration must be given.

The patients who lived long distances from the Limb Fitting Centre were deliberately kept in hospital for rehabilitation as treatment on an out-patient basis would have required unacceptably long travelling times each day. From an economic standpoint alone it would have been more expensive than keeping the patient in hospital. There is no easy answer to this problem. If there were decentralization of the limb-fitting services it would be possible for more patients to attend daily for walking training and rehabilitation. One solution to the problem, which would meet our own needs more adequately, would be the construction of a specialized disabled living unit similar to the Mary Marlborough Lodge at the Nuffield

Orthopaedic Centre in Oxford, described by Hamilton and Nichols (1972). It would then be possible to make sure that patients were rehabilitated to the maximum extent before returning to the outside world. It is our experience that when patients curtail their rehabilitation, full use is not made of artificial limbs and other aids and these people tend to revert to a wheelchair life or become bedridden.

Table IV.—REVIEW OF 52 LIVING AMPUTEES WHO HAD 69 LOWER-LIMB AMPUTATIONS CARRIED OUT BETWEEN JUNE, 1966, AND DECEMBER, 1971

	No. of Cases		
Single amputees	35		
Double amputees	16		
Triple amputees	1		
Males	38 (49 amputations)		
Females	14 (20 amputations)		
Amputations carried out in the Westminster Hospital Group	62		
Amputations carried out in other hospitals	7		
Patients living in London	26		
Patients living elsewhere	26		
Additional existing disabilities			
	Males	*Females*	*Total*
Diabetes mellitus	7	11	18
Ischaemic heart disease	5	3	8
Cerebrovascular accident + hemiplegia	2	2	4
Average ages (yr.)			
At first amputation	69·69		
At second amputation	71·59		
Diabetics (at first amputation)	69·33		
Non-diabetics (at first amputation)	69·88		
	No. of Cases	*Percentage*	
Patients with:—			
Stump pain	9	17·3	
Phantom pain	3	5·7	
Patients who live alone	11	21·2	
Patients who live with other people	41	78·8	
Patients who are independent	27	51·9	
Patients who are dependent	25	48·1	
Patients who have:—			
District nurse	7	13·5	
Home help	7	13·5	
Meals-on-wheels	5	9·6	
Employment			
Patients working before amputation	9	17·3	
Patients working after amputation	7	13·5	
Accommodation	*No. of Cases*	*Percentage*	
Patients who live in:—			
Council property	23	44·2	
Unsuitable	8	34·8	
Private property and	10	19·2	
Rented property	9	17·3	
Unsuitable	8	42·1	
Old people's homes and	8	15·4	
Old people's flatlets	1	1·9	
Unsuitable	0	0·0	
Hospital	1	1·9	

Chilvers and Browse (1971) stressed the difficulty of returning patients to their own homes and 7 out of 20 of their cases were discharged to institutions. While they were waiting for suitable accommodation these patients occupied acute surgical beds for many weeks. Of our 105 patients, 18 were discharged to institutions. Twelve of these patients were admitted from institutions; 6 came from their own home and were discharged into institutional care.

Follow-up of Surviving Amputees.—The 52 surviving amputees had 69 lower-limb amputations carried out between June, 1966, and December, 1971. The details of this group (*Table IV*) show no striking difference from the original 105 amputees. As can be seen in *Table V*, there is a preponderance of single and bilateral below-knee amputees. *Table VI* shows that 92 per cent of the group are over the age of 60.

Twelve patients (23 per cent) had some discomfort in the form of stump or phantom pain. In 5 of these patients this discomfort was severe enough to be contributory to either cessation of walking or limiting the use of the prosthesis.

State of Rehabilitation.—*Table VII* documents the supply and use of prostheses and wheelchairs; it also indicates the state of rehabilitation of the patients and whether this had changed from that listed on discharge from hospital. Thirty-three patients (63·5 per cent) continued to walk, 11 patients (21 per cent) had discontinued walking, and 8 patients (15 per cent) did not walk. This latter group is divided into two sections. The patients listed under 'did not walk' originally tried to use a prosthesis in hospital but failed to attain any degree of competence and were then rehabilitated in a wheelchair. Under the heading 'prostheses not supplied' are listed patients where no attempt at walking was made. Most of the sub-group figures are too small for serious comment, but we should like to draw attention to the fact that 5 out of 8 bilateral below-knee amputees continued to walk, whereas all the bilateral above-knee amputees found a wheelchair existence more satisfactory.

Table V.—FINAL LEVELS OF AMPUTATION IN THE 52 LIVING AMPUTEES

LEVEL OF AMPUTATION	MALE	FEMALE	TOTAL
A.K.	8	3	11
T.K.	2	0	2
B.K.	17	5	22
2 A.K.	3	1	4
2 B.K.	4	4	8
A.K./B.K.	1	1	2
T.K./B.K.	1	0	1
A.K./T.K.	2	0	2
Total	38	14	52

A.K., Above knee. B.K., Below knee. T.K., Through knee.

Table VI.—AGES OF THE 52 LIVING AMPUTEES AT THE TIME OF THEIR FIRST AMPUTATION

SEX	AGE (yr.)		
	40–59	60–79	Over 80
Males	4	31	3
Females	0	10	4
Total	4	41	7

Of the 33 patients who continued to use their prostheses, 5 were not wearing their limbs when visited (1 bilateral, 1 above-knee, and 3 below-knee amputees). The bilateral amputee had not completed his walking training, and his prostheses had been kept at the hospital. The above-knee amputee said she found it difficult to put on her pylon. Of the 3 below-knee amputees, 1 had congestive cardiac failure, 1 was recovering from hemiplegia, and 1 had severe stump pain.

The patient's continued use of his prosthesis was apparently determined to some extent by his social situation, irrespective of amputation level. Of 28 patients who lived at home with relatives, 25 (89·3 per cent) continued to walk. Of 9 patients who lived alone, 5 (55·6 per cent) continued to walk (1 had not completed his walking training and therefore could not be assessed). In these patients difficulty in putting on the prosthesis and fear of falling are deterrents to limb-wearing. Patients who lived in geriatric accommodation were generally not encouraged to use their prostheses, and only 2 out of 7 (28·6 per cent) continued to do so. The patient's own attitude is perhaps the most important factor: those who have the determination to walk will do so in any situation.

Table VII.—SUPPLY AND USE OF PROSTHESES AND WHEELCHAIRS

LEVEL OF AMPUTATION	PROSTHESES SUPPLIED									PROSTHESES NOT SUPPLIED			WHEELCHAIR SUPPLIED						WHEELCHAIR NOT SUPPLIED		
	Continued to Walk			Discontinued Walking			Did not Walk						In Addition to Prostheses			Wheelchair only					
	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.
B.K.	15	3	18	2	1	3	0	1	1	0	0	0	8	3	11	0	0	0	9	2	11
T.K.	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	2
A.K.	6	1	7	1	0	1	0	0	0	1	2	3	2	1	3	1	2	3	5	0	5
2 B.K.	2	3	5	2	1	3	0	0	0	0	0	0	4	4	8	0	0	0	0	0	0
2 A.K.	0	0	0	2	1	3	1	0	1	0	0	0	3	1	4	0	0	0	0	0	0
A.K./B.K.	1	0	1	0	0	0	0	0	0	0	1	1	1	0	1	0	1	1	0	0	0
A.K./T.K.	0	0	0	0	0	0	1	0	1	1	0	1	1	0	1	1	0	1	0	0	0
T.K./B.K.	0	0	0	1	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0
Total	26	7	33	8	3	11	2	1	3	2	3	5	20	9	29	2	3	5	16	2	18

A.K., Above knee. B.K., Below knee. T.K., Through knee.
M., Male. F., Female. T., Total.

Table VIII.—RELATION OF LEVEL OF AMPUTATION TO INDEPENDENCE OR DEPENDENCE

	UNILATERAL AMPUTATION						BILATERAL AMPUTATION						TOTAL
	Below Knee		*Through Knee*		*Above Knee*		*Below Knee*		*Above Knee*		*Others*		
	Limbs	Chair	Limbs	Chair	Limbs	Chair	Limbs	Chair	Limbs	Chair	Limbs	Chair	
Independent													
Male	11	0	2	0	5	0	2	1	0	1	0	1	23
Female	4	0	0	0	0	0	0	0	0	0	0	0	4
Total	15	0	2	0	5	0	2	1	0	1	0	1	27
Dependent													
Male	3	2	0	0	1	2	0	1	0	3	0	2	14
Female	0	2	0	0	1	2	3	1	0	1	0	1	11
Total	3	4	0	0	2	4	3	2	0	4	0	3	25

Every amputee must have some means of getting about when he is not wearing his prosthesis and when other conditions restrict mobility. All bilateral amputees have a wheelchair, but in the case of the single amputee there is a choice between a wheelchair and crutches. *Table VII* shows that 18 single amputees were not issued with a wheelchair. They were supplied with crutches. Many elderly patients cannot walk safely with crutches, and they may not be able to get outside their home without a wheelchair. Fourteen single amputees required a wheelchair in addition to their prosthesis. A wheelchair can enable the elderly amputee to achieve maximum independence (Hamilton and Nichols, 1972), but it should be used as a complement to the prosthesis and not as a replacement for it.

Table VIII shows the relation between the level of amputation and independence. The value of this table depends upon our definition of independence. A patient had to fulfil the following criteria, whether he walked or led a wheelchair life, to be classified as personally independent. He had to be capable of dressing and undressing himself, preparing food and feeding himself, transferring to a chair, bed, and toilet, and washing and personal toilet. It was desirable that he should be capable of venturing outside, at least to the local shops, in an emergency. It was felt to be unfair to call a patient dependent if he fulfilled all the other criteria but could not get outside in a wheelchair because of difficult steps, or because he lived in a high-rise flat. Twenty-seven patients (51·9 per cent) were considered to be personally independent.

To enable them to live at home some patients required the help of a district nurse (7 patients), a home help (7 patients), and some had midday meals provided by the meals-on-wheels service (5 patients).

Accommodation.—Accommodation was assessed for suitability, and was classed as suitable if the patient could obtain ready access to the bathroom, toilet, kitchen, living room, and bedroom, and if he could gain easy entry to the living unit by at least one door. Suitability is listed for council, private, and rented property and for specialized old people's accommodation. In many council and private properties the patient was unable to use the bathroom because of difficult stairs and narrow doorways. Most properties had entrance steps making wheelchair access difficult. Some patients found lift failure in high-rise flats an occasional hazard.

Sixteen patients were living in unsuitable homes. Recommendations for alternative accommodation had been made in each case during the patient's hospital stay following a home visit by hospital staff. Six patients living in council property wished to move and werewaiting for rehousing. Three patients in private accommodation were trying to obtain new housing. The rest of the group had either decided not to move and to accept the shortcomings of their homes or had rejected alternative accommodation.

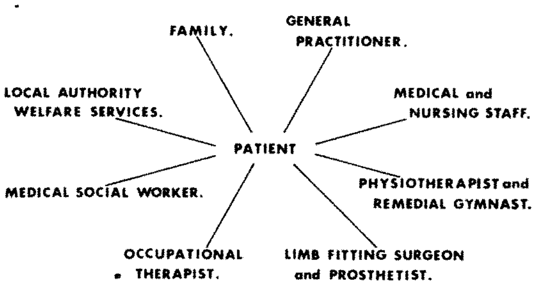
FAMILY.
GENERAL PRACTITIONER.
LOCAL AUTHORITY WELFARE SERVICES.
MEDICAL and NURSING STAFF.
PATIENT
MEDICAL SOCIAL WORKER.
PHYSIOTHERAPIST and REMEDIAL GYMNAST.
OCCUPATIONAL THERAPIST.
LIMB FITTING SURGEON and PROSTHETIST.

FIG. 3.—The amputation team.

Employment.—Nine patients were working in the period prior to admission to hospital, and 7 of these returned to employment after amputation.

Recommendations.—Constructive recommendations were made in 10 cases. Further walking training was thought necessary for a bilateral below-knee amputee and a single below-knee amputee who had given up walking because of lack of confidence. After further training they continued to use their limbs when revisited. In the remaining 8 patients minor structural alterations were required in the homes of 3 patients, rehousing was required by 2, and 1 needed a home help. Two other patients and 3 of those already mentioned needed additional aids and instruction in their use.

The Amputation Team.—Amputation of a limb constitutes a major disaster to any patient. To overcome the physical and mental problems which result, particularly in the elderly, an enthusiastic team approach is necessary (Vitali, 1970). Our own team is illustrated in *Fig.* 3. A close liaison is essential between members of the team. This type of work can be time-consuming and discouraging, but not infrequently a patient who initially appears to be a hopeless medical and social problem learns to walk again and returns to a useful existence within the community. It must be remembered that the patient with an ischaemic limb may have been unable to lead a normal life for some time and that pain and incapacity lead to poor nutrition and depression. Other problems associated with advancing years have already been discussed. The team approach helps to draw attention to all these problems, which can be frequently overlooked in a busy hospital.

CONCLUSIONS

The amputees in this series have a limited life expectancy and require long hospitalization in the post-amputation period. Living units for the disabled would help to reduce the period of time that they occupy acute surgical beds. The experience of an amputation team is beneficial to the quality and rate of rehabilitation.

It is possible for a high percentage of elderly amputees to make a successful return to society, either ambulant or in a wheelchair. Most amputees returning to their own home require some adaptation of the dwelling, and it is important to make certain that recommendations have been carried out, preferably before discharge. Most of the surviving patients had maintained their standard of rehabilitation when visited in their homes. Social services play an important part in enabling the amputee to live within the community. It was disappointing to find some old people's homes discouraging ambulation in patients who had been taught to walk again.

Acknowledgements.—We wish to thank all our colleagues in the amputation team. In particular, we wish to thank Mr. K. P. Robinson and Mr. A. G. Rutter for permission to review their patients and for their encouragement and advice, and Dr. M. Vitali, Dr. I. H. M. Curwen, Dr. P. C. Puddifoot, and Dr. R. G. Redhead for ideas and suggestions.

We acknowledge financial assistance from the Governors' Discretionary Fund of the Westminster Hospital towards our expenses.

We are grateful to the staff of the Biomechanical Research and Development Unit, Roehampton, for their assistance in the drawing and photography of our illustrations.

We are grateful to Mrs. J. P. Bristow and Mrs. D. J. Browning for assistance in the preparation of the manuscript.

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INFARCTION OF FIBRO-ADENOMA OF THE BREAST

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SUMMARY

Infarction of benign lesions of the breast is very uncommon and may lead to difficulties in clinical and pathological diagnosis. Five instances of infarction occurring in a fibro-adenoma are described; in 2 of them thrombo-occlusive vascular changes were seen. The aetiology, pathogenesis, and helpful diagnostic features are discussed.

INFARCTION is an infrequently reported complication of fibro-adenoma of the breast. In a review of the literature we have been able to find only 11 such cases, of which 4 occurred during pregnancy and lactation (Delarue and Redon, 1949; Wilkinson and Green, 1964; Pambakian and Tighe, 1971); in none of these were vascular changes described. This article reports a further 5 cases and describes vascular lesions that were present in 2 of them; only 1 of the 5 cases was associated with pregnancy and lactation.

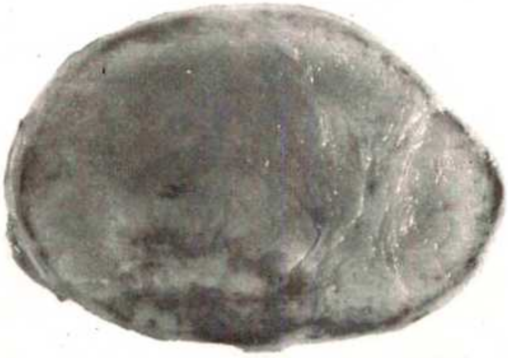

FIG. 1.—*Case* 3. Cut surface of infarcted fibro-adenoma.

CASE REPORTS

Case 1.—A 25-year-old coloured female presented with a tender lump in her breast which she had noticed 10 days prior to her admission in August, 1956. She was not pregnant and there were no other relevant clinical features. An excision biopsy was performed.

The specimen consisted of fibro-adipose tissue weighing 38 g. The cut surface revealed a 4 × 3-cm. well-encapsulated nodule with a variegated appearance. There were soft greyish-pink as well as firm white areas. Histologically, the lesion was well circumscribed and surrounded by compressed but otherwise normal breast tissue. It showed the features of a fibro-adenoma of predominantly intracanalicular type. Except for a viable rim at the periphery, the tumour was necrotic but the original architectural pattern was still discernible. Within the necrotic tissue focal areas of interstitial haemorrhage were evident. Several large vessels were seen at the periphery of the tumour and in the surrounding breast tissue, but they showed no evidence of either thrombo-occlusive or inflammatory vascular disease. Within the necrotic areas many of the vessels were intensely congested. The features were those of a fibro-adenoma which had undergone recent infarction.

Case 2.—In August, 1960, a 40-year-old Caucasian female presented with a 1-week history of a mobile lump in her right breast. An excision biopsy was performed.

The specimen consisted of breast tissue measuring 10 cm. in its greatest dimension. The cut surface showed two lobulated nodules. The larger nodule measured 6·5 cm., had a dark-red colour, and its appearance suggested a necrotic fibro-adenoma. The smaller nodule had the appearance of a typical fibro-adenoma. Histological examination confirmed the features of an intracanalicular fibro-adenoma. However, in the larger nodule there were extensive areas of necrosis with foci of interstitial haemorrhage and congestion. Within these foci the original architecture of the fibro-adenoma was still preserved. At the periphery the tumour tissue was still viable and was infiltrated by acute and chronic inflammatory cells. Within a fibrous septum separating a lobule of viable from necrotic tissue there was a medium-sized vessel which was completely occluded by thrombus. These features indicated a fibro-adenoma with large areas of recent infarction.

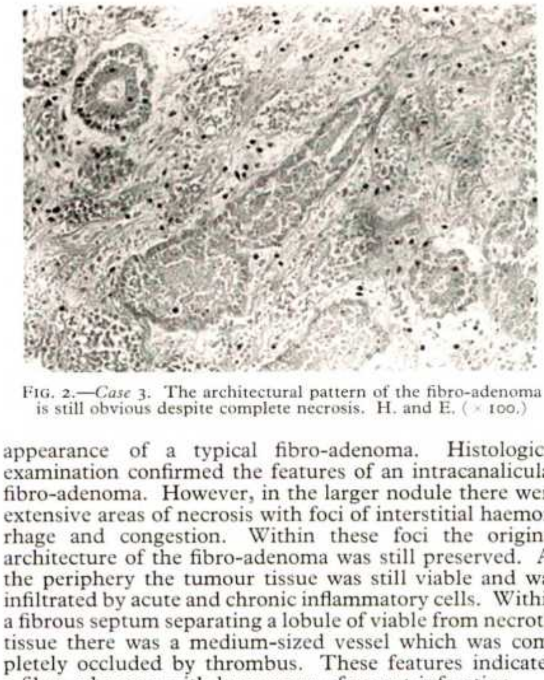

FIG. 2.—*Case* 3. The architectural pattern of the fibro-adenoma is still obvious despite complete necrosis. H. and E. (× 100.)

Case 3.—A 17-year-old coloured female presented in April, 1972, with a history of being aware of a lump in her right breast for 3 months. Before her admission she had developed a throbbing pain in the lump. There was no history of recent pregnancy or of trauma to the breast. On examination the lump was found to be mobile and non-tender; the axillary nodes were not palpable. The breast lump was excised.

The specimen consisted of a circumscribed tumour mass weighing 50 g. and measuring 4·5 × 4 × 3 cm. (*Fig.* 1). It had a lobulated bulging cut surface with geographically outlined haemorrhagic and tan-coloured areas. Microscopically, the lesion was a fibro-adenoma of mixed type. Except for a peripheral rim of viable tumour tissue, most of the lesion was necrotic but with preservation of the architectural pattern (*Fig.* 2). A mild lymphocytic infiltrate was present at the margins of the infarcted areas. A small artery was located adjacent to an infarcted area and its lumen was occluded by recanalized thrombus (*Figs.* 3, 4). The features were those of a fibro-adenoma with large areas of infarction.

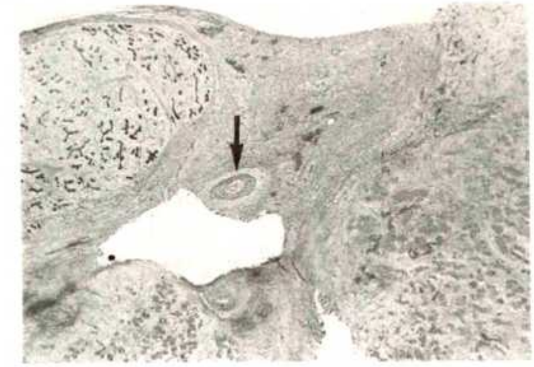
FIG. 3.—*Case* 3. Viable fibro-adenoma is seen on the left and necrotic fibro-adenoma on the right. An artery showing occlusion of its lumen by recanalized thrombus is present in the fibrous septum (arrow). H. and E. (× 90.)

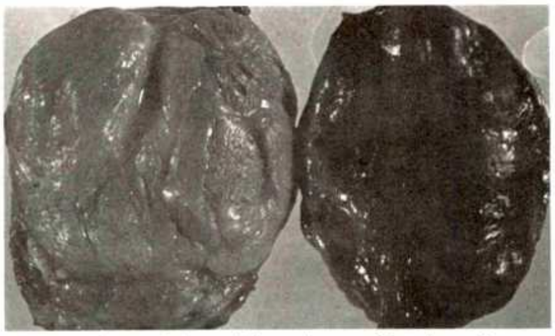
FIG. 5.—*Case* 4. Infarcted fibro-adenoma. Capsular surface on the right and cut surface on the left.

Case 4.—In July, 1972, an 18-year-old coloured female presented with a 2-year history of a lump in her breast. She had first noticed the lump following trauma to her breast during a game of netball. The lump had slowly increased in size and was occasionally painful. Four months prior to her admission she had given birth and had breast-fed the baby from the opposite breast. The lump had not decreased in size during puerperium or lactation. On examination the presence of a mobile lump in the left upper outer quadrant was confirmed. The axillary nodes were not palpable. The lump was excised.

The specimen consisted of a well-circumscribed spherical mass measuring 6 cm. in diameter (*Fig.* 5). It had a bulging cut surface and a distinct tan colour. Most of the tumour mass appeared to be necrotic. Microscopically, the lesion was a fibro-adenoma in which the acinar epithelial cells showed lactational change. The circumscribed mass was surrounded by a compressed rim of breast tissue showing regressive postpartum change. Except for a rim of peripheral viable tumour tissue, most of the lesion was necrotic. In areas of necrosis there was a marked histiocytic infiltrate in response to liberated secretions (*Fig.* 6). At the junction between the viable and necrotic tissue an infiltrate of acute and chronic inflammatory cells as well as fibroblastic proliferation was present. There was no evidence of thrombo-occlusive or inflammatory vascular disease. The features were those of a fibro-adenoma showing lactational change and extensive recent infarction.

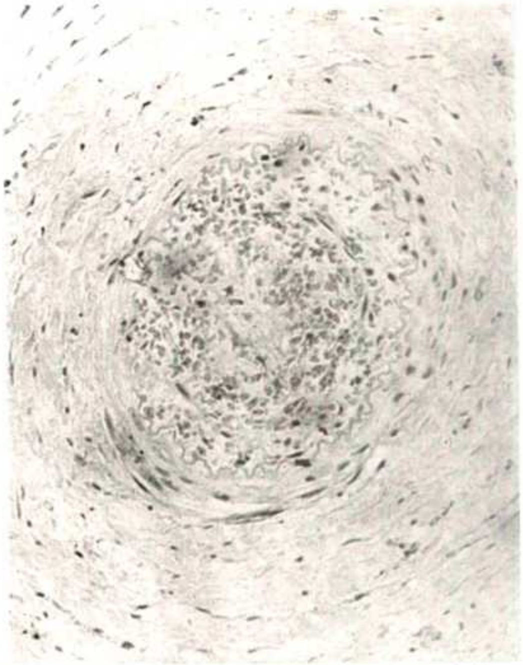
FIG. 4.—*Case* 3. Detail of recanalized thrombus occluding a medium-sized artery in a fibrous septum. H. and E. (× 150.)

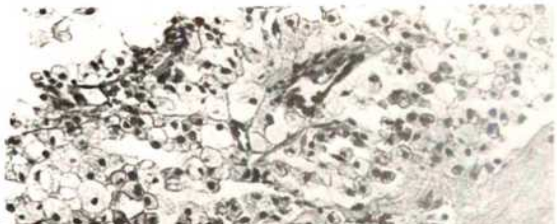
FIG. 6.—*Case* 4. Histiocytic reaction in response to the liberation of secretions from the infarcted fibro-adenoma showing lactational change. H. and E. (× 94.)

Case 5.—A 17-year-old coloured female presented with a mass in the right breast of 1 month's duration. Initially the lump was tender and the patient complained of a throbbing pain associated with it but these symptoms had subsided. She had been given antibiotics by her doctor who had diagnosed a breast abscess. There was no history of trauma. On examination a 5-cm. firm well-circumscribed mass was palpated and was thought to be a treated breast abscess or a fibro-adenoma; it was excised.

The specimen consisted of a well-encapsulated nodule 4·5 cm. in diameter with a necrotic-looking grey cut surface. Histologically, the peripheral rim of the lesion showed features of a pericanalicular fibro-adenoma while the bulk of the tumour was completely infarcted. No occluded feeding vessels were noted.

DISCUSSION

Fibro-adenomas are common benign breast lesions and in one large series (Wright and Symmers, 1966) they constituted 19 per cent of all benign breast lumps. There are very few reports of necrosis occurring in these lesions and several standard textbooks of pathology fail to mention this complication (Wright and Symmers, 1966; Ackerman, 1968; Anderson, 1968; Evans, 1968; McDivitt, Stewart, and Berg, 1968). We have been able to find only a few references to infarction occurring in fibro-adenomas. Six such lesions occurring in non-pregnant women are recorded in the French literature by Delarue and Redon (1949). Wilkinson and Green (1964) have reported 2 instances of infarction in fibro-adenoma occurring during pregnancy and lactation, while Pambakian and Tighe (1971) recently reported 1 case of infarction of a fibro-adenoma unassociated with pregnancy and 2 cases occurring in association with pregnancy and lactation. We have been able to find 5 cases of infarction in a fibro-adenoma recorded in the surgical pathology files of the Groote Schuur Hospital from 1950 to 1972 but we have not systematically reviewed all the fibro-adenomas seen in this department. Two of these 5 cases were seen during the past 6 months; only 1 of the 5 was associated with pregnancy and lactation.

Other authors have been unable to demonstrate an anatomical cause for the infarction of fibro-adenomas and have postulated a relative vascular insufficiency secondary to an increased metabolic requirement such as occurs during pregnancy and lactation. Pambakian and Tighe (1971) were unable to account for the infarction of the fibro-adenoma that occurred in a postmenopausal patient. The infarcted fibro-adenoma in the present *Case* 4, who had recently been pregnant, displayed similar histological features to those described by Wilkinson and Green (1964), viz., a fibro-adenoma with lactational changes and infarction without obvious anatomical cause. Two of the present lesions resembled one of the cases described by Pambakian and Tighe (1971) in that the infarction occurred in the absence of pregnancy and without demonstrable vascular lesions to account for the infarction. However, in the two other lesions we were able to demonstrate thrombo-occlusive vascular changes in the feeding vessels. As far as we are aware this is the first documentation of such changes in this condition. These vessels subtended the areas of infarction and were situated in fibrous septa separating areas of infarcted from viable tumour. The areas of infarction seemed disproportionately large, considering the size of the vessel involved. Although it is possible that these thrombosed vessels may have been the primary cause of the infarction, the possibility of secondary thrombosis following the infarction cannot be entirely excluded. It is interesting to speculate on the possible role of mechanical factors, as fibro-adenomas are usually very mobile in the breast and could theoretically undergo torsion with compromise of their blood-supply. If this were an important aetiological factor it is surprising that infarction is not a more frequent complication in fibro-adenomas. The theory of relative vascular insufficiency occurring during phases of increased metabolic activity and nutritional requirement may explain the necrosis described in fibro-adenomas in pregnancy (Wilkinson and Green, 1964; Pambakian and Tighe, 1971). This same mechanism has been postulated to be the cause of necrosis that occurs in lactational adenomas (Hasson and Pope, 1961). However, it is difficult to understand why infarction of fibro-adenomas during pregnancy and lactation is so infrequently recorded.

It is of paramount importance for the pathologist to recognize infarction in a fibro-adenoma and not to mistake it for necrotic breast carcinoma. Delarue and Redon (1949) described these tumours as having clinically simulated carcinoma, viz., hardness, fixation, and enlarged axillary nodes. The clinical diagnosis of carcinoma was made with such confidence that 4 of their 6 patients underwent mastectomy without the benefit of prior excision biopsy and frozen-section examination. In none of our patients was the diagnosis of carcinoma considered. However, the surgical pathologist always regards necrosis in tumours with suspicion so that examination of necrotic areas in a fibro-adenoma may give rise to diagnostic difficulties, especially on frozen-section examination. The necrotic ductular and glandular outlines may bear a superficial resemblance to adenocarcinoma, while the collection of foamy histiocytes lying loosely within the necrotic tumour tissue spaces, as seen in our *Case* 4, may simulate a mucoid carcinoma. However, the macroscopical features as well as the architectural pattern, even in the necrotic areas, are quite obviously those of necrosis in a fibro-adenoma. Sections taken from the periphery usually reveal viable fibro-adenomatous tissue so that confusion between carcinoma and necrosis in a fibro-adenoma should not occasion diagnostic difficulty, even on frozen-section examination.

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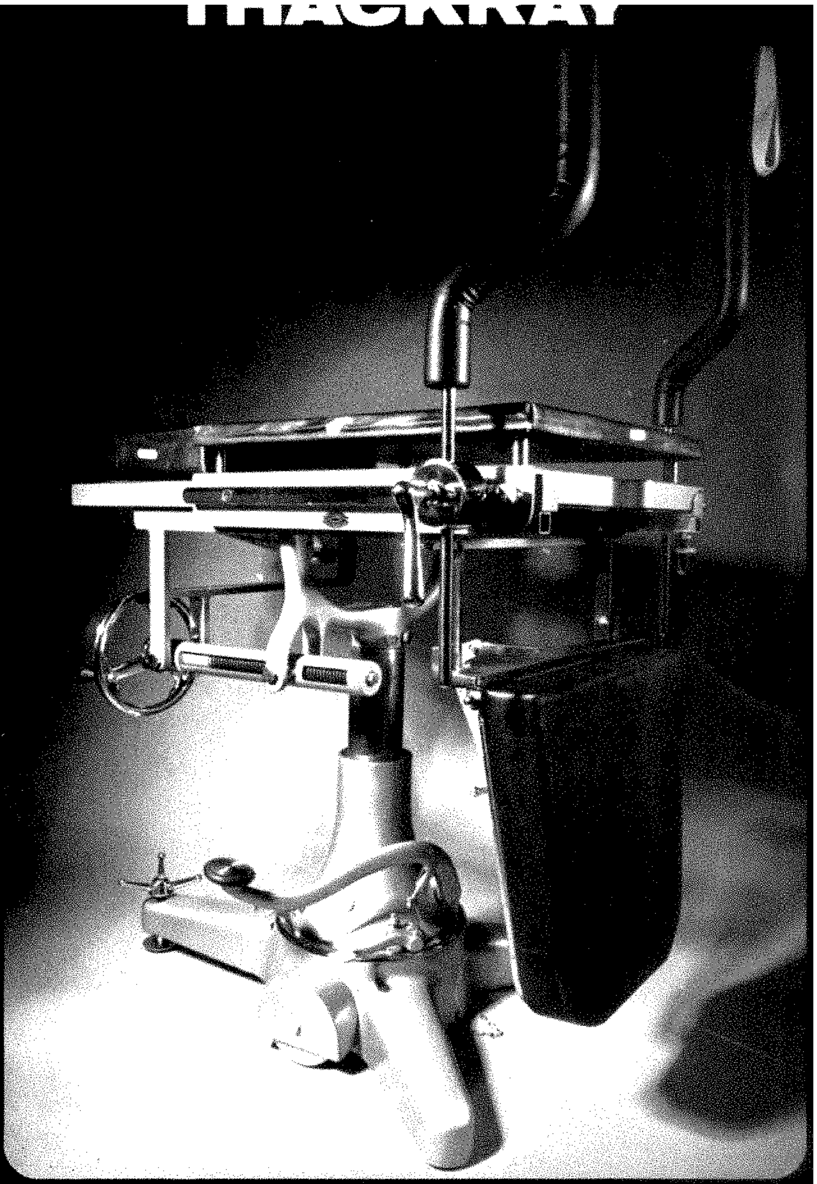

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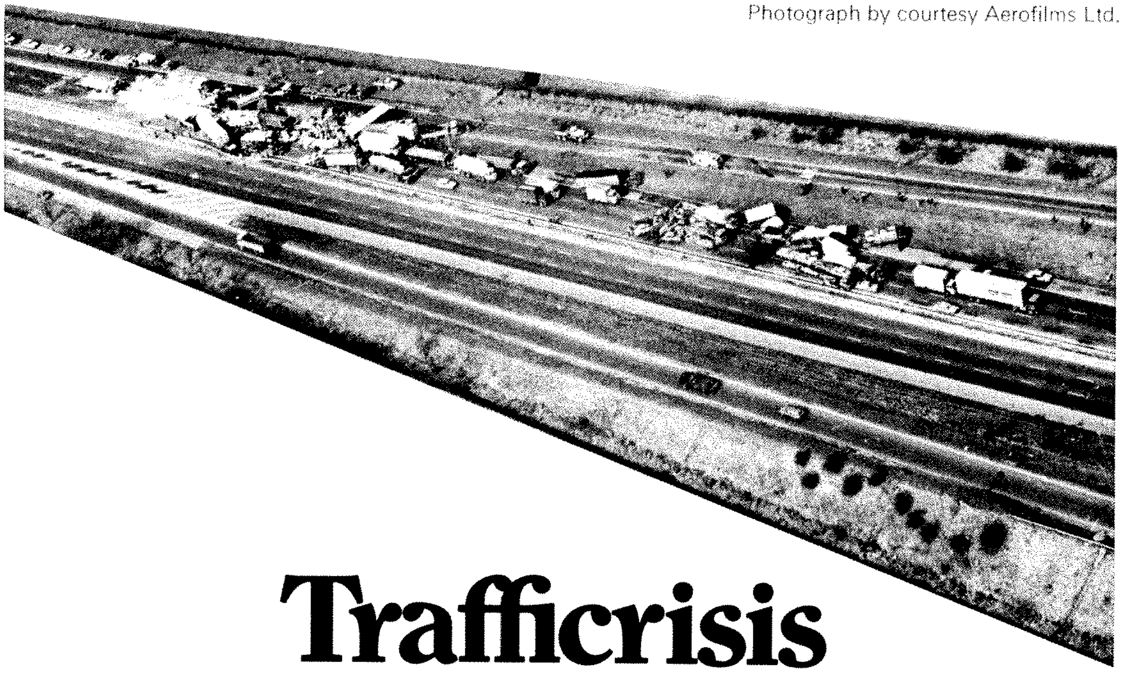

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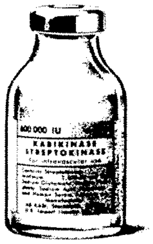

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THE TECHNIQUE AND POSSIBLE APPLICATION OF SUPRA-ORBITAL ARTERY BLOOD-PRESSURE ESTIMATION

By A. P. WYATT, K. RATNAVEL, and G. E. LOXTON

BROOK GENERAL HOSPITAL, LONDON

SUMMARY

An indirect method of measuring systolic blood-pressure in the supra-orbital arteries by an ultrasonic technique is described. The results are repeatable and the expected differences are shown with changes of posture. Calculation of pressure indices has shown significant variation between normal, hypertensive, and arteriosclerotic subjects. The method should be of value in assessing the significance of occlusive lesions of the carotid vessels.

A SIMPLE method of indirect measurement of blood-pressure in the supra-orbital artery should be of value in elucidating the haemodynamics of the cerebral circulation. There are many techniques available at present, such as ophthalmodynamometry (Eastcott, 1969), tonometry with carotid compression (Percival and Ridgway, 1968), and thermography (Maudsley, Samuel, Sumerling, and Young, 1968) of the face which probably reflect changes in cerebral circulation, but these are not as easily understood or interpreted as a blood-pressure measurement. Doppler ultrasound studies of blood-flow in vessels of the carotid distribution have also been reported (Brockenborough, 1973). Reversal of flow, if it can be demonstrated in vessels around the orbit, is certainly of significance.

In this article a device incorporating the probe of a Doppler ultrasound blood-flow detector which enables indirect measurement of systolic blood-pressure in the supra-orbital arteries is described.

The Doppler ultrasonic blood-flow detector now in use in clinical practice in most obstetric and vascular units has been well documented (Yao, Gourmos, Hobbs, and Irvine, 1970). The supra-orbital artery is a branch of the ophthalmic artery which itself is the first major branch of the internal carotid artery, so that lateral blood-pressure in this artery should reflect to a degree, depending on anastomotic vessels, the blood-pressure in the distal internal carotid artery. As the supra-orbital artery leaves the orbit to pass over the forehead it lies over the smooth frontal bone and can be compressed against it. Preliminary experiments showed that the ultrasound beam of a Parkes Model 802 blood-flow detector would pass with little attenuation through a thin rubber diaphragm liberally coated on both sides with coupling jelly. A capsule was therefore developed with a lax rubber diaphragm in which the ultrasound probe could be incorporated and in which the pressure, and thus the pressure of the diaphragm on the forehead, could be raised. Increasing pressure in the capsule, balanced against a mercury column, eventually stops flow in the artery as registered by the flow detector and should give a systolic blood-pressure reading as accurately as a sphygmomanometer placed around an arm. The technique which has previously been briefly reported (Wyatt, Ratnavel, and Loxton, 1971) is now described in detail.

MATERIALS AND METHODS

The Apparatus.—The pressure capsule was made of a Perspex box with external dimensions of 3·0 × 3·0 × 3·75 cm. Into the upper surface the probe of a Doppler blood-flow detector (Parkes Model 802) is introduced through an air-tight 'gland'. A connexion through the lateral wall is attached to an air reservoir, rubber bulb pump, and mercury column. A window 2·0 cm. in diameter is cut in the lower surface of the capsule to which the rubber diaphragm is attached by a circular metal clamp. The diaphragm was initially formed from specially manufactured latex rubber, but the thumb tip of a large rubber surgical glove has been found equally useful. The Perspex capsule is mounted at the corners on small rubber feet which are adjustable to allow for contour differences on the forehead. To prepare the capsule for use a liberal quantity of ultrasound contact jelly is introduced into the capsule to reach the concave surface of the diaphragm and the ultrasound probe is manipulated into the jelly to as low a level as possible without interfering with the action of the diaphragm. The outer surface of the diaphragm is also coated with the jelly.

The Examination.—The subject is examined lying supine on a couch. The arm blood-pressure is recorded. The supra-orbital artery is then identified with an unmodified Doppler probe and the capsule is placed in position over the site of the artery. The legs of the capsule are adjusted so that with firm manual approximation of the capsule to the forehead the rubber diaphragm (but not the end of the Doppler probe) rests on the forehead. Small adjustments of the position of the probe are now required until flow in the vessel is identified. Pressure in the capsule is raised and the values necessary just to obliterate flow and at which flow returns are noted. The mean of these is recorded. This is repeated three times. The readings are then repeated with pressure first on one and then on both temporal arteries to make sure that the vessel concerned is not a branch of these. The brachial systolic pressure is recorded once more. Next the subject sits in a chair against a wall and the measurements are repeated in this position.

Subjects.—Three categories of people were selected for examination in the preliminary investigation of this device.

Normal Subjects.—By this we meant subjects under 40 years of age in normal health. These subjects were nurses, medical students, doctors, and patients in the surgical ward for hernia repair.

Hypertensive Subjects.—These were young patients under investigation for hypertension who, as far as could be ascertained, did not yet suffer from degenerative arterial disease.

Arteriosclerotic Subjects.—These were patients attending the arterial clinic with intermittent claudication but without evidence of cerebrovascular disease, diabetes, or gross hypertension.

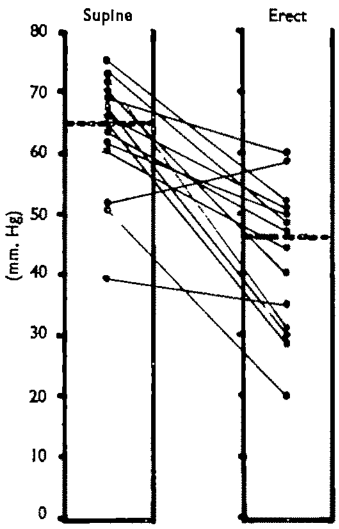

Fig. 1.—Differences between supra-orbital artery pressures in normal subjects in supine and erect positions.

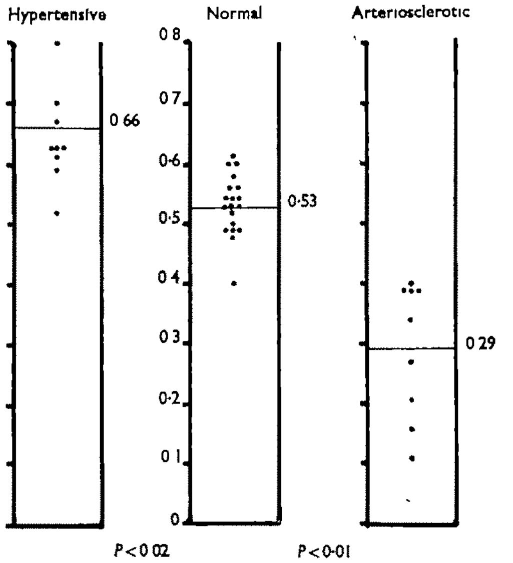

Fig. 3.—Comparison of the pressure index in normal, hypertensive, and arteriosclerotic subjects.

RESULTS

The number of subjects in each category is set out in *Table I*. It will be seen that in 1 'normal' subject only one supra-orbital artery could be found and recorded.

Table II sets out, in a somewhat foreshortened form, the values obtained in 1 subject, illustrating that the results are repeatable.

An analysis was made of the differences measured between right and left arteries in each category of patient in both erect and supine positions. In none of the six categories thus obtained and subjected to Student's t-test was there any significant difference between the left and the right supra-orbital pressures, nor was there any difference in the whole series.

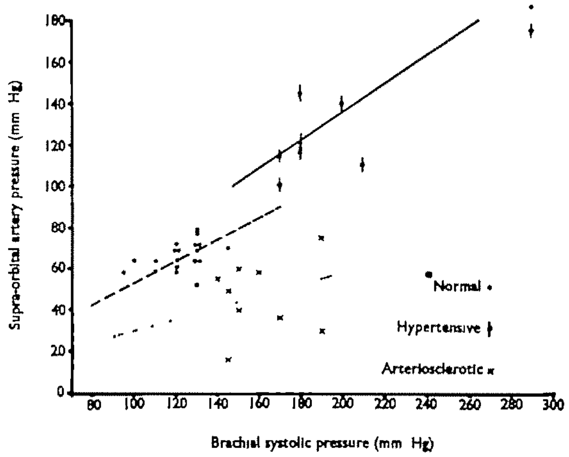

Fig. 2.—Composite graph of all the values obtained in the supine position expressing supra-orbital artery pressure in terms of brachial systolic pressure.

Table I.—Number of Subjects and Arteries examined in Each Category

Subjects	*No. of Subjects*	*No. of Arteries*
Normal	19	37
Hypertensive	9	18
Arteriosclerotic	9	18
Total	37	73

Table II.—Supra-orbital Artery Pressure Estimations obtained in a Normal 29-year-old Male

	Supra-orbital Artery Pressure (mm. Hg)	
	Right	Left
Lying supine*	63 62 63	64 65 68
Ipsilateral temporal artery occlusion	61	68
Bilateral temporal artery occlusion	61	70
Sitting erect†	45	30

* Brachial blood-pressure 110/75 mm. Hg.
† Brachial blood-pressure 110/70 mm Hg

When pressure differences in the supine and erect position were sought significant values were obtained. *Fig.* 1 illustrates these differences in the normal subjects. It can clearly be seen that the pressures are significantly higher in the supine position. The mean difference in the normal group was 19 mm. Hg ($P<0{\cdot}01$), in the hypertensive group it was 18 mm. Hg ($P<0{\cdot}02$), and in the arteriosclerotic group it was 15 mm. Hg ($P<0{\cdot}05$). There is no significant difference between these three means.

Fig. 2 is a composite graph of all the values measured in the supine position. The three categories of patients are clearly grouped. It is obvious that the pressure recorded will be related to the brachial systolic pressure. A valid comparison between these groups must take the variations of systemic blood-pressure into account. A pressure index has therefore been calculated after Yao, Hobbs, and Irvine (1969):—

$$\text{Pressure index} = \frac{\text{Supra-orbital artery pressure}}{\text{Brachial systolic pressure}}.$$

Using the mean of right and left supine supra-orbital artery pressures the mean pressure index in normal subjects was found to be 0·53. In the hypertensive group of subjects the mean pressure index was 0·66. These means are significantly different ($P < 0{\cdot}02$). The mean pressure index of arteriosclerotic subjects was 0·29. This again is significantly different from the normal ($P < 0{\cdot}01$; *Fig.* 3).

DISCUSSION

The results obtained with this apparatus strongly suggest that a function of the blood-pressure in the supra-orbital artery is being recorded, if not the true pressure. Particularly significant is the change in pressure related to the change in posture from supine to erect. The mean difference of 17 mm. Hg found is equivalent to 23 cm. H_2O and this is about what would be expected taking the hydrostatic effect of the blood column in the erect posture into account. The repeatability of the measurements and absence of any significant difference between left and right sides are also arguments for their validity. Occlusion of the superficial temporal vessels should have ruled out erroneous measurement of pressure in branches of the external carotid system. Only 1 out of 74 possible arteries could not be located and examined in this series (1·3 per cent). This may well have been due to an anatomical abnormality.

Somewhat unexpected was the apparently low value of systolic pressure in the supra-orbital artery compared with that in the brachial artery. So far we have not been successful in making direct measurements in this vessel to confirm these values, but one would expect errors as a result of pressurizing the capsule to give readings on the high rather than on the low side of normal. Wisnant, Siekert, and Milliken (1962), using ophthalmodynamometry, suggested that ophthalmic artery systolic pressure is approximately 55 per cent of the corresponding pressure in the brachial artery. This agrees very closely with our figure of 53 per cent amongst the normal subjects.

Hypertensive patients were studied to give a wide spread of systolic pressures and thus indicate the relationship of supra-orbital and brachial pressures clearly. However, a difference in the mean pressure index between the normal and hypertensive groups has been demonstrated and must be due to a difference in resistance of the vessels concerned. In a similar way, with the claudicating patients it appears that we have demonstrated at least a relative increase in resistance of these branches of the internal carotid system which may well reflect the presence of the disease process in these vessels.

This method of measurement is rather more easily learnt and simpler to perform than ophthalmodynamometry. It may be more accurate and should be useful in exactly the same situations. Preliminary measurements in a small number of patients with internal carotid stenoses and occlusions have shown distinct differences in the comparison of right- and left-sided supra-orbital pressure measurements (Wyatt, Ratnavel, and Loxton, 1973).

Acknowledgements.—We wish to acknowledge the help of Mr. J. H. Savage, F.I.E.E., who designed and made the capsule. Thanks are also due to L.R. Industries who made the rubber diaphragms. The ultrasound equipment was purchased with an Ernest Hart Research Award given by the British Medical Association.

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TREATMENT OF COMBINED EXTERNAL ILIAC ARTERY AND VEIN INJURY BY CROSS-OVER FEMOROFEMORAL ARTERIAL AND VENOUS GRAFTS WITH TEMPORARY ARTERIOVENOUS SHUNT

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SUMMARY

The case is presented of a patient whose left external iliac artery and vein were inadvertently divided during attempted intestinal resection for diverticulitis of the sigmoid colon.

Gangrene of the leg was almost inevitable, direct vascular surgery was impossible, but an indirect approach by thrombectomy and double cross-over femorofemoral arterial and venous grafts with temporary arteriovenous shunt fully restored the life of the limb.

During the operation severe bleeding occurred through the mesh of the woven Teflon prosthesis.

THE external iliac artery and vein may together be severed in gunshot wounds or may be intentionally or accidentally divided during pelvic operations, particularly in neoplastic disease.

In the absence of infection, local replacement surgery with an arterial prosthesis and a venous vein-graft may be possible, although for reasons discussed in this paper the latter is often unsuccessful. Likely major complications are arterial and venous thromboses resulting from circulatory stasis.

It is suggested that these problems may be resolved by the surgical treatment described here.

CASE REPORT

Mrs. D. P., a 76-year-old housewife with chronic rheumatoid arthritis, presented at another hospital complaining of a painful mass in the left iliac fossa, fever, and diarrhoea. A barium-enema examination showed extensive diverticular disease and suggested an intraluminal filling defect. After sigmoidoscopy had shown no lesion, laparotomy was performed. During 'trial dissection' of a fixed mass in the lower pelvic colon, which in retrospect was certainly an area of diverticulitis, torrential haemorrhage from the iliac vessels was encountered; this was controlled by ligature, transverse colostomy was performed, and the operation was abandoned.

Postoperatively the left leg was noted to be blue and cold, the toes were hypo-aesthetic, and pulses were absent, but the superficial veins were distended. It therefore seemed certain that both the external iliac artery and the vein had been transected and that in the absence of treatment gangrene was inevitable.

The patient was transferred to Torbay Hospital for vascular surgery. Since direct operation on the iliac vessels was out of the question it was decided to perform combined arterial and venous femoral cross-over grafts with an arteriovenous shunt to improve the chances of maintaining venous patency.

Eleven hours after her first operation the left femoral vessels were exposed in the groin by a vertical incision under general anaesthesia. Already both the artery and vein were solid with thrombus which in the latter case extended down into the calf. After intravenous administration of 5000 units of heparin, arterial and venous thrombectomies were done with Fogarty catheters and complete obstruction of the iliac vessels about 4 cm. above the inguinal ligament was confirmed. The right long saphenous vein was then exposed, divided just below the mid-thigh, and mobilized up to the saphenofemoral junction; this vein was then brought across suprapubically in a subcutaneous tunnel to the left groin wound where the arteriovenous shunt was first formed by joining it end to side* to the left femoral artery (*Fig.* 1A) to provide a venous outflow path from the left leg. The thrombectomy opening in the left femoral vein was then anastomosed side to side to the transposed right long saphenous vein. It was thus arranged that the vein-graft would be perfused by a mixture of arterial and venous blood. With venous drainage now restored, an arterial supply to the left leg was provided by a woven Teflon cross-over femorofemoral graft placed proximally, parallel to the vein-graft, in a separate subcutaneous tunnel. On removing the clamps very severe bleeding through the interstices of the graft ensued despite neutralization of heparin with protamine sulphate and empirical administration of epsilon aminocaproic acid; eventually, when hope was fading after 17 units (8500 ml.) of blood had been transfused, bleeding eventually stopped; subsequent investigation failed to reveal any underlying haemorrhagic tendency. In view o the primary intra-abdominal sepsis trimethoprim and sulphamethoxazole were given in the postoperative period. The only transient complication was a deep venous thrombosis in the left calf on the thirteenth day, which was treated with anticoagulants.

Angiography 10 weeks after operation confirmed that both the arterial and venous grafts were patent (*Fig.* 1).

It is proposed to close the arteriovenous shunt at the time of the patient's elective colonic surgery.

DISCUSSION

Combined injuries of the external iliac artery and vein are usually repaired by direct surgery. Because of the size of the artery a woven or knitted prosthesis is usually employed, and in the case of the iliac vein reliance is placed on a saphenous graft. Unfortunately grafts in the venous system commonly thrombose unless a temporary peripheral arteriovenous fistula is fashioned (Dumanian, Santschi, Park, Walker, and Frahn, 1968). The direct surgical approach, and particularly the use of a synthetic arterial prosthesis, is not uncommonly precluded by bacterial contamination, frank sepsis, or malignancy, and it is in such circumstances that limbs may be saved by an indirect approach with cross-over arterial and venous femorofemoral grafts as described here.

Simple autogenous vein-grafts in the venous system commonly thrombose. Vein walls depend on the vasa vasorum for their arterial supply and venous drainage, but in venous grafts virtually the only source of nourishment to the wall is by diffusion from the lumen; venous blood, however, has a low oxygen content and is also under reduced pressure.

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* For all anastomoses 50 Mersalene was used.

Temporary arteriovenous shunts increase the patency rate of venous vein-grafts (Johnson and Eiseman, 1969; Levin, Rich, Hutton, Barker, and Zeller, 1971). This favourable influence is probably the result of, first, improvement in the diffusion gradients across the vein wall during the critical time before the vein acquires a new blood-supply from the surrounding tissues, and, secondly, increased flow and pressure which discourage thrombosis and help to prevent apposition and adhesion of opposite sides of the ischaemic vein wall during any temporary compression or kinking.

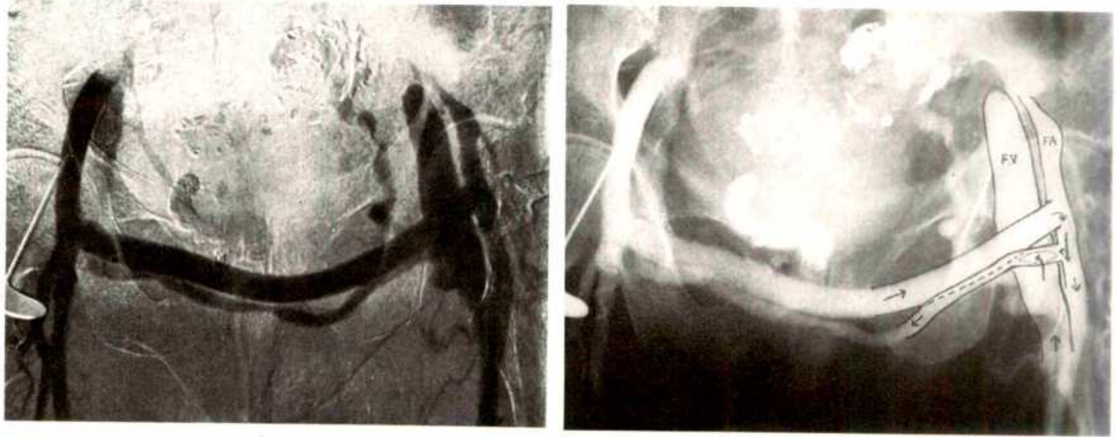

FIG. 1.—Angiograms via the right femoral artery showing contrast medium flowing across suprapubically through the Teflon prosthesis to the left femoral artery whence part is perfusing the left femoral arterial tree and part is returning with venous blood from the left femoral vein through the saphenous graft to the right femoral vein. A is a positive print made by the photographic subtraction technique. B is a diagram superimposed on the photographic negative.

The severe bleeding through the mesh of the woven Teflon graft in our patient seems most likely to have been caused by a consumption coagulopathy associated with recent operation and extensive thrombosis in the iliac and femoral veins and arteries. In such cases prostheses with as fine an impervious mesh as possible seem to be indicated.

Acknowledgement.—I would like to thank Dr. Victor Mitchell, Consultant Radiologist at the Torbay Hospital, for the angiograms.

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PHYTOHAEMAGGLUTININ-STIMULATED TRANSFORMATION OF PERIPHERAL AND LYMPH-NODE LYMPHOCYTES IN PATIENTS WITH GASTRO-INTESTINAL CANCER

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SUMMARY

Phytohaemagglutinin-induced lymphocyte transformation has been studied in 10 patients with gastro-intestinal cancer and in 8 control subjects. When cultured in autologous serum, peripheral lymphocytes from cancer patients exhibited lower transformation indices (L.T.I.) than did those of control subjects. Culture in AB serum resulted in an elevation of the L.T.I. of peripheral lymphocytes from cancer patients whilst those of the controls were essentially unchanged. Of 6 control subjects, 5 showed reduced L.T.I.'s when their circulating lymphocytes were cultured in serum from cancer patients. Mesenteric lymph-node lymphocytes from patients with cancer also showed lower indices compared with the control group and these were elevated by culture in AB serum.

THERE is currently much interest in the role of lymph-nodes in the immunological control of malignant disease in man. In the experimental situation it can be shown that the implantation of tumour cells provokes an increase in the number of transformed lymphocytes appearing in the lymph-nodes draining the tumour (Hall and Morris, 1963), though this is not necessarily tumour-specific. Similarly, the recent work on immunological defence mechanisms in breast cancer has suggested that enhanced lymphocytic activity is present in the axillary lymph-nodes draining the tumour provided that neoplastic involvement has not yet occurred (Humphrey, Barker, Bohesch, Fetter, Amerson, and Boehm, 1971; Deodhar, Crile, and Esselstyn, 1972). Indeed, these findings have influenced the approach to the clinical management of breast cancer (Crile, 1965).

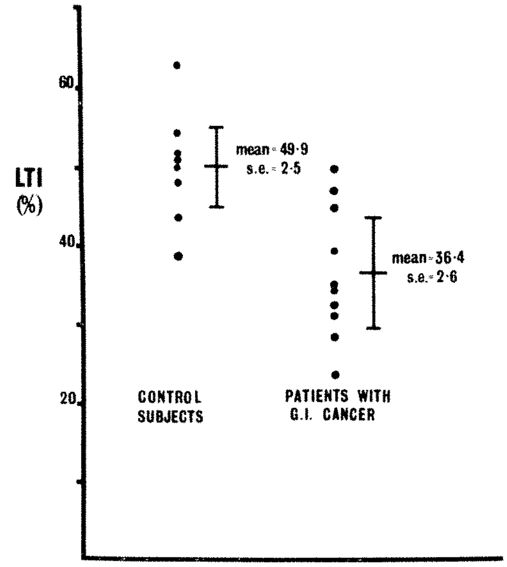

FIG. 1.—The transformation indices of peripheral lymphocytes of control subjects and patients with gastro-intestinal cancer after exposure to PHA and culture in autologous serum.

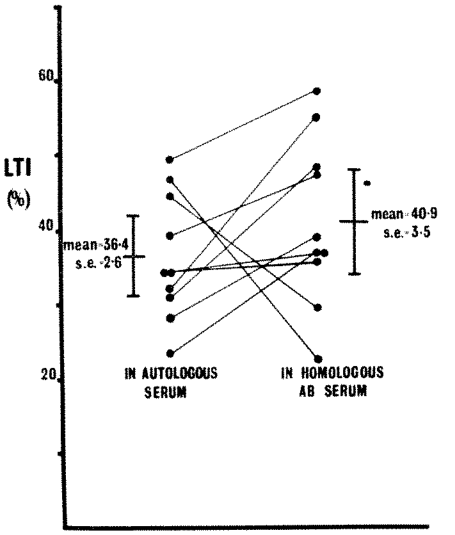

FIG. 2.—The transformation indices of peripheral lymphocytes in response to PHA of 10 patients with gastro-intestinal cancer comparing the degree of transformation obtained by culture in autologous serum with that in homologous AB serum.

Since these observations may apply to other neoplasms we have commenced a series of investigations into the immunological responses of lymph-nodes draining gastro-intestinal cancer in man. The purpose of the present study was to investigate the responses of lymph-node lymphocytes and circulating lymphocytes to stimulation with phytohaemagglutinin (PHA), comparing the results obtained from patients with cancer with those found in control subjects.

MATERIAL AND METHODS

Peripheral lymphocytes were obtained from 20 ml. of defibrinated venous blood by a modification of the method of Coulson and Chalmers (1964), utilizing methyl-cellulose sedimentation with the addition of carbonyl iron to remove polymorphs. Lymph-node lymphocytes were obtained from all lymph-nodes under study by fine mincing and filtration through a sterile 33 μ diameter sieve.

All the lymphocytes were cultured at a cell concentration of 10^6 per ml. of medium 199 (Burroughs Wellcome) containing 20 per cent serum and antibiotics. The serum in use was either autologous serum or homologous AB serum obtained from a pool of 7 healthy donors. PHA was added at a concentration of 0·05 ml. per ml. of culture medium. All the cultures were performed in duplicate in plastic tissue-culture flasks (Falcon Plastics 3012) using 5-ml. aliquots per culture. The cultures were incubated at 37° C. for 72 hours, the final half-hour of culture being accompanied by the addition of 0·1 μc. of tritiated thymidine (Radiochemicals, Amersham). At the end of this period the cells were harvested, washed three times in T.C. 199, and smeared on glass slides. Following fixation in methanol, autoradiography was performed on these smears which were then stained by routine haematological methods (Giemsa). For each culture performed at least 3000 cells were counted microscopically and the number of labelled cells demonstrating radioactive uptake was expressed as a percentage of the total number of cells counted. This expression we have termed the lymphocyte transformation index (L.T.I.).

Clinical Groups.—

1. *Patients suffering from Gastro-intestinal Cancer.*—Ten patients suffering from cancer were studied and consisted of 5 patients with carcinoma of the rectum, 4 with colonic carcinoma, and 1 patient with a carcinoma of the stomach. Peripheral blood and lymph-node lymphocytes were obtained from all these patients and the lymphocytes were cultured both in autologous serum and in pooled homologous AB serum. All the patients underwent laparotomy and resection, at which time lymph-nodes were removed from the root of the mesentery and from an area directly draining the cancer wherever possible. Altogether 15 lymph-nodes were studied from these patients.

2. *Control Subjects.*—There were 8 control subjects who were all undergoing laparotomy for non-malignant conditions (cholelithiasis, duodenal ulceration, hysterectomy, or diverticular disease), at which time mesenteric and juxta-intestinal lymph-nodes were obtained. Seventeen nodes were obtained from these subjects and lymphocytes isolated from them were cultured in autologous serum only. Peripheral blood lymphocytes were obtained from the control subjects just prior to operation and were cultured in

both autologous serum and in pooled homologous serum. In addition, the peripheral lymphocytes of 6 of the control subjects were also cultured in 20 per cent pooled serum from the patients suffering from cancer.

One-half of each lymph-node under study was also fixed in formol–saline for subsequent histological examination.

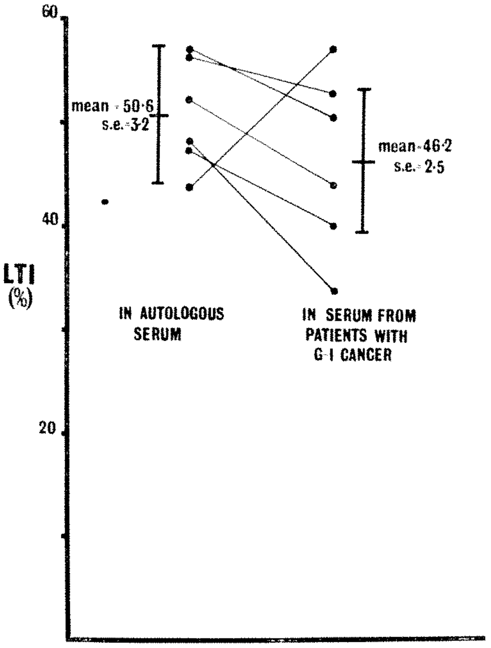

FIG. 3.—The transformation indices of 6 control subjects whose peripheral lymphocytes were cultured in autologous serum and a pooled serum from patients with gastro-intestinal cancer.

RESULTS

Peripheral Blood Studies.—

Culture in Autologous Serum.—The mean L.T.I. of the 8 control subjects whose lymphocytes were cultured in autologous serum was 49·9 ± 5·0 (± 2 S.E.M.). Similar studies using the peripheral cells from the 10 patients with cancer resulted in a mean L.T.I. of 36·4 ± 5·2. The difference between the L.T.I.'s obtained for these two groups was statistically significant at less than the 2 per cent level ($t = 3{\cdot}89$; *Fig.* 1).

Culture in Homologous AB Serum.—The effect of culture in pooled homologous AB serum was variable, with 3 control subjects showing minor elevations in the L.T.I. when compared with culture in autologous serum, 2 showing minor diminutions in L.T.I., and the remainder showing no change. The mean L.T.I. for the group as a whole, however, remained at 50·5 ± 4 and the differences observed for the control group when culture was performed in homologous AB serum rather than autologous serum were not statistically significant ($t = 1{\cdot}49$). When the lymphocytes from the patients with cancer were cultured in homologous AB serum, 8 of the 10 patients demonstrated increased transformation indices when compared with culture in autologous serum (*Fig.* 2). The remaining 2 samples showed marked decreases. The mean transformation index for this group of patients was 40·7 ± 9 and this increase in the mean value above that obtained for culture of the same cells in autologous serum is just significant at the 5 per cent level using the Wilcoxen signed rank test.

Culture of Control Lymphocytes in the Serum of Patients suffering from Cancer.—Of the 6 control subjects whose peripheral lymphocytes were cultured in the pooled serum from the patients with cancer, 5 showed a diminution in their transformation indices but 1 showed a marked elevation (*Fig.* 3). The mean transformation index for this group of 6 subjects fell from 50·6 ± 6·4 when cultured in autologous serum to 46·2 ± 5 when culture was performed in serum from the patients with cancer. This difference, however, does not reach statistical significance.

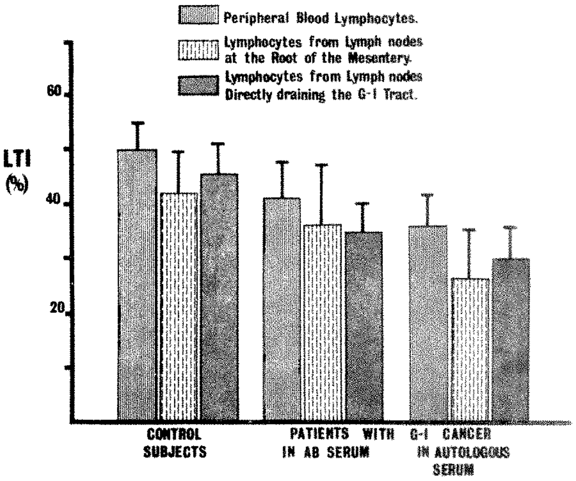

FIG. 4.—The lymphocyte transformation indices of cells obtained from the peripheral blood, root of mesentery lymph-nodes, and lymph-nodes directly draining the colon and associated neoplasm (mean values ± 2 S.E.M.).

Lymph-node Studies.—

Culture in Autologous Serum.—Lymphocyte cultures in autologous serum were prepared from all 17 lymph-nodes taken at laparotomy from the control subjects. The mean L.T.I. for this group was 43·6 ± 4·5 and the results were similar in all respects to those obtained from peripheral lymphocytes in the same subjects. When lymph-nodes in a juxta-intestinal position were considered the mean L.T.I. was 44·9 ± 2·8 compared with a mean L.T.I. of 41·2 ± 8 in lymphocytes obtained from lymph-nodes at the root of the mesentery (*Fig.* 4).

The mean L.T.I. of cells taken from the 15 nodes obtained at operation from the patients with gastro-intestinal cancer was 28·6 ± 5·8. This value was significantly lower than that observed for cells obtained from the nodes of the control subjects ($t = 5{\cdot}11$, $P < 0{\cdot}02$). Lymph-node lymphocyte values were also significantly lower than those obtained for the peripheral lymphocytes of these patients with cancer ($t = 2{\cdot}64$, $P = 0{\cdot}05$). When lymph-nodes directly draining the lesion were considered the mean L.T.I. obtained for these cells was 30·6 ± 6·4 compared with a mean L.T.I. of 26·8 ± 9·6 for cells from the root of the mesentery (*Fig.* 4). This difference, however, was not statistically significant.

Culture in Homologous AB Serum.—Only the lymphocytes isolated from the lymph-nodes obtained from the patients with cancer were cultured in homologous AB serum and this resulted in a mean transformation index of 35·8 ± 6·2. This figure is significantly different at the 5 per cent level from the results obtained for the same nodal lymphocytes when culture was performed in autologous serum ($t = 2{\cdot}48$). Again considering the results with regard to whether the cells were obtained from lymph-nodes directly draining the lesion or those at the root of the mesentery the former gave a result of 34·8 ± 5·4 whilst the latter gave a result of 36·7 ± 11·2. The difference between these two figures is not statistically significant.

Histological Studies.—Foci of metastatic disease were found to be present in the investigated lymph-nodes removed from alongside the lesions of 3 of the patients with gastro-intestinal cancer. The lymphocyte transformation indices of the cells obtained from these nodes varied little from the mean for the group as a whole. In addition, the transformation indices for both the peripheral and lymph-node lymphocytes bore no relationship to the final pathological grading of the lesion, the 10 cases being eventually divided equally between the Dukes classification B and C (Dukes, 1957).

DISCUSSION

Gastro-intestinal cancer may spread by local invasion and along lymphatic channels. Thus, the neoplasms involve mesenteric nodes draining the tumour and ultimately the lymph-nodes alongside the aorta. This tendency has led to the classification of the extent of invasion by these carcinomas described by Dukes (1957) which has proved useful in predicting the eventual outcome for the individual patient. The principles of surgical excision have, therefore, been directed to removal of the primary tumour and the regional nodes draining it as far as the aortic chain. While this is still an accepted surgical procedure, clinicians treating other tumours, notably breast cancer, have argued that not only is this practice unnecessary but that it may adversely affect the ultimate prognosis (Crile, 1968). The rationale of this argument is that the lymph-nodes which drain the tumour may be the site of a delayed hypersensitivity response against antigens present in the tumour and thus removal of these nodes deprives the patient of this natural defence.

Experimentally it has been demonstrated that following the administration of an antigenic inoculum increased numbers of immunoblasts are found in the regional lymph-nodes draining the site of injection. It has been suggested that this recruitment of sensitized lymphocytes involves their recognition of and commitment to particular antigens and is amongst the earliest of events in the initiation of an immune response. Lymphocytes removed from stimulated nodes and labelled with ^{51}Cr will home into the regional nodes of syngeneic animals immunized with the same antigen (Hall and Morris, 1963; Delorme, Hodgett, Hall, and Alexander, 1969; Zatz and Lance, 1971).

However, it has become apparent from the work of Alexander, Benstead, Delorme, Hall, and Hodgett (1969) that lymph-nodes draining experimental tumours will not release these committed cells into the general circulation until the bulk of the tumour has been removed. These observations have encouraged some surgeons to modify their management of early breast cancer in the hope that by extirpation of the tumour alone, immunoblasts will be released from uninvolved axillary nodes and impair the growth of residual tumour (Crile, 1965). It is too early to comment upon the clinical results of this approach.

It has been shown that adenocarcinomas of the gastro-intestinal tract possess surface antigens which may be capable of evoking an immune response in the patient (Gold and Freedman, 1965; Hellstrom, Hellstrom, and Shepard, 1970; Kleinman, Harwell, and Turner, 1971). It therefore seems pertinent to examine the immune competence of lymphocytes present in the lymph-nodes draining such tumours. In this study lymphocytes extracted from the peripheral blood and from mesenteric lymph-nodes have been investigated with regard to their ability to undergo blast-cell transformation *in vitro* in response to PHA. In control subjects 45–50 per cent of lymphocytes from each of these sites were observed to undergo transformation. In patients with gastro-intestinal cancer, however, lymphocytes from the peripheral blood and from the mesenteric nodes exhibited significantly lower transformation indices than those from the corresponding sites in the control subjects. Furthermore, cells from nodes directly draining the tumours of these patients exhibited significantly lower transformation responses than those observed for their circulating lymphocytes. A similar gradient of response of mesenteric lymph-node and peripheral lymphocytes has been described previously by us in relation to Crohn's disease of the ileum (Guillou, Brennan, and Giles, 1973).

The significance of these results is far from clear. Since PHA produces blast-cell transformation only in cells which are thymic-derived, the results of this study might be interpreted as indicating a reduction in the number of such lymphocytes in the circulating and lymph-node populations in patients with gastro-intestinal cancer. An alternative explanation would involve the concept that the immunological function of the lymphocytes of these patients is impaired by factors as yet undefined or that the lymphocytes are already immunologically committed and thus rendered unresponsive to PHA.

It would appear that a lymphocyte depressive factor is circulating in the patients with gastro-intestinal cancer since after thorough washing and culture of these lymphocytes in homologous AB serum, the response to PHA becomes significantly elevated. Similar depressive factors have been reported in a number of chronic infective illnesses associated with massive antigenic stimulation (Gatti, 1971) and in other forms of malignant diseases (Silk, 1967; Whittaker, Rees, and Clark, 1971). The nature of these factors is as yet unknown, though α-globulins, antibody excess, and circulating antigen have been implicated in this role (Cooperband, Boudevik, Schmid, and Mannick, 1968; Currie and Basham, 1972; Oppenheim, 1972). Whatever the nature of these factors, it is apparent that they are only partially responsible for the altered responses to PHA, for even when culture is performed in homologous serum the lymphocytes do not transform as frequently as in control subjects. Thus it must be presumed that the lymphocytes themselves are in some way affected by the presence of the cancer.

It remains unclear whether the lymph-nodes draining gastro-intestinal cancer behave in the same manner as those draining experimental animal tumours. Lymphocyte transformation indices in the nodes containing tumour metastases were similar to those which were free of tumour and it is not clear whether the lymph-node cells were sensitized by the tumour. It will be of importance to test the response of these lymph-node lymphocytes to specific tumour antigens by the use of other techniques. In this way we may be able to determine precisely the role of lymph-nodes in the immunological control of gastro-intestinal cancer.

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SHORT NOTES OF RARE OR OBSCURE CASES

PRIMARY ARGENTAFFINOMA OF THE OVARY

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SUMMARY

A case is presented of primary argentaffinoma of the ovary, without metastases, that gave rise to the systemic manifestation of the carcinoid syndrome. Removal of the tumour led to regression of all symptoms. This case illustrates that single argentaffinoma tumours which drain directly into the systemic venous system may cause the carcinoid syndrome and removal may be curative in that the disease process is arrested.

CARCINOID tumour arising as part of a teratoma of the ovary was first described by Stewart, Willis, and de Saran (1939). Since then, Gabrilove (1941), Falkmer (1956), Betson and Golden (1959), and Evans, Harris, and McDougall (1959) have described cases. Somewhat more rare, however, must be the appearance of the carcinoid syndrome associated with an argentaffin tumour of the ovary. The first case was described by Sauer, Dearing, Flock, Waugh, Dockerty, and Roth (1958), and up to 1965 only 3 more cases had been described (Thorson, Pernon, Soderstrom, Waldenstrom, Winblad, and Wulff, 1958; Torvick, 1960; Kephart, Jackson, and Caylor, 1960). A further case is reported here of the carcinoid syndrome produced by a primary argentaffinoma of the ovary.

CASE REPORT

A 29-year-old woman was admitted to hospital with a 2-year history of amenorrhoea and a 3-month history of weight-loss, diarrhoea, and intermittent dyspnoea. She had been married 6 months prior to admission. On examination she had a marked cyanotic malar flush extending over the bridge of the nose. There was a moderate-sized pleural effusion on the left side, ascites, and a large, hard mass arising out of the pelvis. She had a Grade 3 pulmonary systolic murmur, a Grade 2 tricuspid diastolic murmur, and a marked expiratory wheeze over both lung fields. The haemoglobin was 12·4 g., white-cell count 6300 per c.mm., differential count normal, and erythrocyte-sedimentation rate 41 mm. per hour. The urinary 5-hydroxy-indole acetic acid was 188 mg. per g. of creatinine (normal, 10 mg.).

Laparotomy was performed 1 week later and a large tumour was found arising from the site of the left ovary and was adherent to the left Fallopian tube. While the tumour was being handled the malar flush increased in intensity and spread to involve the whole face and neck. The tumour and Fallopian tube were removed completely. Postoperative recovery was uneventful, the bronchospasm disappeared immediately, and the malar flush gradually faded over the next 4 weeks. Two days postoperatively the urinary 5-hydroxy-indole acetic acid had fallen to normal limits.

The patient has been observed for the past 5 years. Her progress has been excellent; she regained her normal weight in 6 months and began menstruation again at 3 months postoperatively. The malar flush has disappeared completely but the cardiac murmurs have remained the same.

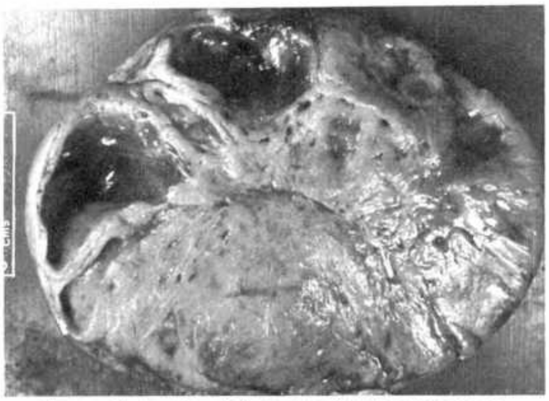

FIG. 1.—Cut surface of the tumour showing cystic spaces.

Three years later she became pregnant but miscarried at 7 months. Repeated checks of the urinary 5-hydroxy-indole acetic acid have remained normal up to the present time.

PATHOLOGY.—Macroscopically, the tumour measured 16 × 12 × 8 cm. and the cut surface showed the presence of three cysts, the largest of which measured 5·5 cm. in diameter. The remainder of the tumour was of solid, slightly yellow tissue of very firm consistency (*Fig.* 1). Microscopically, the picture was that of replacement of ovarian tissue by clumps and columns of uniform, darkly staining cells in a background of fibrous tissue, which was rather hyaline in areas. The appearance was typical of argentaffinoma and the cells showed positive silver- and diazo-staining reactions. No teratomatous tissues were found (*Fig.* 2).

DISCUSSION

The description of the pathological findings is in keeping with that already given by other authors for primary ovarian argentaffinoma (Evans and others, 1959; Willis, 1960). Most ovarian argentaffinomas have clearly shown teratomatous elements, the carcinoid sometimes lying in close proximity to intestinal or respiratory elements (Stewart and others, 1939; Thorson and others, 1958). Williams and Sandler (1963), in their classification of carcinoid tumours, distinguish three divisions on an embryological basis: bronchial, gastric, and pancreatic carcinoids are foregut derivatives; intestinal carcinoids from the mid-duodenum to the proximal half of the colon are of midgut origin; those of the distal colon and rectum are of hindgut origin, and these carcinoids have a trabecular pattern, the cells of which are negative to silver stains. In the present case the tumour cells were reactive to silver and therefore the carcinoid is unlikely to be of hindgut origin.

It is generally accepted that extensive hepatic metastases must be present in intestinal argentaffinomas before the systemic effects are found. The importance of recognizing that the carcinoid syndrome can be caused by argentaffinoma of the ovary lies in the fact that the veins of the ovary drain directly into the caval system and, therefore, the secretion from the tumour is not inactivated in the liver. If the primary tumour is in the ovary its removal, as in the present case, may well be curative, at least in the sense that the disease process is arrested.

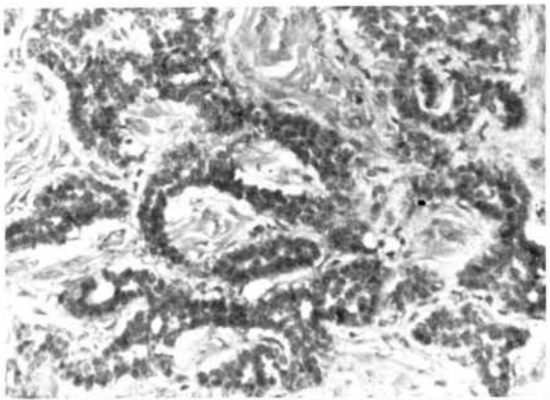

FIG. 2.—Positive silver staining of a section of the tumour showing the distribution of the cells in columns in a background of fibrous tissue (× 25.)

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DUPLICATION OF THE MALE URETHRA

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SUMMARY

A brief report of 3 cases of duplication of the male urethra, 2 of which were complete duplications, is presented.

DUPLICATION of the urethra occurs in association with duplication of the bladder and/or diphallus and other congenital abnormalities. Occurring as the only major deformity, duplication of the urethra has been described as complete or incomplete. In the rarer complete form there is a separate accessory urethra which has an external opening on to the skin, in addition to the normal urethra. Gross and Moore (1950) gave an account of cases reported up to 1950 together with 2 cases of their own of complete double urethra; in 1966 Casselman and Williams added 4 cases of complete duplication to the 34 then already reported in the literature. It is very unusual for the two channels to communicate with one another. The accessory external opening is usually on the penis, dorsal to the normal urethra, but may be on the glans or ventral surface of the penis and occasionally at some point removed from the penis itself. Boissonnat (1961) reported a case with the external opening at the penoscrotal junction, while Karanjavala's (1970) case had the accessory opening inside the anterior lip of the anal orifice, and in both cases the accessory urethra was more functional than the normal urethra. This is also true of the case reported by Selvaggi and Goodwin (1972) with an external opening in the perineum, and Williams (1968) refers to 3 cases with a wide channel descending from the bladder neck to open at or just outside the anus associated with a narrow and poorly functioning urethra in the normal situation.

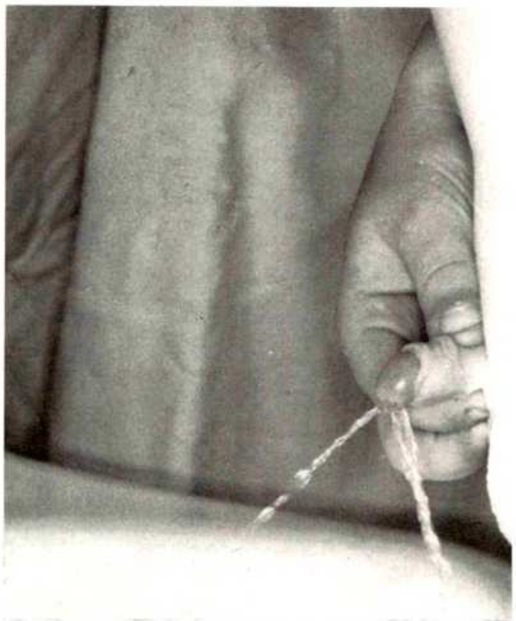

FIG. 1.—*Case* 1. The divergent streams of approximately equal power and volume.

The symptoms associated with complete duplication are listed as incontinence, infection, dorsal chordee, and double stream.

In incomplete duplication there is a segment only of the second urethra which may extend from the bladder outwards or from the penis inwards, usually to end blindly, or occasionally to communicate with the normal urethra. Infection of this accessory channel is the usual cause of symptoms.

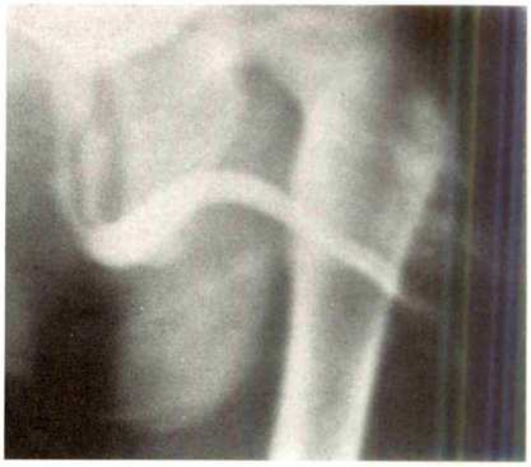

FIG. 2.—*Case* 1. Micturating cystogram which demonstrates the complete double urethra commencing just below the bladder neck.

Three cases are presented here: one of complete double urethra with two channels opening at the normally placed external meatus on the glans penis with a double stream on micturition, a second case with a complete accessory urethra opening externally on the scrotum with urinary incontinence, and one case of incomplete duplication with minimal symptoms.

CASE REPORTS

Case 1.—A. C. was first seen on 8 May, 1967, when he was 5 years old. The history was that he passed his urine in a double stream and tended to wet his legs as the two streams diverged. There was no incontinence or bed wetting. On examination he was a cheerful healthy boy who was normally developed for his age. On the glans penis in the normal situation there were two urethral orifices side by side and on micturition he was seen to pass two separate streams of nearly equal power and volume (*Fig.* 1). Probes were passed up both urethrae and there did not appear to be any connexion between the two in the penile part of the urethra.

INVESTIGATIONS.—An intravenous pyelogram showed no abnormality. A micturating cystogram demonstrated a complete double urethra, commencing just below the bladder neck (*Fig.* 2).

As this little boy had no symptoms at all, except the problem of directing his double stream so that he did not wet himself, no surgical treatment was advised at this time.

He has been followed up at regular intervals. He has managed his double stream very well and it causes him no embarrassment.

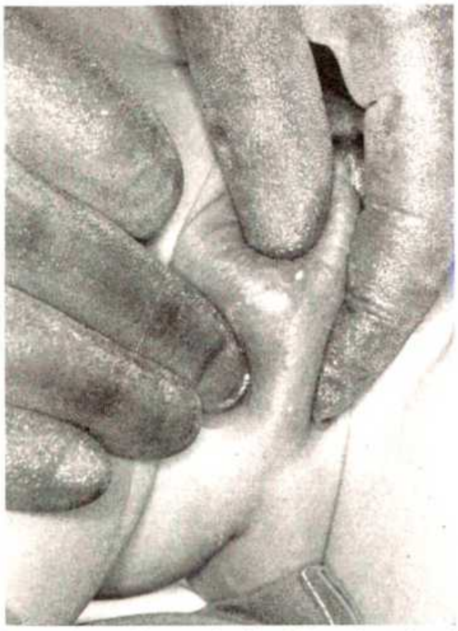

FIG. 3.—*Case* 2. Photograph of the thickened, roughened area on the right side of the scrotum; the small orifice of the abnormal urethra cannot be seen in this photograph.

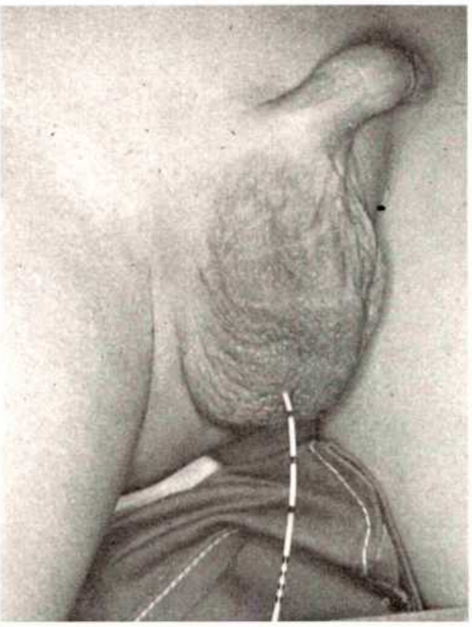

FIG. 4.—*Case* 2. A ureteric catheter inserted into the abnormal urethral orifice.

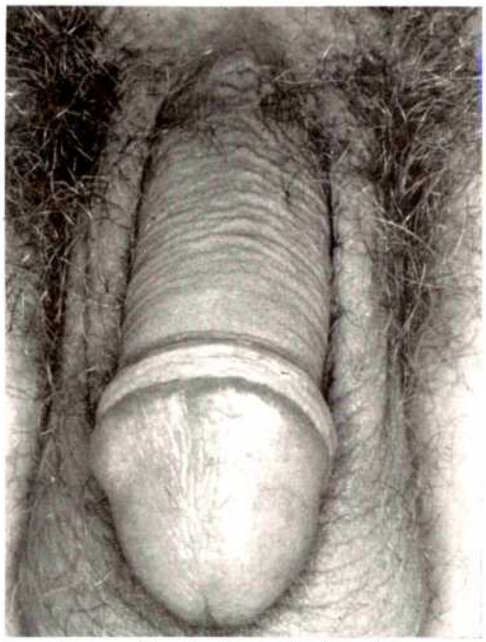

FIG. 5.—*Case* 3. The dimpling and orifice of the accessory urethra can be seen on the dorsal surface of the penis.

Case 2.—S. W., aged 3½ years, was first seen on 17 Jan., 1972. His mother said that he had always been wet since birth. About 3 weeks previously she had noticed urine draining from the right side of the scrotum. She had not observed this before. On examination he was a normally developed child. Both testes were in the scrotum. On the lower part of the right side of the scrotum a small orifice could be seen, around which the scrotal skin was thickened and roughened (*Fig.* 3). From this orifice urine could be seen to ooze out very slowly. A thickening could be felt in the scrotum on this side, separate from the testis. On compressing this thickening, fluid could be expressed from the tiny opening fairly easily. It seemed probable that this was a urinary fistula.

INVESTIGATIONS.—An intravenous pyelogram showed normally functioning kidneys and a urethrogram showed a normal urethra. No communication could be demonstrated between either the urethra or the bladder and the scrotal fistula. No abnormality of the bladder was seen on cystoscopy. A bag was fixed to the scrotum around the fistula, and urine collected in this bag continuously in a considerable quantity although most of his urine was passed via the normal urethra. A ureteric catheter was introduced into the fistula (*Fig.* 4). Injection of Hypaque into the ureteric catheter revealed a cavity in the scrotum, but no communication with the urethra or the bladder could be demonstrated.

Although radiological confirmation was not possible, a diagnosis of duplication of the urethra was made.

OPERATION (27 July, 1972).—The accessory urethra was explored and excised. A ureteric catheter was passed through the orifice and methylene blue was injected into the cavity. A very thick-walled sac was found in the scrotal tissues. It was dissected free and a narrow tube was discovered running from it up to the prostatic urethra. However, neither a ureteric catheter nor a probe could be made to enter the bladder by passing it upwards along this track. The abnormal urethra was traced up to the triangular ligament, pulled down as far as possible, ligatured, diathermied, and divided. The bladder was drained with a Foley catheter.

HISTOLOGICAL REPORT (Dr. H. J. Voss).—'Serial sections through the scrotal tissue show presence of sinus or duct lined partly by squamous epithelium, partly by transitional epithelium. Consistent with heterotopic urethra.'

Convalescence was uneventful. The patient has remained well and dry and passes urine normally.

Case 3.—D. U., aged 35 years, was seen on 5 June, 1967. He gave a history of an opening on the dorsal aspect of the penis which had been present since birth. He had never experienced any trouble with this until 3 weeks prior to being seen, when a painful lump had appeared above this orifice. The swelling had disappeared following discharge of blood from the opening. On examination there was a small orifice on the dorsal surface of the penis (*Fig.* 5) from which a little thin pus could be expressed. No other abnormality was found. Culture of the pus grew micrococci and non-haemolytic streptococci.

INVESTIGATIONS.—An intravenous pyelogram and micturating cysto-urethrogram revealed no abnormality. A urethrogram showed a normal urethra; only a trace of dye could be injected into the abnormal opening on the dorsum of the penis and this outlined a track 2½ cm. long.

In the absence of symptoms no treatment was advised or carried out at that time. A recurrence of infection with discharge of pus from the accessory urethra occurred 3 years later and responded to antibiotics.

DIAGNOSIS

A history of double stream or incontinence should alert one to the possibility of duplication of the urethra; the diagnosis of this condition seems to be long delayed in many cases, particularly with the incomplete duplications, which if they do not produce a dorsal chordee may only cause symptoms if they become infected. The finding of two urethral orifices on examination will suggest the diagnosis very strongly, and observation of a double stream or urine coming from both openings if they are not close together will confirm the diagnosis. Generally, cystoscopy and urethroscopy seem to have been unhelpful. The two urethrae can be visualized on voiding during cysto-urethrography providing that both channels convey a reasonable proportion of the voided urine, but a narrow accessory channel may not be demonstrated. Retrograde urethrograms with injection of dye into both channels may be satisfactory but again this may fail if the accessory channel is small, as in *Case* 2 reported here.

TREATMENT

In the absence of other symptoms a double stream need not be an indication for operation. If there is incontinence from the accessory urethra and a satisfactory lumen and sphincteric control of the normal channel can be demonstrated the accessory urethra should be excised. The passage of most of the urine via the accessory urethra may be a contra-indication to its excision if there is no incontinence from it. The cases described by Karanjavala (1970) and Selvaggi and Goodwin (1972) are examples of this.

AETIOLOGY

The reason for the development of a double urethra remains uncertain; the variable anatomy of the duplication cannot easily be explained by any one of the theories which have been put forward and it is likely that more than one embryological explanation is needed to account for all the cases.

Acknowledgement.—I wish to thank Mr. R. R. Popham for the photography.

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REVIEWS AND NOTICES OF BOOKS

Die Behandlung der hämatogenen und der traumatischen Osteomyelitis. By Stojan Popkirov, Fruhjahr. 9½ × 6½ in. Pp. 408. Illustrated. 1971. Berlin: Veb Verlag Volk und Gesundheit. DM.172.40.

The author, Director of the Clinic for Septic Surgery in Sofia, Bulgaria, gives a detailed account of the general principles and his recommended method of treatment of 380 cases of osteomyelitis. Three-quarters of these patients suffered from haematogenous osteomyelitis, and the remainder from chronic osteomyelitis following trauma.

The radical removal of all necrotic tissue, especially bone, is stressed and the techniques for every bone are well illustrated. Over 300 of the patients received a bone-graft, with homologous grafts being transplanted twice as often as autologous grafts and three times as often as heterologous bone-grafts. In the infected non-union osteomyelitis with fractures, rigid fixation by metal implants or a 'fixateur externe' was used very rarely. Skin and muscle problems were elegantly solved by primary closure of wounds using a closed-irrigation drainage system. When several operations were included in the series 95 per cent of the patients were clinically and radiologically cured.

The book offers valuable advice for anybody who deals with the problems of osteomyelitis. The results obtained from this series of patients should be compared with other methods and experience in the future. It is also interesting to see the references from the Eastern European literature concerning bone transplantation in the presence of infection.

Textbook of Physiology and Biochemistry. Eighth edition. By George H. Bell, B.Sc., M.D., F.R.C.P., F.R.S.E., University of Dundee; J. Norman Davidson, C.B.E., M.D., D.Sc., F.R.C.P., F.R.I.C., F.R.S., University of Glasgow; and Donald Emslie-Smith, M.D., F.R.C.P., University of Dundee. 9½ × 7 in. Pp. 1160. Illustrated. 1972. Edinburgh: Churchill Livingstone. £5.

Whenever the reviewer attempts any systematic reading of texts of physiology he is impressed by the diversity of concepts, techniques, and methods which are needed in the study of human and animal function. This book is written by a physiologist, a biochemist, and a clinician; it has always had a lively and dramatic presentation and in this new edition it seems, with two-column pages and lithographic methods, more attractive than ever. This is a volume with a strong chemical bent and it contains brief but authoritative summaries of such topics as protein structure, metabolic reactions, enzyme kinetics, and chemical genetics. The presence of a clinician has ensured that the relevance to human medicine is continually emphasized. A book of this kind must have good illustrations, and these are outstanding in number and variety; the radiographs of normal chests to show the extent of variation of the cardiac shadow and the reproduction of the original print showing Forssmann's self-catheterization are particularly interesting. A number of the illustrations are in colour, and these are well reproduced.

Since physiology is primarily an experimental science, the authors have taken the trouble to include accounts of the classic experiments to enable the reader to appreciate something of the evidence on which the descriptive sections are based. In a book of this size the topics have to be condensed, but an extensive series of references and reviews for further reading is given at the end of each chapter. This is a basic text in human physiology which can be recommended to students of all ages.

Fundamental Techniques of Plastic Surgery. Fifth edition. By Ian A. McGregor, M.B., Ch.M., F.R.C.S., Glasgow. 8½ × 5½ in. Pp. 301 + x. Illustrated. 1972. Edinburgh: Churchill Livingstone. £4.

The first edition of this book was published in 1960 and the appearance of the fifth only 12 years later is testimony of its great popularity with trainee plastic surgeons and those in other surgical specialties alike; it provides basic information about which all surgeons should be aware and on which plastic surgeons can build.

There have been a number of advances in basic techniques since the fourth edition and most of these are now included in the text. Thus, the deltopectoral flap and other axial pattern flaps have almost completely replaced the tube pedicle; delayed exposed grafting is increasingly popular; sophisticated haloes have outclassed the plaster head cap in maxillofacial surgery; hand incisions other than the classic one are now widely used. Mr. McGregor's continued diligence in keeping his textbook up to date should make this edition as much sought after as its predecessors.

Transplantation. Edited by John S. Najarian, M.D., Minnesota, and Richard L. Simmons, M.D., Minnesota. 11 × 8¼ in. Pp. 797 + xiv. Illustrated. 1972. London: Henry Kimpton. £21·80.

This beautifully produced and expensive volume on transplantation is edited by clinically orientated surgeons who must, of course, have a deep interest in basic science as it affects their sub-specialty. The first part of the book is devoted to the immunobiology of transplantation—the basic science involved. The contributors to this section are able to give a most authoritative and definitive description of the processes which occur in transplanted organs and the ways in which treatment can, at least in part, circumvent them. There is always an overall clinical relevance in the book, although many of the contributions are from authors who are somewhat obliquely concerned with the care of patients.

The section on clinical transplantation covers ethical, legal, and organizational aspects as well as surgical problems. The discussion of transplantation of tissues and organs other than the kidney is somewhat more extensive than in similar volumes, and stresses the interest of the editors in transplantation as a technique in surgery rather than a specialist concern with transplantation of one organ. It seems likely that within the next decade transplantation as a surgical tool will tend to fall into place in several areas of surgery as one of a number of techniques available for the treatment of damaged or diseased tissues. For that reason the approach of the editors will continue to be a valuable one in helping the practice of surgery, in all areas, to use the best available technique for the treatment of a particular patient.

Handbuch der allgemeinen Pathologie. Volume 3, Part 6, **Lymphgefäss-System.** Edited by H. MEESEN, Dusseldorf. 9¾ × 6½ in. Pp. 708 + xiv. Illustrated. 1972. Berlin: Springer-Verlag. DM.396.

THIS volume deals in immense detail with advances in the knowledge of the lymphatic system. Each chapter is written by an authority actively engaged in research in the field, and some chapters are in English. For the research worker this is an essential reference book. The surgeon who is especially interested in this field will find much to stimulate him, and there are excellent chapters on chemistry, pharmacology, and immunology. Perhaps of greatest interest to the surgeon are the sections on pathology and the discussion on lymphangiography. The volume is unlikely to find a place in the surgeon's personal library unless he has a special interest in the lymphatic system.

Handbuch der medizinischen Radiologie. Volume 19, part 1, **Spezielle Straleuntherapie maligner Tumoren.** Edited by A. ZUPPINGER, Bern, and E. KROKOWSKI, Kassel. 10½ × 7¾ in. Pp. 824 + xix. Illustrated. 1972. Berlin: Springer-Verlag. DM.360.

THIS volume is entirely devoted to the treatment of malignant tumours and is written in German except for chapters in English on cancer of the oral cavity and cancer of the lip. Tumours of the skin and gastro-intestinal tract receive special attention, and there are comments on the use of hormonal treatment and chemotherapy.

It is a large volume with many excellent illustrations and adequate references. The text is conventional and at times somewhat didactic. It will be read with interest by the radiotherapist, and the general surgeon will benefit from consulting particular sections within his own field.

Modern Management of Myelomeningocele. By WILTON H. BUNCH, M.D., Ph.D., Virginia; ALEXANDER S. CASS, M.B., F.R.C.S., Minnesota; ALAN S. BENSMAN, M.D., Minnesota; and DONLIN M. LONG, M.D., Ph.D., Minnesota. 9 × 6 in. Pp. 251 + ix. Illustrated. 1972. St. Louis: Warren H. Green Inc. $15.00.

THIS brief book claims to be written for all who see and treat myelomeningocele, its avowed aim being to bring together the various medical specialists concerned with this condition, but also to be written for both medical and paramedical personnel. The four authors are a neurosurgeon, an orthopaedic surgeon, a urologist, and a rehabilitation expert; in addition, there is a chapter on intellectual and emotional development by two psychologists. There are reasonable references to the literature but the book in fact reports the methods and views of a single group of enthusiasts. Inevitably the orthopaedic and urological chapters reflect the approach of the respective authors, because views differ widely in these areas; these two chapters contain many pages of radiographs. Probably the best chapter, because it would be of use to a wide range of readers, is that on 'Habilitation of the Child with Myelomeningocele'. Incidentally the book also makes reference to the treatment of spina bifida occulta in patients with only dimples on the spine which really presents quite different problems to myelomeningocele.

Although the authors make reference to the view that treatment may sometimes be unwise or unjustified, it is clear that they themselves are committed to treating virtually all children. The term 'aggressive team approach' occurs five times in two pages and this indicates a degree of optimism which was common five or ten years ago in Britain but which is currently giving way to a more realistic and sober assessment of the therapeutic possibilities.

General Thoracic Surgery. Edited by THOMAS W. SHIELDS, M.D., Chicago. 10 × 7 in. Pp. 1007 + xxi. Illustrated. 1972. London: Henry Kimpton. £20·25.

THE publication of this book is timely; because of the striking advances made in cardiac surgery there is a danger that surgical training programmes may overlook the great volume of general thoracic surgery that has to be done throughout the world. Dr. Shields has mustered a fine team to add much to his own considerable contribution in this comprehensive book. In a graceful foreword Dr. Paul Sampson writes: 'Dr. Shields has picked his 56 contributors for their specialised knowledge, their professional reputation and their ability to write.' Multiple authorship often leads to patchiness, but this cannot be said of this work.

The division of the book into 14 sections, subdivided into 43 chapters, laid out in a clear style encourages the reader from the moment that he opens the book; the 3 Contents pages are elegantly designed and printed. The basic science contributions in Sections 1 and 2 are clear, up to date, and fit in well with accounts of the supporting disciplines, which are essential for good thoracic surgery, including anaesthesia, radiology, bacteriology, mycology, and parasitology.

The section on operative procedures contains much information of value to senior residents and practitioners of general surgery who may find themselves involved, because of local conditions of time and place. Perhaps the omission of oesophageal surgery may be regretted by many 'general' thoracic surgeons. There is a good account of diaphragmatic and hiatal hernia practice.

In a book written by so many experts it is difficult and unnecessary to single out particular chapters; the reviewer found much of interest in the accounts of tracheal surgery, the correction of sternal deformities, and the section on the mediastinum.

'Pulmonary' conditions are thoroughly covered by a large section containing much valuable information in the 290 pages devoted to the subject. The present practice of surgery for cancer is excellently stated. The less common lung diseases, which from time to time deceive the most experienced thoracic surgeons, such as anomalies, hydatid cyst disease, and other 'rarities', are clearly outlined. The chapter on the present state of lung-transplantation research is short but authoritative.

It was a pleasure to read this outstanding contribution which should find its way to the shelves of every medical library.

Urologische Operationslehre. Volumes 9 and 10. Edited by G. W. HEISE, Magdeburg, and E. HIENZSCH, Jena. 10½ × 7¼ in. Vol. 9, pp. 180; Vol. 10, pp. 172. Illustrated. 1972. Leipzig: Veb Georg Thieme. Vol. 9, 58M.; Vol. 10, 53M.

TWO further volumes of this multi-author work on operative urology have now appeared. Volume 9 deals first of all with those procedures which come somewhere between gynaecology and urology, and there is an extensive section on the management of vesicovaginal and other types of lower urinary fistulae. The question of incontinence is also dealt with, and as the author of this section is a gynaecologist the preference for vaginal procedures is not surprising. The many different types of operative procedure are described in detail and are extremely well illustrated by clear line diagrams. The second section of this volume deals with intersexuality and the various problems of pseudohermaphroditism. The differential diagnosis is clearly pointed out and the operative management is again well illustrated by diagrams. Both sections of this book have an extensive bibliography.

Volume 10 deals with operations on the kidney and has an excellent section on the various methods of surgical exposure of the kidney. This section is also extremely well illustrated. There follows a chapter on the surgical technique of the removal of parathyroid tumours which is probably outside the scope of the average British urologist. The final two chapters in this volume deal with the medical treatment of urinary calculi in general and the conservative treatment of cystine stones.

Both volumes should be of interest to urologists, especially because of their extremely clear diagrammatic illustrations of operative procedures. These publications also show that the present trend of thinking in the German Democratic Republic is very similar to that in other European countries.

Clinical Neurosurgery, Volume 19. Edited by GEORGE T. TINDALL, M.D., Galveston. 9 × 6 in. Pp. 598 + xlvi. Illustrated. 1972. Edinburgh: Churchill Livinsgtone. £12.

THIS rather expensive volume contains the edited proceedings of the Twenty-first Annual Meeting of the (American) Congress of Neurological Surgeons held in Miami in 1971. The congress was devoted to the topic of head trauma and the book is dedicated to the congress's honoured guest, Dr. E. S. Gurdjian. The volume also contains a cumulative index of the 19 volumes of *Clinical Neurosurgery* so far published.

The chapters, in the form of edited papers given at the Miami meeting by 36 distinguished contributors (mostly from the United States but Canada, Australia, and the United Kingdom are also represented), cover a wide variety of clinical and scientific subjects concerned with head injury. Mostly they deal with problems of prevention and management which are currently uppermost in the thoughts of those concerned with the care of cerebral trauma.

The chapters deal with the experimental mechanisms of head injury, patient monitoring, circulatory changes, lung function, diagnostic procedures, medical management, metabolic disturbances, prevention and mechanisms of road and sports accidents, cerebrospinal fluid 'leaks', vascular trauma, and many other subjects. There is a particularly valuable chapter by Professor Jennett indicating how better and earlier prognosis of the severe cerebral injury may be achieved.

Each chapter is a study in some depth and represents the clinical or research interests of the contributor. As a survey of current thought this is an excellent volume for reference and contains good subject bibliographies, but like all conference compendia of this nature it is expensive and its value is likely to be ephemeral. A less expensive format might have enabled earlier publication and wider dissemination. Nevertheless, for the libraries which can afford it the book is a very worth-while purchase and the cumulative index is especially valuable.

Diagnostic Orthopaedic Pathology, By C. G. WOODS, B.Sc., M.B., Ch.B., M.R.C. Path., Consultant Pathologist, The Nuffield Orthopaedic Centre, Oxford. 9½ × 7½ in. Pp. 297. Illustrated. 1972. Oxford: Blackwell Scientific Publications. £8·50.

THIS book is a lucid presentation of much of the field of orthopaedic pathology. It begins with technical considerations and then outlines the normal and articular tissues, the latter in detail. The subsequent chapters deal with congenital and acquired abnormalities of growth, and there are further chapters on acquired bone disease, including tumours. Emphasis is placed on the need to use all the information available in order to reach a valid conclusion in cases where there are similarities in the histological appearances of different bone lesions.

In each chapter the text precedes the illustrations, which are well chosen, clear, and well described. The book contains few references and is more the personal expression of the author's viewpoint, which is sound, realistic, and practical. This is a book for anyone who wants to learn about orthopaedic pathology.

Supportive Care of the Surgical Patient. By WILLIAM M. STAHL, M.D., New York. 9 × 6 in. Pp. 270 + xvii. 1972. New York: Grune & Stratton, Inc. $13.50.

THIS book will fulfil an important role in furnishing both undergraduate students and those destined for examinations such as the primary F.R.C.S. with factual knowledge about facets of patient management which are so often acquired haphazardly. Because the book is clearly based on physiology it will have particular appeal to students grappling with what are considered by clinicians to be the basic sciences. In a sense it is applied physiology, covering cardiorespiratory, renal, metabolic, and endocrine functions with a glance at the skin, the emotions, and the autonomic nervous system. The author presents them in terms of survival systems for which he creates an original nosological classification—exchange systems (e.g. O_2 exchange), transport systems, and regulatory systems. It is a useful book with an adequate bibliography, although it is expensive for a work without illustrations.

Recent Advances in Gastroenterology. Edited by JOHN BADENOCH, D.M., F.R.C.P., United Oxford Hospitals, and BRYAN N. BROOKE, M.D., M.Chir., F.R.C.S., St. George's Hospital Medical School, London. 9¼ × 6¼ in. Pp. 350 + ix. Illustrated. 1972. Edinburgh: Churchill Livingstone. £6.

THIS book is not only for gastro-enterologists but for all who are involved with the treatment of abdominal disease. Each chapter is written by an authority and the text is lucid and well illustrated. The contents range widely through some of the topics of current interest in gastroenterology, dealing with basic science in some chapters and with treatment in others. There are liberal references and the cost for such a volume is very reasonable.

The need for authoritative review articles is ever increasing. The succinct appraisal of new methods and ideas demands a technique of writing which requires judgement and experience if it is to educate and not confuse the reader. The editors are to be congratulated in achieving precisely this object.

Symposium on Myelomeningocele. AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS. 9¾ × 7¾ in. Pp. 317 + xiii. Illustrated. 1972. London: Henry Kimpton. £10·80.

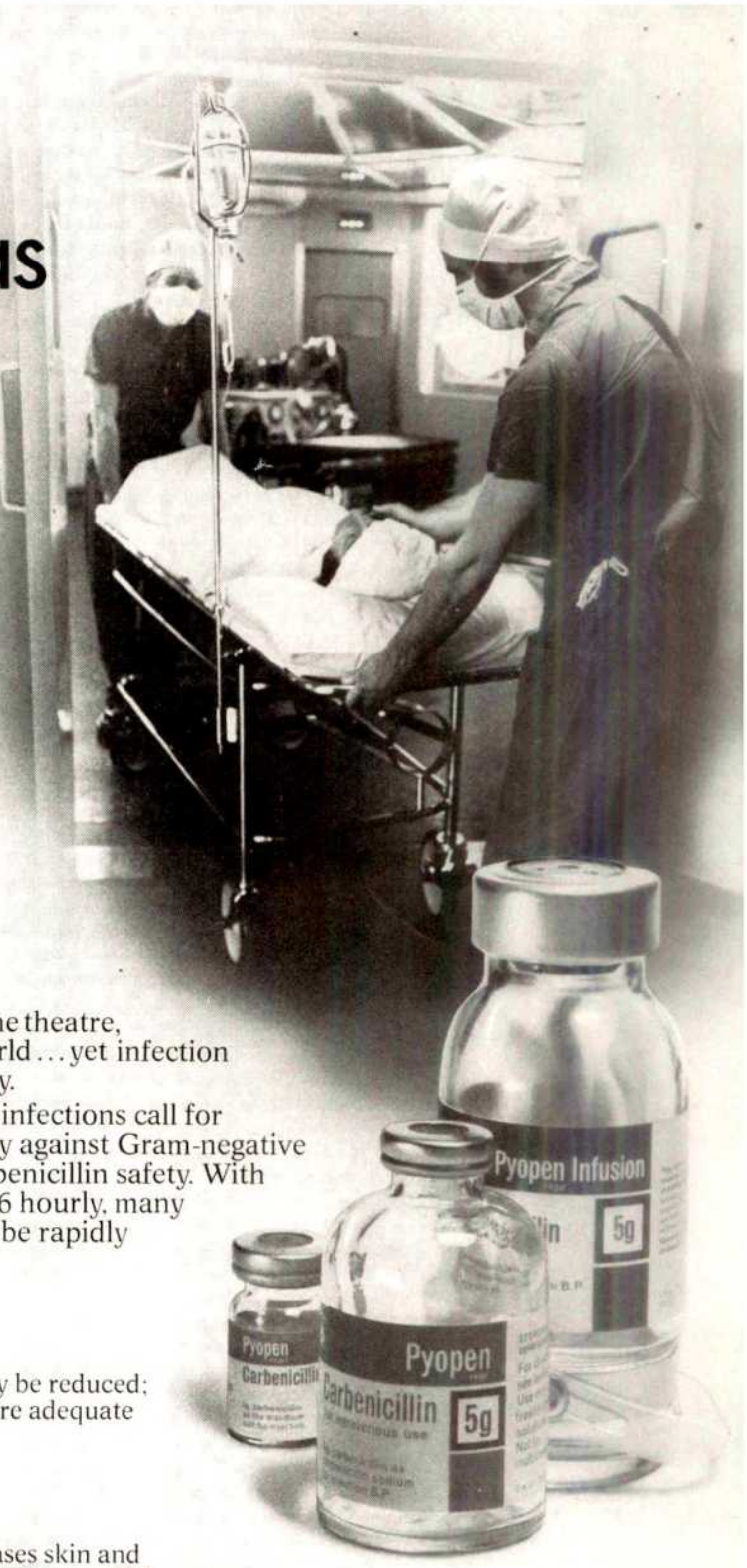
THERE are surgeons in the fields of genito-urinary, orthopaedic, paediatric, and even neurological surgery who have yet to encounter the challenge presented by the child with myelomeningocele. For them and for those who already struggle with the problem this book would provide much enlightenment.

The 31 chapters are drawn from the papers and discussions at a course on myelomeningocele in 1970 under the aegis of the American Academy of Orthopaedic Surgeons. Most of the authors are from North America, but the Sheffield group in Britain, a *pioneering team* in the management of children with myelomeningocele, is worthily represented.

The book, which is well printed, has illustrations of an exceptionally uniform excellence. The first few chapters deal with embryology, pathology, and the evaluation of the potential ability of the newborn baby with myelomeningocele, followed by sections on hydrocephalus and genito-urinary and bowel disorders. Orthopaedic and developmental problems are next discussed; the psychosocial aspects are considered and long-term follow-up data are presented. Finally, there are two chapters on the team approach to the care of these unfortunate children.

Many of the subjects are controversial and are a source of disagreement among surgeons of experience. Due regard for other views is shown by most contributors to the book and their clear presentation of personal data and opinions will be of interest and value to a wide variety of readers.

When pseudomonas threatens the success of surgery



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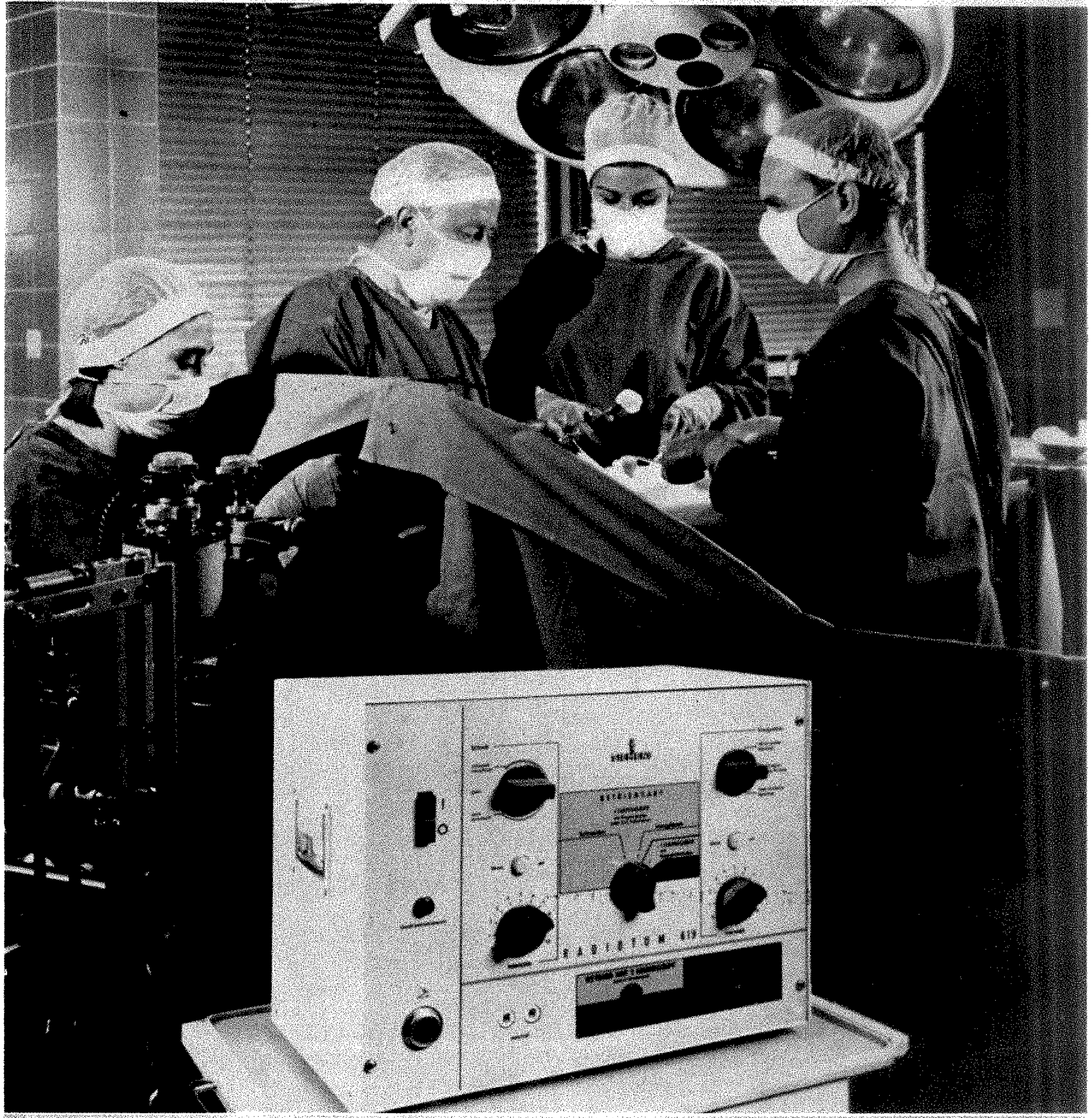

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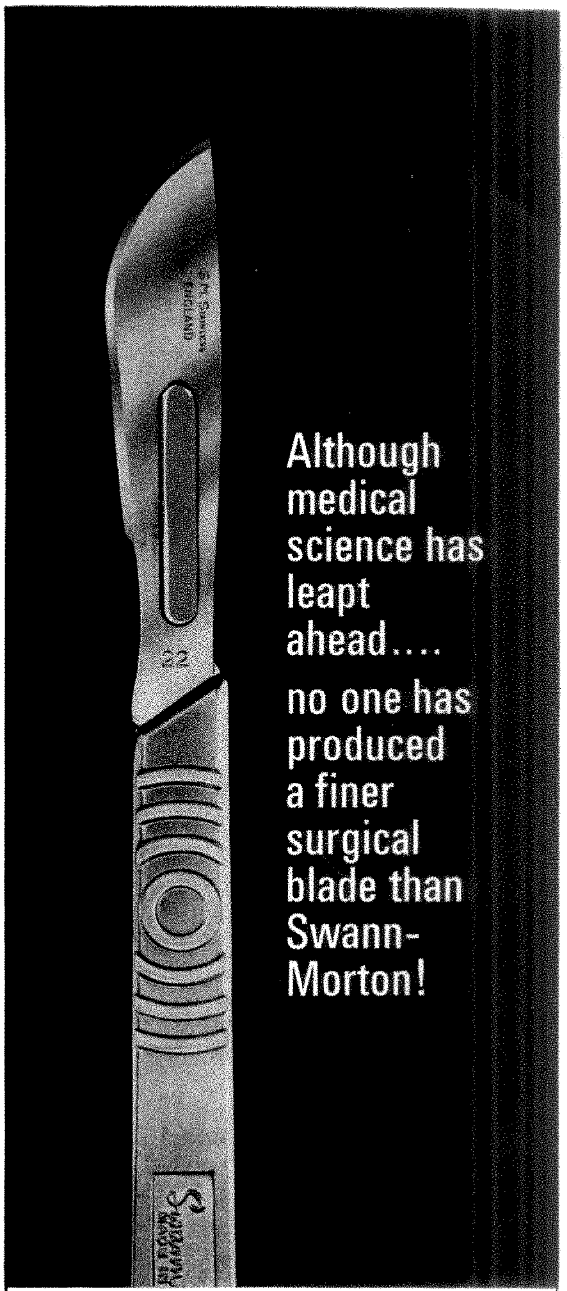
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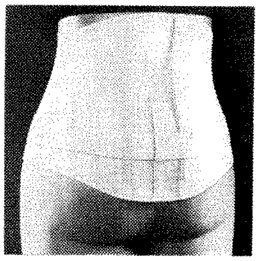

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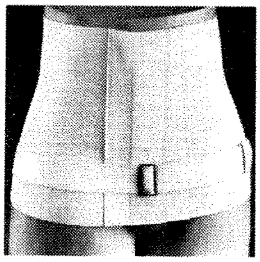

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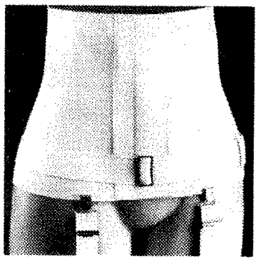

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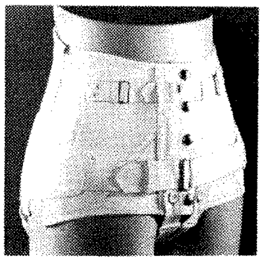

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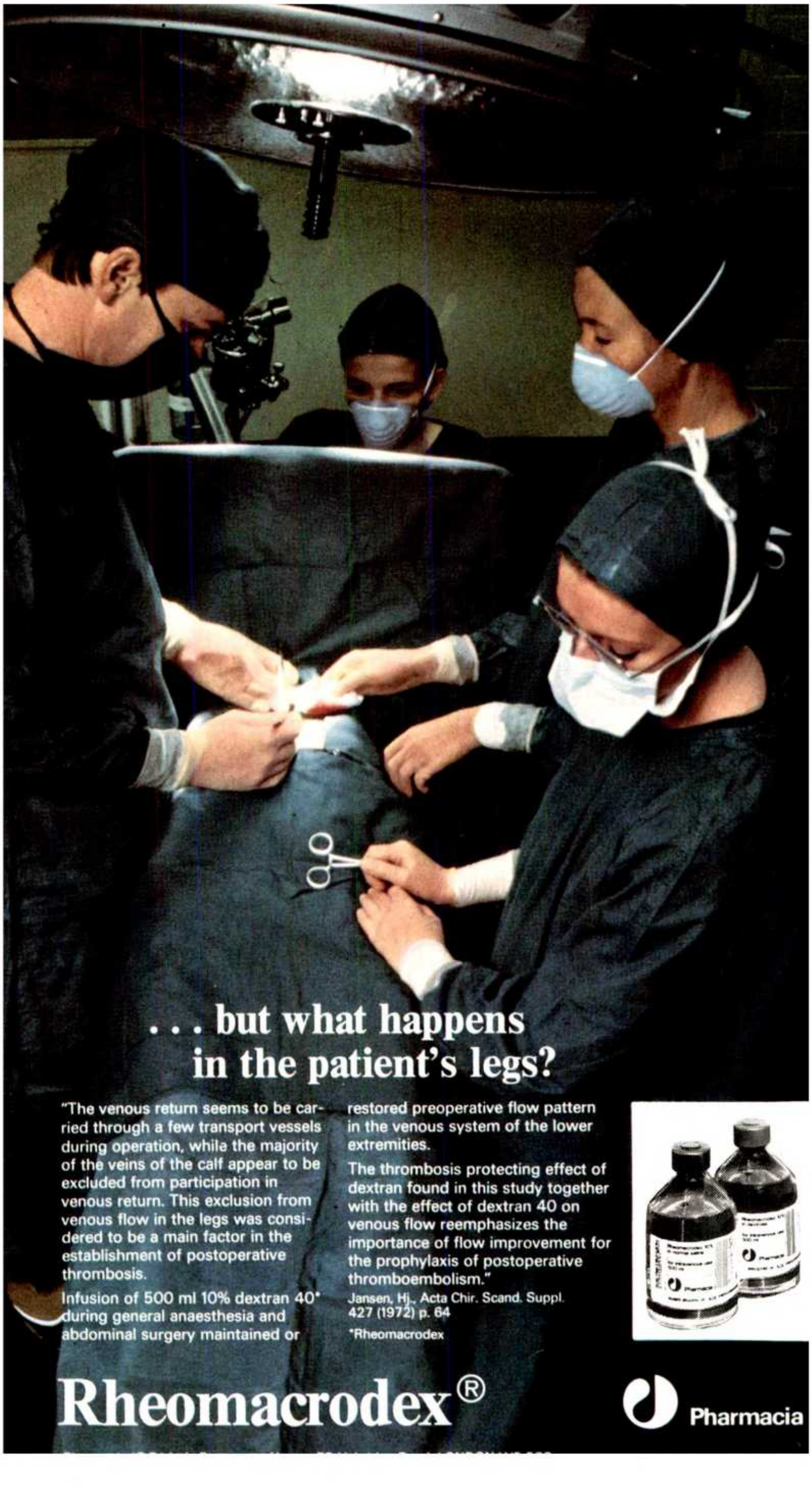

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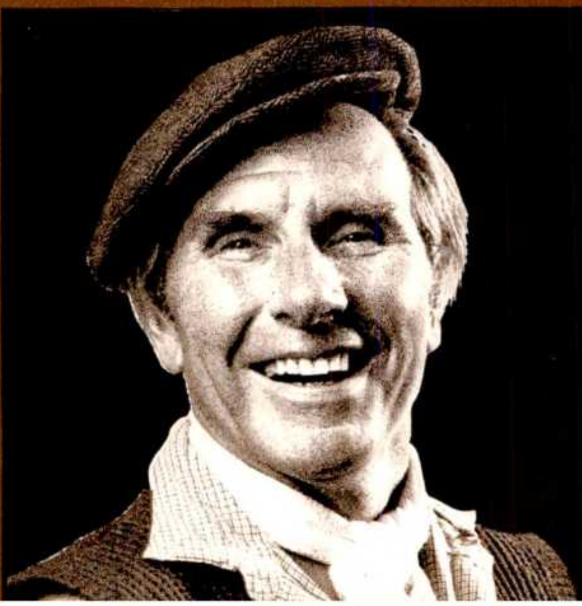

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2 *Postgrad med J*, (1969), **45**, Supplement (November), 91
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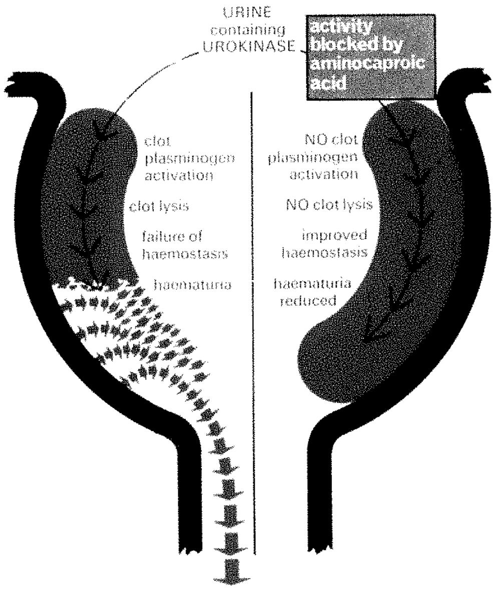
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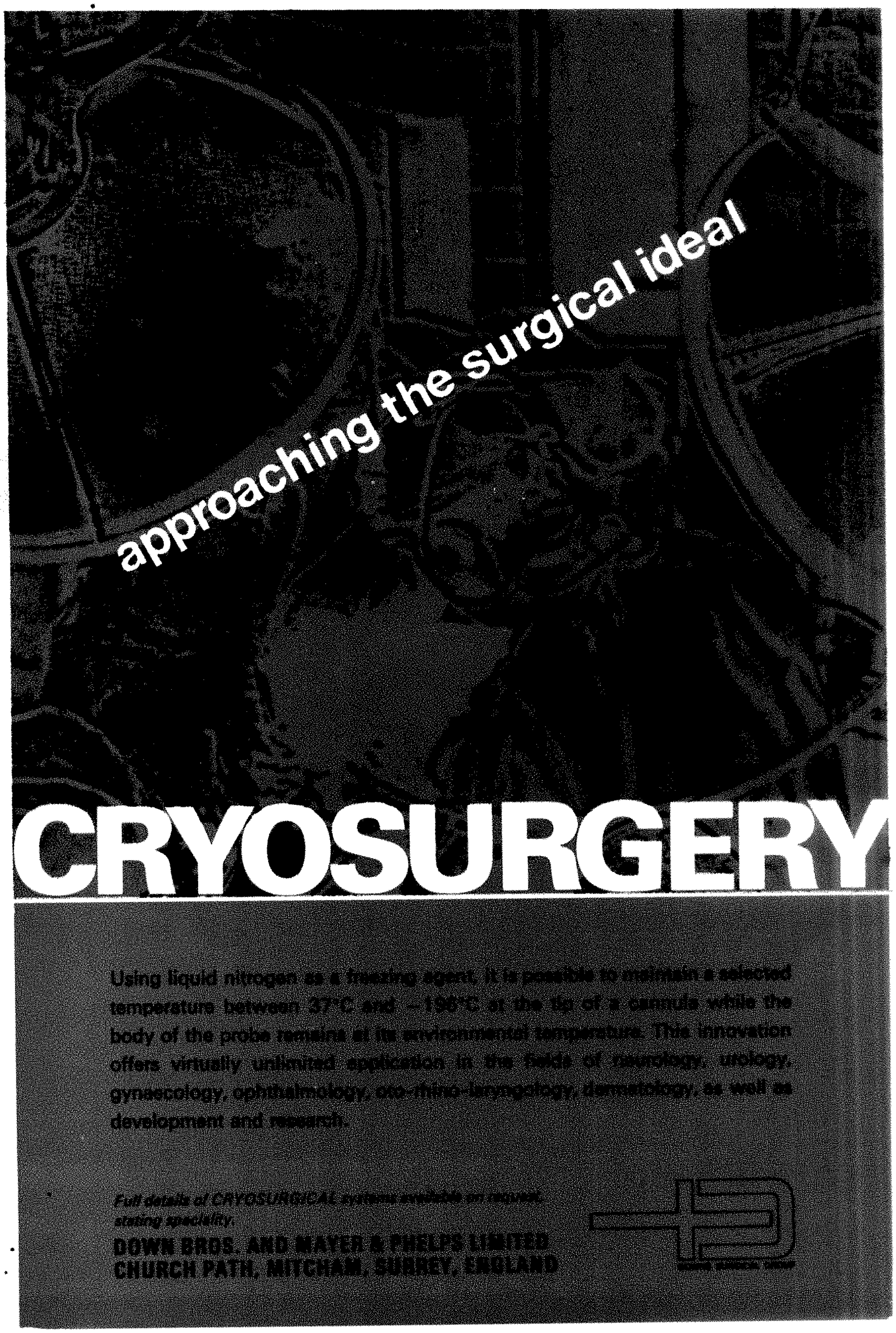

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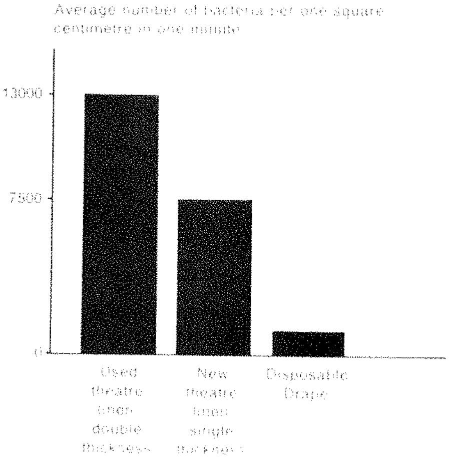

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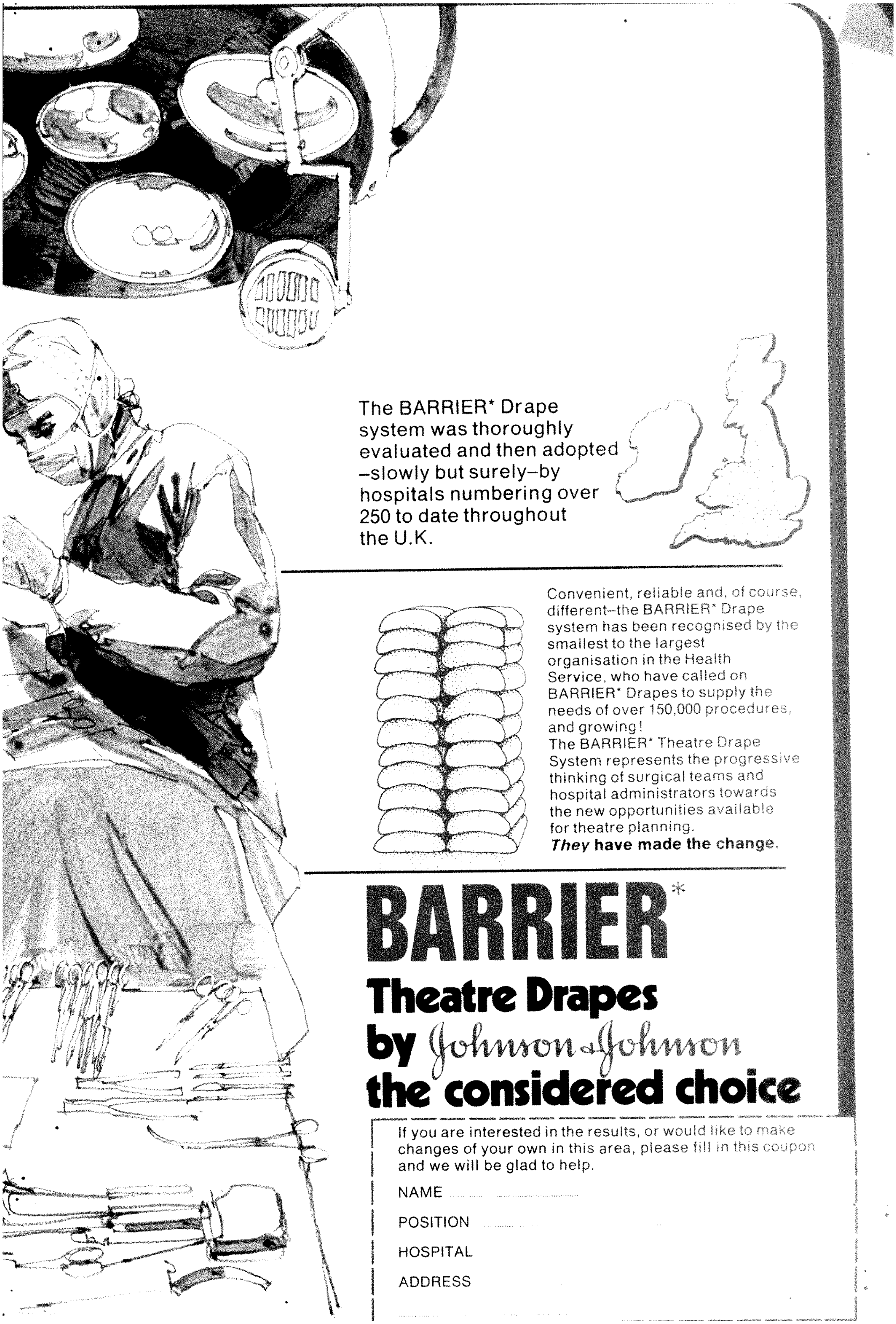

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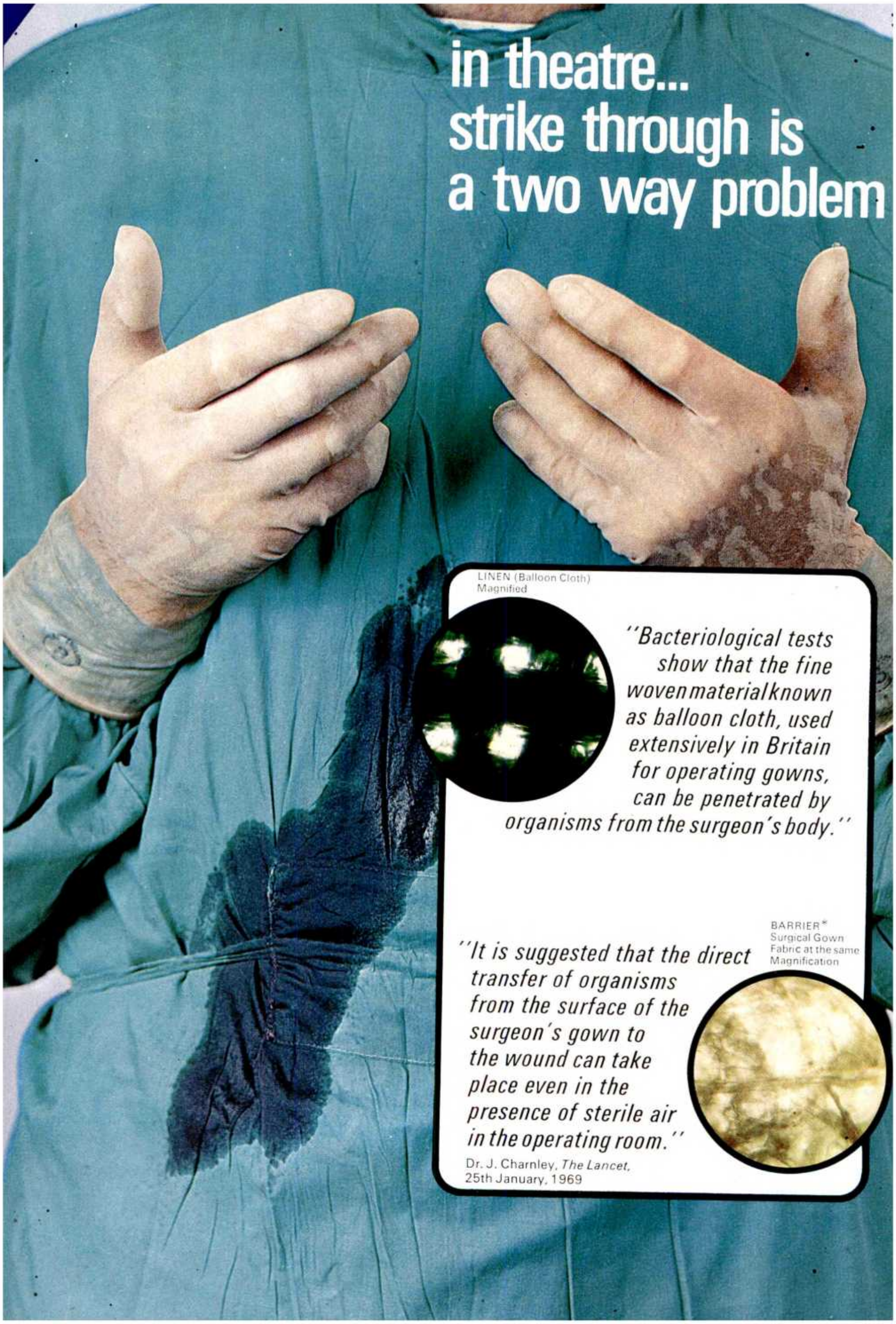
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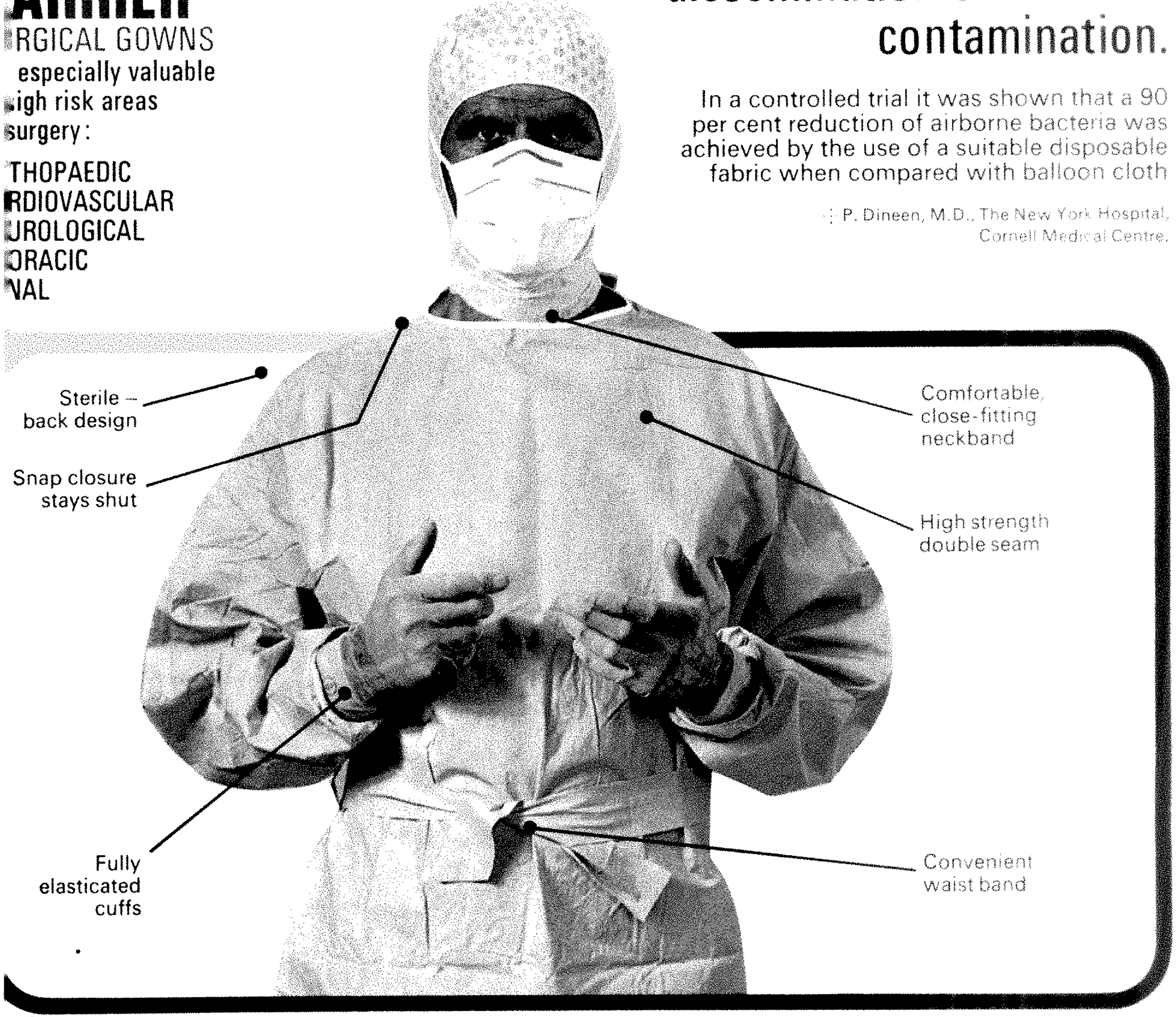

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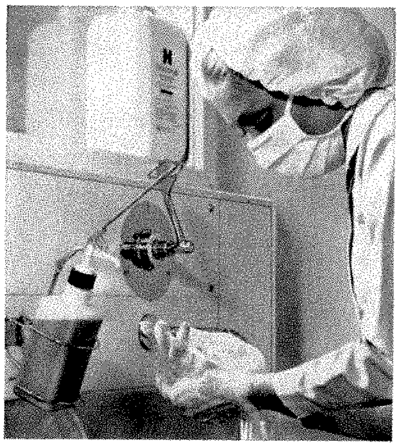

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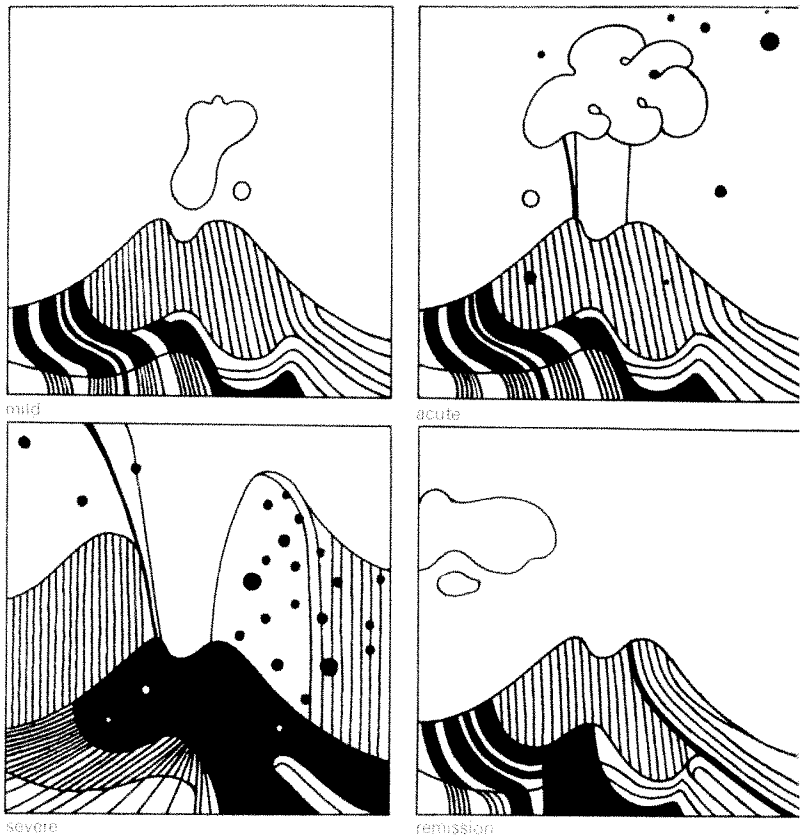

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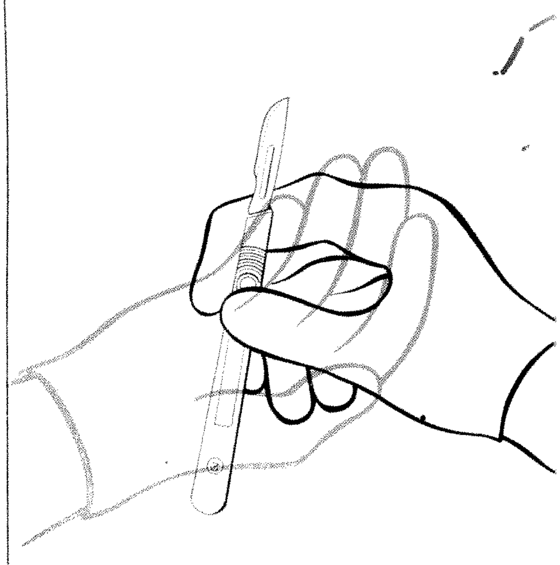

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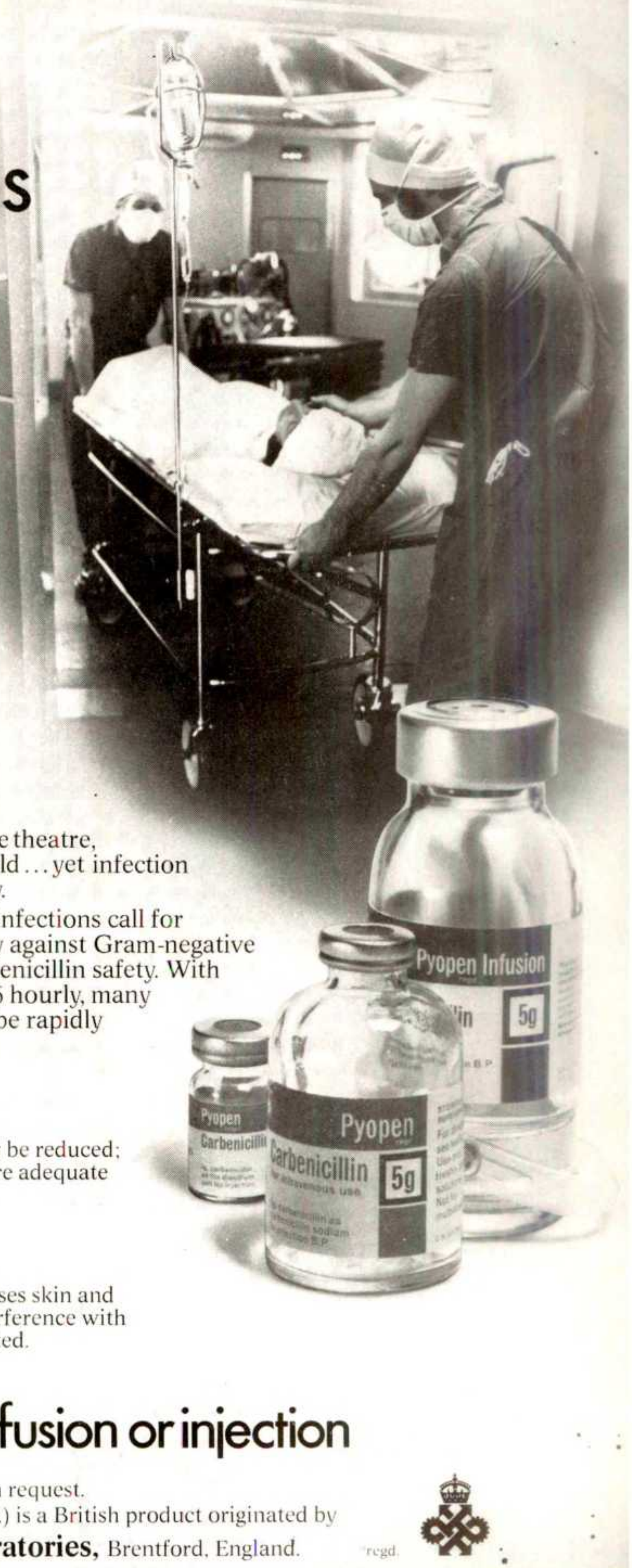

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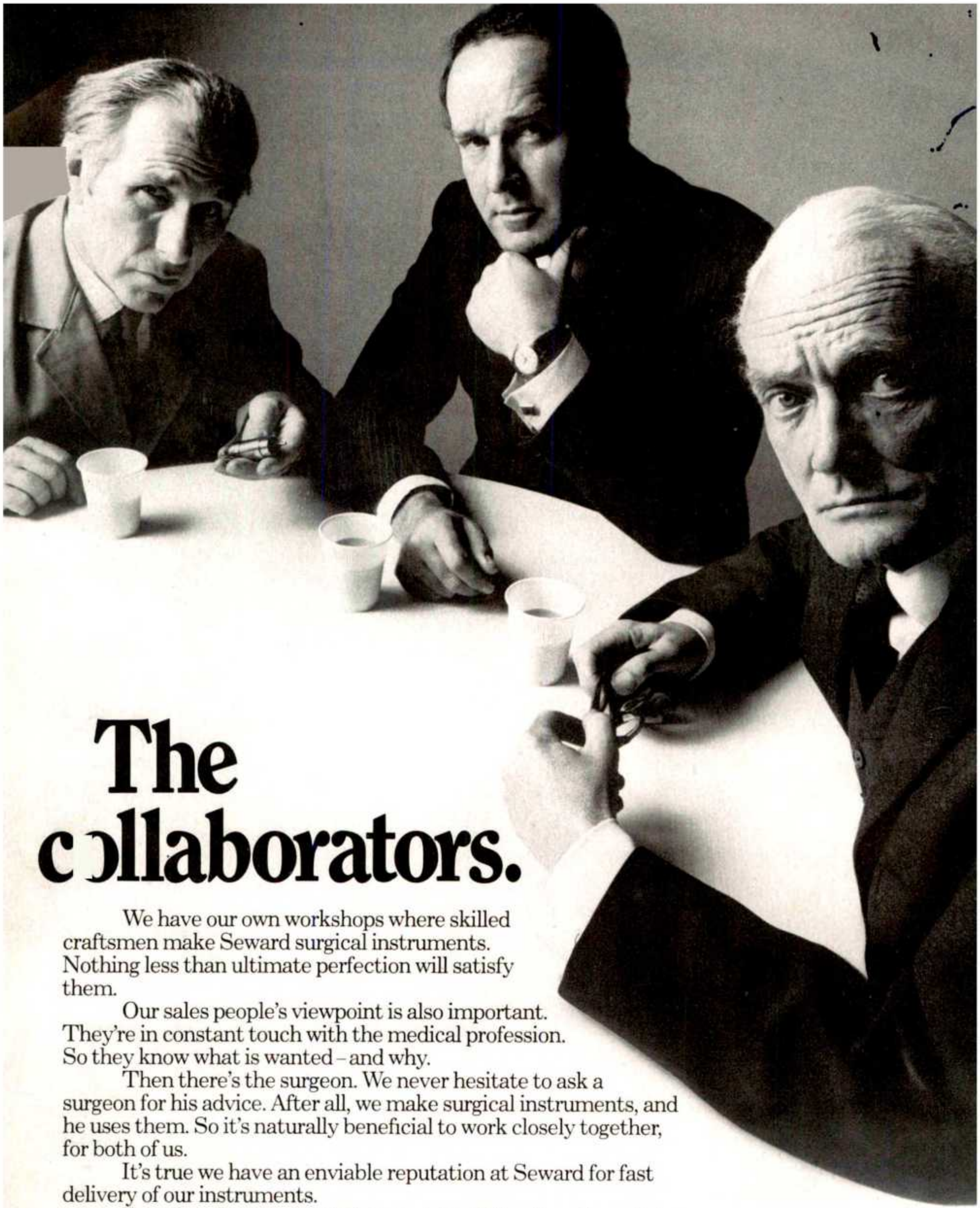

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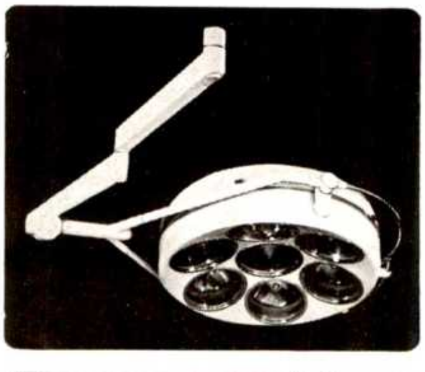

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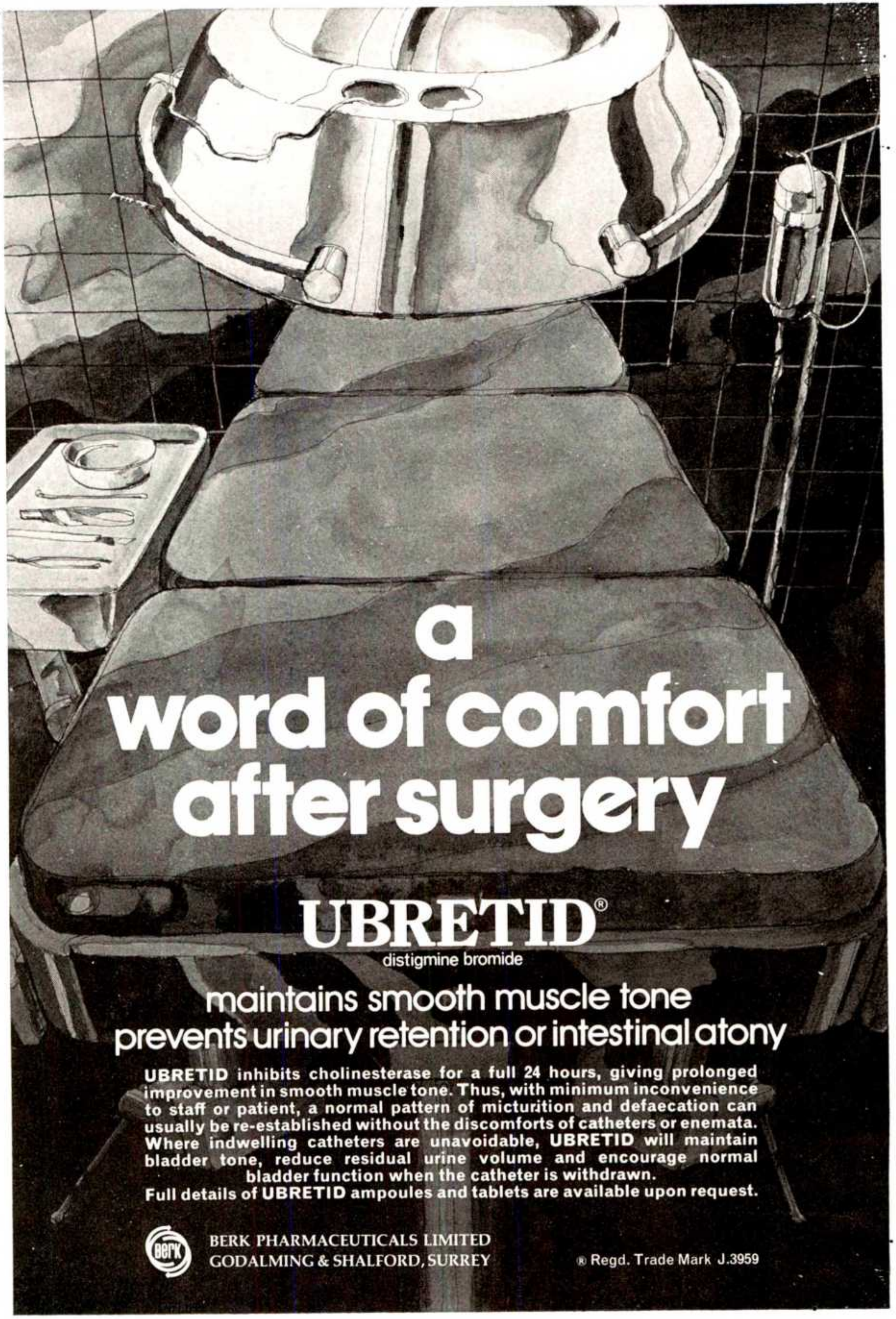

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ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND

The annual meeting of the Association took place in Aberdeen on 4, 5, and 6 April, 1973, with the President, Mr. W. Michie, M.B.E., in the Chair.

The major symposium was entitled 'Modern Trends in the Management of Thyrotoxicosis'. These papers, and others in the subsequent sections of Short Papers and Short Papers for the Moynihan Prize, follow in the order in which they were read. A report of the symposium on General Surgical Training has been contributed by Mr. M. R. Williams (Canterbury).

SYMPOSIUM ON MODERN TRENDS IN THE MANAGEMENT OF THYROTOXICOSIS

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BY W. MICHIE
ABERDEEN ROYAL INFIRMARY

THYROTOXICOSIS is a relatively common disorder with a recorded annual rate of 30 per 100,000 of female population and 20 per 100,000 for both sexes (Furszyfer, Kurland, McConahey, and Elveback, 1970). Despite its frequent occurrence its aetiology remains obscure, its management debatable, and its aftercare problematical. Current thinking involves aetiological factors outwith the hypothalamic–pituitary–thyroid axis, and implicates auto-immune reactivity, either directly from the deposition of immunoglobulins in the basement membrane of the thyroid follicle (Werner, Wegelius, Fierer, and Hsu, 1972) or indirectly by delayed hypersensitivity from defective lymphocytic immune surveillance (Volpé, Edmonds, Lamki, Clarke, and Row, 1972). Yet again the manifestations of Graves' disease have been ascribed to defective thyroid autoregulation of iodine excess and depletion and consequent loss of ability to modulate thyroid function and activity (Ingbar, 1972).

Were the aetiological factors of Graves' disease elicited and understood, it is possible that treatment would be on a defined and rational basis. A generally acceptable treatment has yet to be evolved, and the plurality of therapies currently in vogue merely confirms the aphorism first expressed in 1905 by Dr. Hector Mackenzie, a physician of St. Thomas's Hospital, that when for a particular disease there are many remedies, none will be very efficacious. At present the thyrotoxic patient is treated by destructive therapy by radio-isotopes or surgery, or by long-term surveillance on anti-thyroid drug therapy in the hope of eventual spontaneous remission. Each method has its advantages, disadvantages, and complications. The commonest complication of both methods of destructive therapy is hypothyroidism, though the time interval and incidence differ considerably in each. Provided that an adequate remnant is left, the hypothyroid rate 1 year after operation is in the region of 30 per cent, and if the index of clinical suspicion during this year is sufficiently high, hypothyroidism will rarely develop later than 1 year after operation (Michie, Pegg, and Bewsher, 1972). In contrast, the hypothyroid rate after radio-iodine therapy has been recorded as high as 41 per cent at 1 year, with an annual increase thereafter of

2·8 per cent (Nofal, Beierwaltes, and Patno, 1966). Radio-isotopes are presumed to act by interference with the replicative mechanism of the thyroid follicular cell (Greig, 1965), and the implication is that the eventual end-point of radio-iodine therapy is hypothyroidism in all patients.

While a reasonable prediction of the incidence of hypothyroidism can be made for a group of patients treated by either radio-iodine or surgery, the fate of the individual patient cannot be predicted with any accuracy. It is for this reason that a renewed attempt is being made to assess the value of long-term antithyroid drug therapy supplemented by the evidence of serial 20-minute uptake of radio-iodine or pertechnetate (Alexander, McLarty, Horton, and Pharmakiotis, 1973). While it is unlikely that antithyroid drugs affect the fundamental nature of the disease, they inhibit hormone production until a natural remission, estimated variously as occurring in between 30 and 50 per cent of patients, becomes apparent. The programme which this form of therapy imposes on the patient, with the demands on trained personnel for continuing supervision and the uncertain nature of the outcome, are factors which might tend to limit its general acceptance.

Irrespective of whether control of thyrotoxicosis is actively pursued by destructive therapy or passively awaited from the long-term use of anti-thyroid drugs, there devolves upon the clinician an ethical responsibility for continuing supervision and follow-up of his patient, and this responsibility cannot be lightly undertaken. Overt hypothyroidism can be readily confirmed by routine tests of thyroid function, but forms less clinically obvious exist whose detection rests on elevation of serum thyroid-stimulating hormone levels (Hedley, Hall, Amos, Michie, and Crooks, 1971). This is of some importance for the younger patient with mild persisting hypothyroidism who may be at long-term risk of developing ischaemic heart disease (Bastenie, Vanhaelst, Bonnyns, Neve, and Staquet, 1971).

The number of patients each year may remain relatively constant, but the total number of patients at risk of iatrogenic hypothyroidism accumulates and becomes part of an increasing clinical burden. This burden has in some measure been solved for selected populations in Scotland by an annual follow-up programme controlled by a computer-based register, which has been formulated as a joint venture between general practitioner and hospital consultant (Hedley, Scott, Weir, and Crooks, 1970).

One further aspect of the management of the thyrotoxic patient merits investigation. The cost of treatment to the health service and the economic burden of frequent attendance at hospital for the patient, taken in conjunction with overburdened facilities and an inadequate number of trained personnel, are factors which cannot any longer be ignored. A study of comparative costs of different forms of treatment might prove rewarding. Such a study is now overdue.

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RADIOACTIVE IODINE THERAPY FOR THYROTOXICOSIS

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SUMMARY

Radioactive iodine has been used to treat over 300,000 thyrotoxic patients since 1946. This paper reviews the knowledge gained in the past 23 years about the efficacy and safety of ^{131}I therapy for thyrotoxicosis. Modifications with reference to case selection, dosage, and follow-up are discussed.

RADIOACTIVE iodine (^{131}I; half-life 8 days) in therapeutic amounts destroys thyrotoxic follicular cells and damages the stroma of the gland; there is very little radiation given to, and very rarely any damage incurred by, tissues adjacent to the thyroid, and the same applies to the adult body as a whole.

More than 20 years' experience of the use of ^{131}I in the treatment of thyrotoxicosis has shown that it is safe and effective and is undoubtedly the treatment of choice in all elderly patients and especially in those who are frail and have complications. ^{131}I therapy is also advised for adult patients with a postoperative recurrence of thyrotoxicosis and for those in whom drug therapy has failed for some good reason and in whom operation is refused or contra-indicated.

Children and adults of less than 25 years of age should be considered for ^{131}I therapy only in exceptional circumstances, and it is absolutely contraindicated if the patient is pregnant or likely to be. If the patient is fertile, contraception is advised for up to 1 year after successful therapy.

The size and characteristics of the goitre influence the amount of ^{131}I required, but a large nodular goitre is not a contra-indication to ^{131}I therapy unless it is causing mechanical trouble; in this situation surgery should be considered but it is not mandatory since a sufficient dose of ^{131}I will cause a very large goitre to shrink.

^{131}I therapy can be given a few days after cessation of anti-thyroid drugs, and in cases of severe thyrotoxicosis it is probably wise to induce at least some remission by drugs before a dose of ^{131}I is given. The anti-thyroid drugs can be re-prescribed 1 week after therapy.

It is of importance that successful ^{131}I therapy depends on a sufficient uptake of the dose by the gland. A check tracer uptake is a prerequisite and if it is blocked owing, for example, to iodide excess (medications, radiographic contrast media) therapy has to be postponed.

The only serious drawback to ^{131}I therapy is the high rate of hypothyroidism which is about 10 per cent at 1 year and rises to about 80 per cent at 15 years. This has led to a number of trials in which ^{131}I therapy has been modified or an alternative radionuclide, ^{125}I, has been used. Research in this area will be discussed. Methods have also been devised to follow and supervise patients treated with radioactive iodine (*see* p. 771).

SELECTION OF PATIENTS FOR ^{131}I THERAPY (1950–70)

Experience during the 1900–40 era showed that two-thirds of patients failed to recover from thyrotoxicosis and suffered either chronic relapsing morbidity or death; a third ran a fluctuating course and eventually became euthyroid (Wilson, 1967; Havard, 1969). Thus, physicians faced with a clinically thyrotoxic patient have tended to plan definitive treatment from the outset.

The choice of treatment was basically between anti-thyroid drugs for up to 2 years, anti-thyroid drugs and then operation, or ^{131}I therapy. When ^{131}I became generally available in 1946 for the treatment of thyrotoxicosis its efficacy and simplicity were quickly established in early trials (Chapman and Evans, 1946; Werner, Hamilton, and Nemeth, 1952). There were, however, real fears that the doses of irradiation used might have one or more of the following effects:—

1. Shorten the life span of the treated person by some unknown mechanism.
2. Have a somatic effect on tissues leading to thyroid and other malignancies.
3. Lead to unfavourable reproductive events and/or genetic abnormalities in the children born of treated patients.

As a consequence ^{131}I therapy was rightly confined by the majority of physicians to the following groups of patients:—

1. Patients of over 40 years of age and only in the infertile or when pregnancy was deliberately avoided.
2. Patients of less than 40 years of age in whom the life span seemed to be limited. This group included patients with diabetes and rheumatic heart disease.
3. Patients who were less than 40 years of age in whom other treatments for thyrotoxicosis had been tried but were unsuccessful, dangerous, or unacceptable. This group, who comprised in the United Kingdom about 10 per cent of all the patients treated with ^{131}I in the interval 1950–70, included patients who had an undesirable reaction to or poor control with anti-thyroid drugs. It also included those who refused or were for some good reason not fit for operation. In addition patients with thyrotoxicosis which had recurred after surgery were treated with ^{131}I.

In the United Kingdom ^{131}I therapy was very seldom used in patients of less than 25 years of age and only exceptionally in children (Macgregor, 1957). In the United States, however, some physicians did treat children and young fertile women and men. As a consequence they have been able to accumulate and to report on their experience in relation to clinical outcome, reproductive events, and genetic effects on living offspring (Starr, Jaffe, and Oettinger, 1969; Hayek, Chapman, and Crawford, 1970; Becker and Hurley, 1971; Chapman, 1971).

CALCULATION OF DOSE OF ^{131}I

^{131}I was chosen because it seemed the most appropriate on physical and radiobiological grounds; in early trials it was obviously effective. In addition, it had been released for general use and was available in large amounts at acceptable prices.

^{131}I decays with the emission of energetic beta-rays which travel up to 2200 μm. (average 500 μm.) in thyroid tissue. The beta-rays, which have a finite path, constitute more than 95 per cent of the radiation energy deposited within the thyroid. Moreover, the radiation doses immediately outside the gland fall off very sharply because of the finite paths of the beta-rays. This means that the radiation doses to tissues adjacent to the thyroid and in the neck are exceedingly small in comparison to those within the gland itself. The radiation doses given to the marrow and blood and gonads are about equal and are around 20 rad from an average effective therapy dose (Green, Fisher, Miller, and Wilson, 1961). The radiation doses to the salivary glands, stomach, and kidneys are likewise small, and a tiny fraction of that within the thyroid tissue, which during effective therapy receives an average of 10,000 rad (*see below*). ^{131}I also emits gamma-rays which travel many centimetres through the tissues and out of the body, but the contribution to the thyroid or body dose is negligible compared with that of the beta-radiation. They are, of course, the radiation used for diagnostic tracer tests, but this is another matter.

As might be appreciated, pioneers were cautious in the use of the ^{131}I therapy, starting with small single doses which were repeated until the patient became euthyroid. It soon became apparent, however, that the best philosophy was to attempt control of the thyrotoxicosis with a single drink of ^{131}I alone within 3–4 months, to shrink the thyroid when it was enlarged, and to avoid hypothyroidism if possible. It was assumed that damage in the thyroid depended on the total radiation energy deposited there—the absorbed dose (in rad).

The rad dose is dependent on a number of variables:—

1. Amount of ^{131}I given (μ.c. dose).
2. Proportion of ^{131}I taken into the gland (uptake).
3. Mass of the gland and to some extent shape.
4. Stay of ^{131}I in the gland (biological half-life).
5. Distribution of ^{131}I throughout the tissue and cells.

In turn, the net damage within the thyroid from a given radiation dose in rad depends on distribution and on cell and tissue radiosensitivity (Greig, 1965).

Dose prescription procedures had in common measurement of a tracer uptake, measurement of gland mass by palpation or more recently by scanning, and some empirical estimate of biological half-life, distribution, and radiosensitivity. Some clinicians attempted to be precise and deposit a stated radiation dose in rad within the thyroid; a typical dose was 7000 rad (Blomfield, Eckert, Fisher, Miller, Munro, and Wilson, 1959). Some accepted that this could not be possible because of uncertain variables and aimed at being accurate at getting a given amount of ^{131}I into the thyroid: a typical régime was 150 μc. per g. of thyroid (Chapman and Maloof, 1955). Other clinicians prescribed ^{131}I on an empirical basis, having gained clinical and therapeutic experience with a more rational approach such as that of Blomfield and others (1959). This experience allowed them to adjust amounts of ^{131}I for the size and nodularity of the thyroid with adjustments for factors such as the urgency for rapid control (Macgregor, 1957). It is now known that any one of the three methods gave or gives similar results (Becker and Hurley, 1971).

EFFICACY

In the early 1960's the author reviewed (Greig, 1963), in some detail, the progress of 242 patients from the start of therapy through 8 years of complete follow-up. In this group the régime was to titre the amount of ^{131}I given to deliver about 7000 rad to the thyroid (Crooks, Buchanan, Wayne, and Macdonald, 1960). The results were very similar to those reported throughout the world before (Beling and Einhorn, 1961) and after (Becker and Hurley, 1971). In the author's series 60 per cent of the patients were rendered euthyroid within 3–4 months with one dose, but a further 25 per cent required a second dose and the remainder responded to a third dose. It is of importance that all the patients were eventually rendered euthyroid within about a year and it is of equal importance that in this series, as in others (McGirr, Thomson, and Murray, 1964), the recurrence rate was negligible.

HYPOTHYROIDISM

After the patients were euthyroid, however, more and more of them became hypothyroid with progressive follow-up until after 8 years 41·3 per cent were hypothyroid and only 52·5 per cent were euthyroid; in this series the remaining 6·2 per cent were deceased or could not be traced. In the same study (Greig, 1963) a review of 134 patients who had had ^{131}I therapy after a course of anti-thyroid drugs and 59 patients who had had ^{131}I therapy for a post-operative recurrence was also carried out. The clinical outcome in these two groups of patients was substantially the same as those treated with ^{131}I from the time of presentation.

These data highlight two of the outstanding problems caused by what might be termed 'conventional' ^{131}I therapy: these are a slow rate of control and after a variable interval of euthyroidism a progressive risk of thyroid failure. It is now well established that when ^{131}I is used alone to control thyrotoxicosis it will ultimately cure the condition in every case (that is, the recurrence rate is negligible), but the sufficient amount (or amounts) of isotope given nearly always leads to hypothyroidism; the rate is 80 per cent after a 15-year follow-up. If the initial dose prescription philosophy is set at a low range the rate of control will be unacceptably slow owing to a slow response to the first dose and the frequent need for multiple doses. In this case adjuvant therapy will be required. If the initial dose prescription philosophy is set at a very high range rapid cures will be obtained in the majority of patients but the same patients will become hypothyroid at a faster rate than with conventional doses.

SAFETY

Early Effects.—No demonstrable effects have been observed referable to the recurrent laryngeal nerves, the larynx, the pharynx, the oesophagus, the salivary glands, stomach, breast, or kidneys. A few minor radiation effects are, however, occasionally encountered. Radiation thyroiditis is very rare and seldom is there more than slight discomfort; sometimes the gland may be tender and exceptionally the pain may be severe and referred to the teeth and gums. Radiation thyroiditis occurs within a few days of the treatment and settles spontaneously or very quickly with a short descending course of prednisone. Radiation sialitis producing pain and swelling in the submaxillary and parotid glands is very rare, seldom requires medication, and subsides quickly.

An exacerbation of thyrotoxicosis is very difficult to measure so that its true frequency is not known. Those of us who treat large numbers of ill patients are seldom convinced that ^{131}I therapy can cause an increased degree of thyrotoxicosis. Thyroid crisis when it does occur usually does so in people who were severely thyrotoxic before therapy. When there is a risk in, for example, those with established cardiac failure this is reduced by giving carbimazole for a few weeks before introducing ^{131}I therapy. Carbimazole depletes the gland of hormone stores and at the same time lessens the degree of thyrotoxicosis. The true incidence of an exacerbation of thyrotoxicosis is not known but in my opinion it is very unusual.

Late Effects.—No effects referable to the recurrent laryngeal nerves, the larynx, pharynx, oesophagus, breast, stomach, or kidneys have been demonstrated and the late effects, other than those of hypothyroidism, are directly concerned with the risks or otherwise of thyroid cancer, leukaemia, or undesirable genetic consequences.

Thyroid Cancer.—The United States Public Health Thyrotoxicosis Follow-up Study was started in 1961 by the National Center for Radiological Health, and they have ascertained and reported (Sheline, Dobyns, Workman, Tomkins, McConahey, and Becker, 1969) on the incidence of thyroid cancer in 22,000 patients treated over the years with ^{131}I and they have similar data from 11,000 thyrotoxic patients treated by surgery. There was no difference in the thyroid cancer rate, the rate being negligible in both groups (Sheline and others, 1969; Becker and Hurley, 1971). It would thus appear that the 10 cases of thyroid cancer reported in the literature in association with a history of ^{131}I-treated thyrotoxicosis represent remote and incidental cases (McDougall, Kennedy, and Thomson, 1971). The consensus of opinion is that ^{131}I therapy does not cause thyroid cancer if the patients treated are aged 25 years or more.

Leukaemia.—Leukaemia was one of the somatic radiation effects feared by those pioneering ^{131}I therapy (Stanbury, 1970). In the thyrotoxicosis follow-up study referred to above, data were collected from 22,000 ^{131}I-treated patients to give a patient follow-up of 119,000 years; 17 patients developed leukaemia. In 14,000 thyrotoxic patients treated by surgery there were 114,000 years of patient follow-up and 16 cases of leukaemia (Saenger, Thoma, and Tompkins, 1968). Pochin (1960) found 18 cases of leukaemia in a total of 59,200 patients treated with ^{131}I in this country and followed for a number of years. It would thus appear that the incidence of leukaemia, a condition which is unlikely to be under-diagnosed, is not increased in ^{131}I-treated patients compared with either surgically treated patients or the general population (Becker and Hurley, 1971).

Chromosome Abnormalities.—These are found in the peripheral lymphocytes of ^{131}I-treated patients (Speight, Baba, and Wilson, 1968) but not in surgically treated patients. The lymphocyte cells carrying these abnormalities persist in the circulation for many years but they do not appear to represent clones of leukaemic cells (Boyd, Ferguson-Smith, McDougall, and Greig, 1973).

Genetic and Related Effects.—Genetic effects was another major concern of the pioneers (Holcomb, 1970). This aspect was not evaluated in the United States Public Health Thyrotoxicosis Follow-up Study because of an avowed difficulty in obtaining control data, but Starr and others (1969), Hayek and others (1970), and Chapman (1971) have gone a long way to providing the necessary data. *Table I* shows data from the study of Chapman (1971) and demonstrates that reproductive events such as fertility, pregnancy, and its outcome are not influenced by successful ^{131}I therapy.

Table I.—REPRODUCTIVE HISTORY OF 103 WOMEN TREATED WITH ^{131}I (FROM CHAPMAN, 1971)

	FULL-TERM CHILDREN	PREMATURE	MISCARRIAGES
Before ^{131}I	174	11	28
After ^{131}I	142	10	27

The dose to the ovaries after successful ^{131}I therapy is about 17 rad. In a group of more than 300 children above 3 years of age born of parents (male or female) treated at any age with ^{131}I, 219 have been seen and the incidence of disease determined. These data (Chapman, 1971) when analysed against the actuarial risks of congenital abnormalities, which for the whole population seem to be about 4 per cent of all live births, show a miniscule increase in the average risk of birth defects which might reasonably be attributed to ^{131}I therapy. This reassuring information is similar to that reported (Hayek and others, 1970) for treated females; 12 who were given ^{131}I therapy before the age of 18 gave birth to 18 normal children. Starr and others (1969) treated 73 children with ^{131}I many years ago and now find that the 28 females in the series eventually gave birth to 52 normal children.

The effects of ^{131}I therapy on the germ cells of individuals or the population as a whole can be looked at in another way. The International Commission on Radiological Protection, reporting in 1966, estimated that for each rad of parenteral gonad radiation above background the risk of producing a child with a transmissible trait is 1·6 per 100,000 live births. When patients are rendered euthyroid with ^{131}I the ovaries receive on average 16·6 rad (Weijer, 1964). The spontaneous incidence of these anomalies is about 0·8 per cent, so that ^{131}I therapy will increase the risk by not more than 0 025 per cent (Becker and Hurley, 1971).

Most mutations are, however, recessive and are not expressed in the first generation. The concept 'genetic death' is used to evaluate the effects of mutations on future generations. Genetic death is 'the extinction of a gene lineage through the premature death or reduced fertility of some individual carrying the gene' (Crow, 1957). It is estimated that if each member of the parental generation received 1 rad to both gonads there would be an increase of 0·1 per cent in the genetic deaths occurring in each generation for the next 10 generations (International Commission on Radiological Protection, 1966). Means, De Groot, and Stanbury (1963) think that the incidence of hyperthyroidism is 0·02 per cent per year or 1·4 per cent in a normal lifetime. If 50 per cent of thyrotoxicosis occurred during child-bearing years and if they all received ^{131}I therapy the average gonadal dose to the population would be $0{\cdot}014 \times 0{\cdot}5 \times 16{\cdot}6 = 0{\cdot}116$ rad. This would increase the incidence of genetic death by roughly 0·01 per cent per generation. Radiation from natural background is about 100 mrad per year and X-rays add another 55 mrad to this (Brown, Roney, and Hilberg, 1968). It would thus appear that the use of ^{131}I therapy in younger people is unlikely to increase the prevalence of transmissible genetic defects in succeeding generations.

^{131}I Therapy during Pregnancy.—Effects arising from ^{131}I given during pregnancy should, of course, not be amenable to study since pregnancy is an absolute contra-indication to this treatment. Nevertheless, the population currently receiving therapy is predominantly female, some of whom are fertile and occasionally pregnant without knowing it. Foetal hypothyroidism has been reported on 6 such occasions as reviewed by Pfannensteil, Andrews, and Brown (1965) and McDougall (1972). Usually, however, the baby is otherwise perfectly healthy (Silver, 1968). In fact, more often than not the baby is completely unaffected, although one would presume that if the foetal thyroid was irradiated there would be an increased risk of thyroid cancer in later life.

Abnormalities of Calcium Metabolism.—Damage to thyroid 'C' cells has been suspected after ^{131}I therapy. Certainly 'C' cells resident in the thyroid must be destroyed in the long term as the thyroid atrophies. ^{131}I-treated patents do tend to dispose of an intravenous calcium load at a slower rate than normal people or untreated thyrotoxic patients (Williams, Hargis, Galloway, and Henderson, 1966) and the effects seem to increase as the thyroid atrophies. Nevertheless, plasma-calcitonin levels are normal in patients without thyroid tissue (Gudmundsson, Galante, Woodhouse, Matthews, Osafo, McIntyre, Kenny, and Wiggins, 1969), and in untreated and treated thyrotoxics the serum-calcitonin levels are the same as in healthy people (Fraser and Wilson, 1971). It is true that in females thyrotoxicosis produces a relative demineralization of bone but this apparently decelerates as the hyperthyroidism is controlled, whether by ^{131}I, operation, or anti-thyroid drugs (Fraser, Smith, Anderson, and Wilson, 1971).

Damage to the parathyroids is a possibility during ^{131}I therapy. Very rarely, relative hypocalcaemia, spontaneous or induced by stress tests (Better, Carty, Brautbar, and Barzilac, 1969), has been reported after ^{131}I therapy, an effect attributed by some to radiation loss of parathyroid reserve (Eipé, Johnson, Kiamko, and Bronsky, 1968). In practice, however, neither blood-calcium levels nor bone density seems to be any different in age- and sex-matched patients treated by ^{131}I therapy and compared with those treated by anti-thyroid drugs (Fraser and others, 1971). It can, therefore, be stated that ^{131}I destruction of the thyroid does not result in significant abnormalities of calcium metabolism.

^{131}I THERAPY—THE CURRENT POSITION

^{131}I is still the isotope of choice. Recent evidence shows that it has no side-effects even when used in young adults, apart from the inevitable hypothyroidism. This being so, several questions should now be posed and answered:—

Which patients should be treated with ^{131}I?
What should the dose philosophy be?
What steps should be taken to supervise follow-up?
When is a patient hypothyroid?
What is the treatment for hypothyroidism?

Which Patients should be treated with ^{131}I?—The indications for ^{131}I therapy need to be reviewed now that we know that it is safe. All patients over 40 years of age should continue to have ^{131}I therapy by choice and without doubt the elderly, frail, and those with associated disorders, such as atrial fibrillation and cardiac failure. The size and nature of the thyroid should not influence this decision except that operation might be considered when the goitre is exceptionally large, causing mechanical trouble, or is retrosternal. In the author's opinion, however, even the largest glands will shrink provided that enough ^{131}I is given. There is now no doubt at all that ^{131}I therapy is indicated for a postoperative recurrence of thyrotoxicosis (McLarty, Alexander, Harden, and Clark, 1969) irrespective of the patient's age, sex, or fertility, provided, of course, that pregnancy is excluded at the time of therapy and avoided for up to 1 year after successful control. There is also much less reluctance to use ^{131}I therapy in young patients who have experienced a reaction to initial drug therapy. The alternatives are to change to another drug such as from carbimazole to propyl thio-uracil (Wilson, 1967; Havard, 1969) and to plan operation. The author's view is that this group should have ^{131}I therapy since the morbidity is less than that from surgery. The presence of significant titres of serum-anti-thyroid antibodies is not a contra-indication to ^{131}I therapy and, in fact, probably makes the case for it stronger. It is known that serological evidence of auto-immune thyroiditis increases the risk of post-operative hypothyroidism by a substantial fraction (Irvine, Macgregor, and Smart, 1962). Similarly, patients who for some good reason are not obtaining control from drug therapy or who relapse after a course of anti-thyroid drugs given for 1–2 years (50 per cent relapse) should have ^{131}I therapy rather than operation.

Patients of less than 40 years of age with a large gland have in the past been treated in this country by surgery, but this approach is not universal. Some clinics in the United States seldom refer any thyrotoxic patients for surgery and have experience in either controlling patients with anti-thyroid drugs on a long-term basis or referring them for ^{131}I therapy (Hershman, Givens, Cassidy, and Astwood, 1966).

Certainly the total morbidity from surgery may add up to as much as 50 per cent (McNeill and Thomson, 1968; Editorial, 1970), and perhaps if anti-thyroid drugs and ^{131}I therapy had been introduced in the 1920's surgery would seldom have been indicated in the management of thyrotoxicosis. On the other hand, expert surgeons may safely render a large proportion of patients euthyroid and they remain so provided that there is no auto-immune thyroiditis.

There are now very few absolute contra-indications to ^{131}I therapy. Thyrotoxicosis at birth or shortly afterwards and thyrotoxicosis in pregnancy certainly should not be treated with radiation. Similarly, thyrotoxicosis in children and young adults should first be treated with anti-thyroid drugs and if this is not satisfactory by surgery or ^{131}I therapy. It is well to remember, however, that the results of surgery in children are not very good (Saxena, Crawford, and Talbot, 1964; Havard, 1969) and there is a place for ^{131}I therapy here too, since it does not seem to affect fertility, pregnancy, or its outcome (Chapman, 1971).

What should the Dose Philosophy be?—The details of treatment are, of course, the province of the specialist in nuclear medicine or radiotherapy working in close collaboration with an endocrinologist. ^{131}I therapy should be organized on a regional basis with a central facility for patient assessment, dose calculation and prescription, and follow-up.

In the elderly, frail, and those with diabetes, heart disease, rheumatoid arthritis, atrial fibrillation, and cardiac failure, for example, a large dose designed to destroy the gland quickly should be given. The author now uses doses twice those advocated by Macgregor in 1957. If there is some risk of increasing the severity of the hyperthyroidism a course of carbimazole in a dose of, say, 15 mg. every 6 hours can be given for a few weeks. This has the merit of initiating some control and depleting the gland of hormonal stores. The technique is to stop the carbimazole for 1 week, measure thyroid uptake by tracer, assess thyroid mass, and prescribe a large amount of ^{131}I. Some loading of the dose is probably necessary in this category of patients (Crooks and others, 1960). Carbimazole can be recommended 1 week after the ^{131}I has been given in an amount of about 5 mg. every 6 hours, but a careful watch must, of course, be kept for the rapid onset of hypothyroidism. Deliberately large doses of ^{131}I should also, in the author's opinion, be prescribed for younger patients who have suffered prolonged or fearsome morbidity due to a postoperative recurrence, drug reaction, poor control with drugs, or relapse after a long course of drugs.

How should we use ^{131}I in patients who have, however, uncomplicated thyrotoxicosis? This group comprises mainly the relatively fit thyrotoxic in the 40–60-year age range or indeed in young patients, depending on treatment philosophy. Most of these patients have moderately enlarged thyroids. There are two possible approaches here and each has its supporters. They may be summarized as follows:—

1. Give large doses of ^{131}I from the start, anticipate hypothyroidism, and either give replacement therapy at about 1–2 months or when the criteria for hypothyroidism are satisfied (*see below*).

2. Give small doses of ^{131}I and expect only a small proportion to become euthyroid at 3 months. If at 3 months the patients are still thyrotoxic, and on the assumption that ^{131}I will gradually create a progressive effect and the disorder will remit, give non-destructive anti-thyroid drugs or symptomatic therapy. In practice, this means adding either carbimazole in a dose of 5 mg. three or four times a day (Smith and Wilson, 1967) or iodides in a dose of potassium iodide, 30 mg. three times a day (Hagen, Quellette, and Chapman, 1967), or propranolol in a dose of about 20 mg. four times a day provided that there are no contra-indications (Hadden, Shanks, Montgomery, and Weaver, 1968).

Of the three adjuvant treatments the author's preference is for carbimazole. Smith and Wilson (1967) used carbimazole in this way. They found, however, that 64 per cent of patients treated with 3500 rad from ^{131}I required drug treatment for a few months but 5 years later, when all drugs had been discontinued, only 7 per cent were hypothyroid. It is interesting that no case given ^{131}I therapy and drugs became hypothyroid. The approach of Smith and Wilson (1967) could be combined with the suppression test described by Alexander, Harden, Shimmins, McLarty, and McGill (1967). If after a small dose of ^{131}I followed by carbimazole for some months thyroid-uptake suppressibility returns there might be a case for stopping the anti-thyroid drugs with a reasonable expectation of a permanent remission. The approach outlined does reduce the incidence of hypothyroidism to very low levels. The relapse rate is also less than that encountered in surgical cases (Wilson, 1967).

What Special Steps should be taken to supervise Follow-up, diagnose Hypothyroidism, and treat it?—*See* contributions by Hall (not published here) and Hedley, p. 771.

Special Problems.—

1. *Poor Thyroid Uptake of Therapy Dose.*—Potassium perchlorate stops iodide trapping so that the occasional patient who is taking this drug temporarily as a substitute for one of the thio-uracils or imidazolines must stop it for at least a week before ^{131}I therapy is planned.

Patients who have taken stable iodides or iodine either intentionally or accidentally pose a special problem because the thyroid uptake of tracer and therapeutic dose is blocked. The degree of blockage and the time that it takes for recovery obviously depend on the amounts, character, route, and duration of the iodide excess. Although the therapeutic dose can be adjusted to take account of very low thyroid uptakes, there is not much point in using this therapy unless the thyroid takes up at least 25 per cent of the dose. There is no easy way of discharging stable iodide from the gland, but in thyrotoxicosis the best that can be done is to prescribe anti-thyroid drugs and at a later date, perhaps a few months, these can be stopped. If after a week the radio-iodine tracer uptake is 25 per cent or more ^{131}I therapy can be prescribed.

2. *Very Large Goitres.*—A very big thyroid is not a contra-indication to ^{131}I therapy but treatment of such patients raises two issues: the amount of the therapy dose and the risk of an exacerbation of thyrotoxicosis owing to the bulk of the tissue being irradiated and the possibility of releasing stored hormone into the circulation. A nodular thyroid of 100 g. in an ill patient might require 50 μ.c. of ^{131}I or more. There is not much to be gained from pretreatment with drugs in this situation since the gland may increase in size and the drugs may at any rate induce relative radioresistance (Crooks and others, 1960). In this situation it is important to ensure that any complications such as atrial fibrillation and cardiac failure are firmly treated before ^{131}I is given. Similarly, if the patient has no cardiac problems, asthma, or glaucoma, propanolol may be prescribed to subdue any slight exacerbation of hyperthyroidism. If there is a serious risk of exacerbation of hyperthyroidism there is no reason why the therapy could not be divided into, for example, two doses of 25 μ.c. separated by an interval of 1 month.

3. *Radiation Risks to Others.*—Some ill patients are, of course, treated in hospital and they should be placed in a side-room and the advice of the radiation safety officer sought. In general though, simple precautions suffice. These include a radiation sign on the door, lead aprons, and advice that the patient flushes the toilet several times. After a week no special precuations are required; no children should be allowed to visit during that week. If the patient has urinary incontinence she should be catheterized. If the patient vomits or soils the bedclothes these should be collected by the radiation safety officer for incineration.

The radiation hazard to relatives and the public arising during ^{131}I therapy of an out-patient has been discussed by the International Commission on Radiological Protection (1966) and more recently by Buchan and Brindle (1971) and Pochin (1972). It is estimated that a husband might be expected to receive about 30 rad for every μ.c. of ^{131}I given to his thyrotoxic wife; walking children receive much less. A working rule is that a patient receiving more than 30 μ.c. ^{131}I should be in hospital in a special room for up to 1 week; thereafter the patient may return home. No special precautions are required at home, but in general the patient should avoid contact with pregnant contemporaries and with young children for the first week.

4. *Exophthalmos*.—The link between thyrotoxicosis due to Graves' diesase and exophthalmos has not been fully identified. The balance of opinion is against an association with long-acting thyroid stimulator (Munro, 1971), but Kriss, Pleschakou, Rosenblum, Holderness, Sharp, and Utiger (1967) studied the progress of eye signs in patients treated with ^{131}I. Serial serum long-acting thyroid stimulator titres and serum anti-thyroglobulin antibody titres showed a rise in those whose eye signs deteriorated following this therapy. Others, however, have not found this (Munro, 1971). Kriss (1970, 1971) believes that energetic ^{131}I therapy does tend to lead to a deterioration in the ophthalmopathy when it is significant at the start of treatment. The mechanism for this, he believes, may lie in some common immunological link between thyroid antigen and an antigen in one or all of the extraglobal intra-orbital tissues.

In practice, ^{131}I therapy given to people with uncomplicated moderate exophthalmos leads to a slight increase in this during initial control and is similar to the increase following anti-thyroid drugs (Greig, Mohammed, Aboul-Khair, and Crooks, 1965). However, in the small minority of patients whose eye signs are severe or progressive it is probably wise to avoid ^{131}I therapy because of the anxieties expressed by Kriss (1970, 1971). Certainly the induction of hypothyroidism in this group of patients has a deleterious effect on the ocular signs; flexible anti-thyroid drug treatment is preferable. Incidentally it was at one time thought that total thyroid destruction by removing some speculative but unknown antigen in the thyroid might lead to an improvement in severe ophthalmopathy. This theory has now been discounted in practice as shown by studies of Boyle, Greig, Thomson, Winning, and McGirr (1969) and Volpé, Desbarats-Schonbaum, Schobakm, Row, and Egrin (1969). The specific management of the eye signs are, of course, a special problem and a decision about corticosteroid therapy or orbital decompression must in general be taken independently of the treatment for the hyperthyroidism.

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THE SURGICAL MANAGEMENT OF THYROTOXICOSIS

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SUMMARY

Preparation of selected thyrotoxic patients for partial thyroidectomy can be safely and quickly achieved using propranolol, the duration of preoperative therapy and the number of out-patient attendances being reduced by over 50 per cent. No problems have been encountered during preparation or intraoperatively in patients pretreated with propranolol when compared with patients pretreated with conventional preparations. The commonest form of morbidity following destructive therapy for thyrotoxicosis is hypothyroidism. In surgically treated patients hypothyroidism can be defined within 1 year of operation. The factors influencing postoperative hypothyroidism are discussed.

PARTIAL thyroidectomy has for many years been an established form of treatment for thyrotoxicosis. Refined anaesthetic and surgical techniques have reduced operative and perioperative mortality to virtually nil. Certain forms of morbidity, however, persist and though the incidence of complications such as wound haemorrhage, nerve injury, and hypocalcaemia are now less significant, hypothyroidism following surgery remains a major and possibly *the* major complication. Hypothyroid rates have been variously recorded as 3·3 per cent (Riddell, 1962) and 4·5 per cent (Cattell, 1949), but more recent studies have shown rates of 35 per cent (Hedley, Flemming, Chesters, Michie, and Crooks, 1970) and 48 per cent (Beahrs and Sakulsky, 1968).

The great variation in these figures is difficult to understand, but it is possible that the higher figures may merely represent a more critical evaluation of postoperative thyroid status. Historical evidence of the behaviour of untreated thyrotoxicosis does suggest that the higher recorded incidence of postoperative hypothyroidism may be more realistic. Studies at the turn of the century (*Table I*) indicated that approximately 20 per cent of untreated thyrotoxic patients died acutely in crisis while 40 per cent pursued a chronic course of exacerbation and remission into thyrocardiac disability. Approximately 40 per cent of untreated thyrotoxic patients ultimately improved spontaneously (Williamson, 1896; Ord and Mackenzie, 1897; Mackenzie, 1905; Sattler, 1908; Campbell, 1921), and while some remained euthyroid, others lapsed into hypothyroidism over the course of several years (Baldwin, 1895; Campbell-Gowan, 1895; Sattler, 1908). It would seem, therefore, that in some thyrotoxic patients there is a naturally progressive thyroid impairment leading to decreased reserve of function or frank failure, and it may be that in these patients surgery merely accelerates the natural course of the disease, compressing the events of many years into a matter of months.

SCOPE OF THE STUDY

The enigmatic and unpredictable appearance of hypothyroidism in some of the untreated thyrotoxic patients is mirrored in the postoperative behaviour of thyrotoxic patients who have been treated surgically. The present position is that though a reasonable estimate of the incidence of hypothyroidism can be made for a group of patients, the fate of individual patients can be predicted only within wide limits (Michie, Pegg, and Bewsher, 1972). In an endeavour to determine the factors which might influence the development of hypothyroidism after surgery and which might be of value in determining its early diagnosis and subsequent management, we have studied 373 patients who were subjected to surgery for thyrotoxicosis during the years 1965–71 inclusive. Hypothyroidism was assessed by a standard clinical diagnostic index (Billewicz, Chapman, Crooks, Day, Gossage, Wayne, and Young, 1969), on electrocardiographic evidence, and on serial serum protein-bound ^{127}I and cholesterol estimations. Patients were reviewed at 1, 4, and 12 months after operation and thereafter on a yearly basis until the services of a computer-assisted register became available (Hedley, Scott, Weir, and Crooks, 1970). The factors that were examined were preoperative preparation, surgical management, and early postoperative behaviour. Preoperative preparation in the earlier years was along conventional lines using carbimazole and Lugol's iodine. In the later years propranolol was employed, initially in conjunction with carbimazole but later on its own, excluding conventional preparations. More recently still, patients have been operated upon after a short course of propranolol, sometimes of a week's duration, and without preoperative Lugol's iodine.

We became acutely aware of the importance of the thyroid remnant size, as indicated by the high incidence of hypothyroidism in the early years of the study (*Table II*). This led from mid-1967 to a policy of leaving larger remnants with a resulting decrease in the hypothyroid rate to around 30 per cent.

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The factors of age, blood-group, anti-thyroid drug influence, and anti-thyroid antibody titres determined preoperatively have also been studied in relation to subsequent behaviour.

Table I.—FATE OF UNTREATED THYROTOXIC PATIENTS

AUTHOR	DIED		CHRONIC COURSE LEADING TO THYROCARDIAC DISABILITY		SPONTANEOUS IMPROVEMENT	
	No.	Per cent	No.	Per cent	No.	Per cent
Williamson (1896)	6	26	10	44	7	30
Ord and Mackenzie (1897)	8	24	11	34	14	42
Campbell (1921)	15	18	40	45	33	37
Total	29	20	61	42	54	38

Table II.—INCIDENCE OF HYPOTHYROIDISM IN RELATION TO MEAN ESTIMATED REMNANT WEIGHT FOR EACH YEAR FROM 1965 TO 1971

	YEAR						
	1965	1966	1967	1968	1969	1970	1971
Mean estimated remnant weight (g.)	3·6	4·1	5·5	8·1	8·0	7·2	6·8
Hypothyroid rate (per cent)	63	73	40	36	26	26	28

Table III.—INCIDENCE OF HYPOTHYROIDISM IN RELATION TO DURATION OF ANTI-THYROID DRUG THERAPY

PATIENTS	DURATION (mth)				TOTAL NO.*
	0–2	2–6	6–12	>12	
Euthyroid	52	73	22	22	169
Hypothyroid	35	69	23	24	151
Percentage hypothyroid	40	48	51	52	47

* Fifty-three patients received propranolol and have been excluded

RESULTS

Factors not influencing Hypothyroidism.—The duration of anti-thyroid drug therapy varied from a month to several years, and usually was determined by the physicians who supervised the preoperative care of the patient. No correlation was found between postoperative hypothyroidism and the duration of treatment (*Table III*), nor did the amount of drugs prescribed affect the incidence of hypothyroidism (*Table IV*). The titre of anti-thyroglobulin antibodies (Fulthorpe, Roitt, Doniach, and Couchman, 1961) measured preoperatively was higher in hypothyroid patients, but this difference did not reach statistical significance. Preoperative anticytoplasmic antibody (Beck, 1971) was equally prevalent in hypothyroid and euthyroid patients (*Table V*). Despite considerable variation in the size of the thyroid glands (65 weighed less than 30 g., 40 more than 100 g.) no relationship between total gland mass and hypothyroidism could be demonstrated (*Table IV*).

Factors influencing Hypothyroidism.—A study of the blood-group distribution of thyrotoxic patients in this study showed the distribution of ABO blood groups to be almost identical with the general population of the North-east region of Scotland (Mourant, Kopec, and Domaniewska-Sobczak, 1958) (*Table VII*). Blood-group O was significantly more common in the hypothyroid group of patients ($P<0\cdot05$). Blood-group A was less common but this difference did not reach statistical significance ($0\cdot05<P<0\cdot1$; *Table VIII*). Postoperative hypothyroidism also showed a higher incidence in female patients over the age of 40 years who were pretreated with carbimazole than in the younger age-group ($P<0\cdot05$; *Table IX*).

Table IV.—INCIDENCE OF HYPOTHYROIDISM IN RELATION TO TOTAL AMOUNT OF ANTI-THYROID DRUG PRESCRIBED

PATIENTS	DOSE (g.)				TOTAL NO.*
	<3	3–6	6–10	>10	
Euthyroid	85	54	11	19	169
Hypothyroid	69	47	18	17	151
Percentage hypothyroid	45	47	62	47	47

* Fifty-three patients received propranolol and have been excluded.

The most significant factor which determines the behaviour of a group of patients after partial thyroidectomy is the size of the remnant left at operation. Remnants of 4 g. or less carry the highest hypothyroid rate, whereas those of 10 g. or more carry the lowest ($P<0\cdot001$; *Table X*). It must be emphasized, however, that the size alone is not the only criterion, for with a remnant size of 4 g. or less there is a 36 per cent incidence of euthyroidism while with a remnant of 10 g. or more hypothyroidism still occurs in 20 per cent of patients.

MANAGEMENT

What advice can be offered in the avoidance of postoperative hypothyroidism? Although the 'ideal' remnant size must remain conjectural for the individual patient, average remnant size for the group should be in the region of 7–9 g. It would also seem logical to leave larger than smaller remnants in patients who belong to blood-group O and in female patients of over 40 years of age. Against this we have found unhelpful the response to anti-thyroid drug therapy, either in the duration of treatment or in total dosage. Our findings also suggest that antithyroid antibody titres should not influence the decision on remnant size.

Table V.—RELATIONSHIP BETWEEN ANTI-THYROID ANTIBODIES DETERMINED BEFORE OPERATION AND INCIDENCE OF HYPOTHYROIDISM

PATIENTS	TANNED RED CELL			TOTAL NO.
	NEGATIVE (0–1 : 25)	POSITIVE (1 : 250–1 : 2500)	STRONGLY POSITIVE (1 : 25,000–1 : 2,500,000)	
Euthyroid	174	18	17	209
Hypothyroid	131	12	21	164
Percentage hypothyroid	43	40	55	44

PATIENTS	ANTICYTOPLASMIC ANTIBODY			TOTAL NO.
	NEGATIVE (0, ±)	POSITIVE (+)	STRONGLY POSITIVE (++, +++)	
Euthyroid	89	33	87	209
Hypothyroid	55	28	81	164
Percentage hypothyroid	38	46	48	44

Table VI.—INCIDENCE OF HYPOTHYROIDISM IN RELATION TO TOTAL GLAND MASS

PATIENTS	WEIGHT (g.)					TOTAL NO.
	10–29	30–49	50–69	70–99	>100	
Euthyroid	38	66	47	32	26	209
Hypothyroid	27	69	40	14	14	164
Percentage hypothyroid	42	51	46	31	35	44

Table VII.—COMPARISON OF ABO BLOOD GROUPS (PER CENT) OF GENERAL POPULATION OF NORTH-EAST SCOTLAND WITH THYROTOXIC PATIENTS IN THE PRESENT SURVEY

SUBJECTS	BLOOD GROUP			
	O	A	AB	B
General population of North-east Scotland	51	35	3	11
Thyrotoxic patients	54	35	4	7

Table VIII.—INCIDENCE OF ABO BLOOD GROUPS (PER CENT) IN EUTHYROID AND HYPOTHYROID PATIENTS AFTER SURGERY

PATIENTS	BLOOD GROUP			
	O	A	AB	B
Euthyroid	48	38	5	9
Hypothyroid	62	29	3	6

Table IX.—POSTOPERATIVE HYPOTHYROIDISM IN RELATION TO THE AGE OF THE PATIENT AT TIME OF OPERATION

PATIENTS	AGE (yr.)		TOTAL NO.*
	<40	>40	
Euthyroid	97	50	126
Hypothyroid	67	59	147
Percentage hypothyroid	41	56	53

* Female patients prepared with carbimazole only.

The surgeon, like the radiotherapist, must accept a measure of post-treatment hypothyroidism, and for the surgeon the figure is unlikely to be less than 30 per cent. Whichever the method of treatment there is a clinical and ethical responsibility for the continuing supervision of these patients. It has been our practice to estimate protein-bound ^{127}I levels at 1 and 4 months after operation and thereafter yearly. From a study of 1- and 4-month figures a distinct pattern emerges. When both levels are 4 μg. per 100 ml. or more we have not observed hypothyroidism in the subsequent follow-up period. Where both levels are below 4 μg. per 100 ml. there is a 77 per cent incidence of hypothyroidism. When one of these levels is below 4 μg. per 100 ml. the incidence of hypothyroidism is around 20 per cent, but a rising level holds a more favourable prognosis than a falling one ($P < 0{\cdot}001$; *Table XI*).

Contrary to published reports (Nofal, Beirwaltes, and Patno, 1966; Olsen, Nishiyaric, and Graber, 1970), we have not observed hypothyroidism occurring later than 1 year after operation. Thus within 1 year it becomes possible to define the thyroid status of an individual patient. Approximately 70 per cent will be euthyroid, while the remaining 30 per cent will require thyroxine replacement. This is a matter of some importance for the busy surgeon for whom a computer-assisted register may not be available. Although ideally all patients subjected to surgery merit lifelong supervision, the surgeon can concentrate his attention on those patients whose early postoperative protein-bound ^{127}I levels have been less than 4 µg. per 100 ml.; in this respect the surgeon has an advantage over his medical colleagues.

Table X.—INCIDENCE OF HYPOTHYROIDISM IN RELATION TO ESTIMATED REMNANT WEIGHT

PATIENTS	REMNANT WEIGHT (g)				TOTAL NO.
	2–4	5–7	8–10	>10	
Euthyroid	45	89	62	13	209
Hypothyroid	84	56	21	3	164
Percentage hypothyroid	64	39	25	19	44

Table XI.—INCIDENCE OF HYPOTHYROIDISM IN RELATION TO PROTEIN-BOUND ^{127}I LEVELS AT 1 AND 4 MONTHS AFTER OPERATION

Level at 1 month (µg per 100 ml)	<4	>4	<4	>4	TOTAL No.*
Level at 4 months (µg. per 100 ml.)	<4	<4	>4	>4	
Patients					
Euthyroid	47	11	42	107	207
Hypothyroid	155	6	2	0	163
Percentage hypothyroid	77	35	5	0	44

* Data incomplete for 3 patients.

Table XII.—COMPARISON BETWEEN PATIENTS PREPARED FOR OPERATION WITH CARBIMAZOLE AND PROPRANOLOL

	PROPRANOLOL	CARBIMAZOLE
Mean No. of out-patient attendances	4	9
Mean duration of treatment (d.)	46	314

A further advantage in management will accrue to the surgeon from the use of the beta-adrenergic blocking agent propranolol. The ability of propranolol to control the haemodynamic changes of hyperthyroidism has been recorded (Rowlands, Howitt, and Markman, 1965; Turner, Granville-Grossman, and Smart, 1965; Howitt and Rowlands, 1966; Parsons and Jewitt, 1967; McDevitt, Shanks, Hadden, Montgomery, and Weaver, 1968; Shanks, Hadden, Lowe, McDevitt, and Montgomery, 1969), and an improvement in other symptoms and signs has also been demonstrated (Marsden, Gimlette, McAllister, Owen, and Miller, 1968; Pimstone, Marine, and Pimstone, 1968; Shanks and others, 1969). The use of propranolol as a preoperative agent has also been described (Barroso and Laczano, 1968; Vinik, Pimstone, and Hoffenberg, 1968 Granger, Wolf, and Strazielle, 1969; Shanks and others, 1969; Giardina, Bellotti, De Gregori, and Ghidiri, 1971; Turner, 1971). We have used it in approximately 100 patients; in 50 propranolol was used in conjunction with carbimazole, whilst in the remainder preparation was by propranolol alone *Table XII* compares patients treated concurrently, either with carbimazole or propranolol in respect of preoperative out-patient attendance and duration of treatment. In both respects propranolol seems to offer considerable advantages. The use of propranolo in the preoperative management of thyrotoxic patients is still under joint evaluation by physician surgeon, and anaesthetist, and we have been carefu to exclude patients with a history of bronchospasm and myocardial decompensation. In patients where propranolol has been employed there have been no problems during preoperative preparation or intra-operative complications for either the anaesthetist or the surgeon. With increasing confidence in its use we have reduced the duration of preoperative preparation and more recently several patients have come to operation within 10 days of commencement of treatment, the shortest being 3 days, and withou the use of preoperative iodine. With experience it should be possible to operate on the florid thyrotoxic patient after a preoperative course of a week or less.

Present indications are that the incidence of postoperative hypothyroidism is the same after propranolol as after conventional therapy. The curtailment of preoperative preparation that propranolol allows and the ability to define postoperative thyroid status for the individual patient within a year offers considerable advantages for the surgically treated thyrotoxic patient.

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LYMPHOID TISSUE IN THE THYROID GLAND AND THYMUS OF PATIENTS WITH PRIMARY THYROTOXICOSIS

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Summary

The amount of lymphoid tissue in the thyroid gland and thymus at the time of partial thyroidectomy was measured quantitatively with the point-counting technique.

The normal pattern of age involution of the thymus was established in patients with non-toxic nodular goitre. In all the patients with thyrotoxicosis the thymus is hyperplastic; after pretreatment with anti-thyroid drugs, such as carbimazole, the pattern of age involution is similar to that in the control subjects, whereas after propranolol therapy very little age involution is seen. Patients treated with anti-thyroid drugs show much less lymphoid infiltration of the thyroid gland than those prepared with propranolol.

There is good historical evidence that the thymus is enlarged in patients dying with untreated primary thyrotoxicosis and this feature was apparently so prominent that unsuccessful attempts were made to treat the disease by thymectomy at the beginning of this century (Fisher, 1964). More recently, it has been shown that the thymus is enlarged (Irvine and Sumerling, 1965) and hypertrophied (Michie, Beck, Mahaffy, Honein, and Fowler, 1967) during life in primary thyrotoxicosis patients in whom the disease activity had been controlled with anti-thyroid drug treatment. Focal thyroiditis formed of aggregates of lymphoid cells is a not infrequent finding in the thyroid gland of patients with primary thyrotoxicosis; there is evidence that in patients prepared for subtotal thyroidectomy with anti-thyroid drugs, such as methyl thio-uracil and carbimazole, those with extensive lymphoid infiltrate in the thyroid gland at the time of operation are much more likely to become hypothyroid after the operation than those with little thyroiditis (Greene, 1950–1; Levitt, 1951).

In view of these indications of an abnormality of the lymphoid tissues in primary thyrotoxicosis and the evidence that auto-immunity complicates and may in fact be responsible for the thyroid hyperfunction in this disease, the present investigation was undertaken to determine quantitatively the changes in the fixed lymphoid tissue in the thyroid gland and thymus in this disease. Since some of the patients had been prepared for operation with carbimazole and others with propranolol, we were able to compare the influence of these drugs on the fixed lymphoid tissues in this disease. This paper reports our preliminary findings.

METHODS

Conventionally fixed and stained sections of thyroid gland and thymus removed at operation were studied with the point-counting technique which allows calculation of the relative volumes of various tissue components in these organs (Dunnill, 1968). With a graticule fixed in the eyepiece of the microscope, the number of appositions of the graticule on particular tissue components was counted in every field examined. The whole of the section of each thymus was counted field by field, and the cumulative total of appositions on thymic parenchyma (and its components, cortex, and medulla) and on the intervening stroma was determined. The ratio of these counts gives an accurate estimate of the relative volumes of these components in the whole organ. The area of the thyroid gland sections was much greater, and consequently fields were selected using six-figure random numbers to define the co-ordinates of the mechanical stage and the counts were continued until the standard error of the observations was less than 5 per cent.

RESULTS

Histometry of the Thymus.—

Non-toxic Nodular Goitre.—In an attempt to define the pattern of age involution in patients who do not have evidence of immunological disease, thymic biopsies from 89 patients (51 women and 38 men) undergoing thyroidectomy for this disease were studied. The lymphoid parenchyma in the thymus declines from about 50 per cent in late teenage to about 10 per cent in late middle age. There is a striking sex difference; in men age involution is linear, whereas in women it is biphasic owing to a 'hump' in the first half of the fifth decade. The sex difference is due entirely to a difference between the cortex in the two groups.

Primary Thyrotoxicosis in Patients prepared for Operation with Anti-thyroid drugs.—One hundred and thirty-one female patients were studied. In these patients the thymus is hyperplastic, but the pattern of age involution of the whole parenchyma is similar to, but at a higher level than, that in non-toxic nodular goitre patients. The main difference between these two groups of patients is the much more abundant medulla in the thyrotoxic patients.

Primary Thyrotoxicosis in Patients prepared for Operation with Propranolol.—Twenty-seven female patients were studied. These patients show little evidence of age involution of the thymic parenchyma and the findings are spectacularly different from age-matched anti-thyroid drug patients ($P < 0{\cdot}001$); this difference is largely explained by the more prominent hyperplasia of the cortex in the propranolol-treated patients.

Histometry of the Thyroid Gland in Treated Primary Thyrotoxicosis.—When the thyroid glands of the 131 female patients treated with carbimazole were compared with those of the 27 women treated with propranolol, no histological features were noted in either group that were absent from the other group. The glands in both treatment groups showed the well-documented features of treated primary thyrotoxicosis, such as epithelial hyperplasia, small acini, and colloid depletion. Thus there was no absolute difference in the qualitative histological appearances between the two groups.

Histometry showed that there were minor differences between the two groups in the proportion of the gland occupied by epithelial cells and colloid: the thyroid glands of the propranolol patients were marginally 'more florid'. The most marked difference between the two groups was that lymphoid infiltrate was more frequent and in general more abundant in the propranolol-treated patients than in the carbimazole group; the distributions were not normal, but a Willcoxon test showed that the difference between the two treatment groups was highly significant ($P < 0{\cdot}001$).

DISCUSSION

The enlargement of the fixed lymphoid tissues in the thyroid gland and thymus of untreated primary thyrotoxicosis patients is a marked feature of the disease. It is likely that this is at least partly due to the stimulatory effect of raised circulating thyroid hormone levels since lymphoid hyperplasia can be induced in experimental animals by feeding thyroxine. This is probably not the only influence, since thymic hypertrophy is a feature of certain auto-immune diseases, such as myasthenia gravis where the patients are euthyroid and here the lymphoid infiltrate in the thyroid gland probably indicates active destructive auto-immunity.

Our measurements have shown that the thyroid gland is enlarged and also hypertrophied in patients with treated primary thyrotoxicosis. After carbimazole treatment the medulla is proportionately larger, but the thymus shows a normal pattern of age involution; after propranolol treatment both the cortex and the medulla are enlarged and little age involution is seen. Lymphocytic infiltration is present in the foci of chronic thyroiditis in the two treatment groups and this is much more prominent in the thyroid glands of patients treated with propranolol.

The marked differences between the amounts of fixed lymphoid tissue in the thyroid gland and thymus of the primary thyrotoxicosis patients treated with carbimazole and propranolol may be related to the pharmacological action of these drugs. The conventional anti-thyroid drugs reduce thyroid function and so make the patient euthyroid. By contrast, propranolol is a β-adrenergic blocking agent that can neutralize the effects of raised circulating thyroid hormone levels on cardiovascular receptors. Consequently, the most plausible explanation of our findings would be that the lymphoid tissues in carbimazole-treated patients have been released from excessive thyroid hormone stimulation and have partly reverted to normal by the time of operation, whereas the lymphoid tissues in propranolol-treated patients continue to be subjected to excessive thyroid-hormone stimulation.

Two other explanations for our findings should be considered. First, it is possible that the conventional anti-thyroid drugs have immunosuppressive properties in view of their chemical similarity to uracil, but this pharmacological action has not been investigated (Berenbaum, 1973); if this were so, then it would be possible that this action would induce lymphoid tissue atrophy in the patients treated with carbimazole. Secondly, it is remotely possible that propranolol could cause hyperplasia of lymphoid tissues by direct stimulation, but this explanation is unlikely since the appearances of the lymphoid tissues in propranolol-treated patients are similar to the historical pathological descriptions of untreated primary thyrotoxicosis.

Primary thyrotoxicosis is a complicated disease in which it is probable that immunological and endocrinological mechanisms interact. It is possible that investigation of the pharmacological effects of the drugs used in its treatment will assist the understanding of the pathogenesis of the diseases.

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LONG-TERM AFTERCARE FOR PATIENTS TREATED FOR THYROTOXICOSIS

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THE CLINICAL PROBLEM

THE nature and magnitude of the clinical problem of providing effective aftercare for patients with thyroid disease can be clearly defined.

Destructive Therapy.—All the patients treated with radioactive iodine for thyrotoxicosis remain at risk of developing hypothyroidism within their lifetime (*Table I*), and patients treated surgically carry the double risk of either early hypothyroidism or late-onset recurrent hyperthyroidism (*Table II*).

Table I.—RESULTS OF FOLLOW-UP STUDIES AFTER ^{131}I THERAPY

AUTHOR	MAXIMUM FOLLOW-UP PERIOD (yr.)	PERCENTAGE OF PATIENTS WHO WERE HYPOTHYROID
Cassidy and Astwood (1959)	8	26·0
Beling and Einhorn (1961)	7	26·5
Burnett and others (1962)	7	16·5
Green and Wilson (1964)	10	29·0
McGirr and others (1964)	1½	17·2
Crooks (1965)	8	41·3
Hagen and others (1967)	—	33·0
Smith and Wilson (1967)	5	29·0

Anti-thyroid Drugs.—This form of treatment, which is simple, cheap, and effective and leaves the gland intact, is preferred by many clinicians and also undoubtedly by their patients. Although many patients achieve a prolonged remission, particularly when their response to treatment is monitored by the assessment of thyroid suppressibility, all the patients remain at risk of a recurrence at a later and unpredictable point in time.

Thyroxine Replacement Therapy.—There is clear evidence from several follow-up studies that the prescription of replacement therapy for patients with spontaneous or iatrogenic hypothyroidism does not provide infallible protection against the future development of hypothyroidism.

The actual numbers of patients involved on a national scale can only be estimated with difficulty because of the inadequacy of our records systems. Many patients are investigated and treated solely on an out-patient basis. Out-patient departments invariably lack a comprehensive diagnostic index facility and unless separate registers are kept for all patients with thyroid disease then much vital information is lost. It can be shown, however, that in countries such as the United Kingdom and United States the number of new patients at risk of iatrogenic thyroid disease lies between 10,000 and 30,000 a year. It is clear that the health services should be able to provide effective medical care in response to such a specific need.

It is important to emphasize that the reported results of treatment in many centres have only been realized after *ad hoc* retrospective surveys have been carried out. This is an extremely unsatisfactory method of assessing the outcome of any form of treatment. The results of incomplete retrospective studies may be very misleading when used in the assessment of clinical management or the future planning of services.

In the present state of our knowledge it is unlikely that the outcome of treatment, which is influenced by a great many variable factors, can be significantly affected by the manipulation of one of them. Much attention has been given in recent publications to modifications of treatment régimes designed to reduce the incidence of later complications. None of these has met with sufficient success to obviate the need for long-term follow-up. Thyrotoxicosis can be effectively treated by the currently available empirical methods; if hypothyroidism is an inevitable consequence of this it should be diagnosed early and treated adequately. Emphasis in the past on the active and early stages of treatment has resulted in a high level of undetected iatrogenic disease.

WHY FOLLOW-UP HAS FAILED

The development of a solution to the problem of long-term aftercare for these patients was preceded by an appraisal of the parts of the health service responsible for the patients' care and an examination of the reasons why follow-up has failed in the past.

In a study of post-thyroidectomy patients in North-east Scotland (Hedley, Flemming, Chesters, Michie, and Crooks, 1970) no difference could be found between patients recalled by the follow-up survey itself and those on the survey list who were referred specifically by their general practitioner. This suggests that many patients' use of the medical services is random and not related simply to the presence of symptoms or their severity but also to other factors.

Table II.—Long-term Results of Subtotal Thyroidectomy

Author	Maximum Follow-up Period (yr)	Percentage of Patients who were Hypothyroid	Percentage of Patients with Recurrence	Total Morbidity
Crile and McCullagh (1951)	10	4·5 21·0	15·0 2·1	19·5 23·1
Green and Wilson (1964)	14	5·0	8·0	13·0
Nofal and others (1964)	16	28·0	—	>28·0
Roy and others (1967)	9	5·0	11·0	16·0
McNeill and Thompson (1968)	14	6·5	12·5	19·0
Hedley, Flemming, and others (1970)	21	35·6	4·0	39·6

The Patient and the Presence of Disease.—The reasons why patients will admit to but not spontaneously complain of symptoms of considerable severity which are present for long periods are not easily defined. At least part of the problem is related to the treatment act itself, the way in which it is carried out, and the nature of the complications which occur later. In common with many other forms of definitive treatment (for example, partial gastrectomy) nothing has been done, understandably, to dissuade the patient from the view that the treatment will effect a cure. Less understandable is the fact that no account has been taken of the possible concomitant disruption of normal physiological processes and many of these complications have only been recognized long after the treatment has become established as a standard practice. As a result neither the patient nor the general practitioner has been prepared for the onset of late complications; when symptoms do occur they are frequently dissociated from the treatment act both in time and in the patient's mind. The symptoms of hypothyroidism occurring late are frequently attributed to the ageing process. The onset of recurrent hyperthyroidism may be equally as insidious and sometimes the symptoms may be mild or absent in contrast to other aspects of the metabolic disturbance. Hypothyroidism usually occurs early after subtotal thyroidectomy for thyrotoxicosis and here it is often not clear that symptoms, if they are present at all, are related to thyroid dysfunction, because they are opposite in nature to the complaint for which the patient has recently received successful treatment. In both hypothyroidism and hyperthyroidism there is often a profound disturbance of mental function, which probably occurs to a greater extent in hypothyroidism (Whybrow, 1969). The slow onset of apathy, somnolence, and listlessness may be accompanied by abnormalities of cognitive function and depression, all of which contribute to the failure of the patient to rationalize the situation and seek medical advice.

In retrospective follow-up studies, failure to find more than 50 per cent of the population 'at risk' can easily be ascribed to the behaviour or idiosyncrasies of individual patients. Untraced patients can be shown to have migrated, emigrated, joined an organization which obliges them to move about (e.g., military forces), changed their name (e.g., marriage), or encountered other problems such as separation, divorce, prison, and debilitating physical or mental illness, all of which complicate their follow-up or modify their responses to recall which takes place some considerable time after the original treatment. It would be quite wrong to lay the responsibility for this failure in communication solely on the patient, particularly as it can be clearly shown that the machinery for either retrospective or prospective follow-up is not provided within the framework of the existing health services.

Medical Records.—One major defect has been in the organization of the medical records systems through which these patients must be identified. Retrospective studies have shown that the present methods of recording and updating basic identification information in hospital, general practice, and executive council records are wholly inadequate, and in many instances are non-existent. Furthermore, there is very little cross-communication between these information stores.

The identification data and allied information collected for the patient's record at the time of admission to hospital are not necessarily the same as those required when long-term follow-up begins. The present format of the hospital case record is often unsatisfactory for its intended purpose and altogether unsuitable as a follow-up document. With the present system of medical records, follow-up should be carried out as a separate but parallel exercise to the routine work of wards and clinics. However, the follow-up records should be complementary to those in hospital and the latter should be constantly updated with any changes in the patient's follow-up status.

The Hospital Service and the General Practitioner.—The responsibility for follow-up must either lie with the general practitioner (providing primary care) or the hospital clinic (which gave the special treatment). The sharing of responsibility for patients of mutual interest between these two parts of the health service has never been clearly defined and in addition they both face special problems.

Because of the overwhelming demand on curative medicine the hospital services are deeply committed to the treatment of new patients and have no additional resources to provide a comprehensive follow-up scheme to detect iatrogenic disease. If the hospital accepts the responsibility for aftercare for patients 'at risk' it is usurping the responsibility of the general practitioner. Furthermore, even if the number of new referrals remained constant the cumulative clinical commitment would soon reach prohibitive proportions. When patients continue to attend an out-patient department for long periods there is an implication that they are better handled in this way than by their general practitioner. This may occasionally be true, but as a routine method of patient care it can only be justified if a special skill is required throughout the long period of attendance. In fact this is infrequently the case and many patients continue to attend hospitals because the onus is on no one to discharge them.

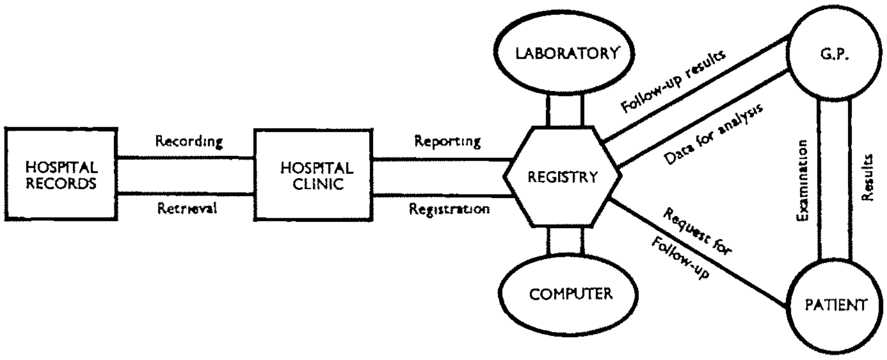

FIG. 1.—Flow diagram of the Scottish Automated Follow-up Register showing the relationship between hospital, general practitioner, patient, and registry. (*Reproduced by permission of the Editor, 'Scottish Medical Journal'.*)

The responsibility for primary care must lie with the patient's own doctor. However, general practitioners seldom have access to appropriate laboratory and data-processing facilities which would enable them to carry out the kind of follow-up which is needed. Several centres do include thyroid-function tests in the range of laboratory investigations routinely available to general practitioners, but in any one practice the patients who require the test are usually small in number and widely dispersed, which makes efficient use of the laboratory facility extremely difficult. However, many difficulties would be avoided and advantages gained if the follow-up arrangements were under the control of the family doctor; for example, within the health service our patients are automatically divided into small manageable groups within each general practice unit. The general practitioner is working in a community which is relatively static and he therefore has, or should have, greater opportunity than most doctors to practise continuity of care. The importance of the general practitioner in follow-up is also linked to the need to motivate patients to seek help; most patients usually prefer to be attended by their family doctor rather than the comparatively hostile environment of the out-patient department. At the same time care must be taken to avoid the deep involvement of the general practitioner in complicated and unproductive routine examination of his patients.

Migration and Emigration.—A feature of the age in which we live is the increasing mobility of the population, which equally applies to the population of 'at-risk' patients under study. When patients leave a district they leave their general practitioner, out-patient clinic, and often their medical records behind them (Acheson, 1967). The movement of patients is increasing at a considerable rate. For example, in the 50 years up to 1970 the population in North-east Scotland fell by almost 7 per cent whereas the population of the whole of Scotland increased by 9 per cent. The process of depopulation is particularly marked in the highlands and islands. For example, the population of Orkney and Shetland fell by 43 per cent in the hundred years before 1951 and the rate of decline is increasing, having been 6·6 per cent in the 20 years before 1951 and 10 per cent in the 10 years since then (Registrar-General, 1961; Hall and Baldwin, 1968).

Changes of this kind are not confined to patients. Doctors move and retire, or even change their interests, and their successors are not always willing or obliged to adopt the same mantle, and as a result continuity of patient care often suffers.

The Regional Geography.—Many thyroid clinics serve thinly populated rural areas. The difficulty, inconvenience, and expense (not recoverable without a means test), and often the hazards associated with travelling to central clinics, reduce the likelihood that successful contact will be maintained with patients over a long period of time. For patients in outlying districts such as the Scottish islands, attendance at a central clinic on the mainland for a check-up examination is not possible.

Conclusions.—It is clear that traditional methods of medical care are not sufficiently developed or flexible enough to overcome the kind of organizational problems which confront those responsible for patient follow-up. Provision of general practitioner facilities for investigation of thyroid function is not sufficient; unless the aftercare of small selected groups in each general practice unit can be co-ordinated and controlled, then follow-up may fail no matter how sophisticated are the scientific aids at the doctor's disposal.

THE NEW SYSTEM

A new system of aftercare for patients treated for thyrotoxicosis and spontaneous hypothyroidism has been developed through the collaborative efforts of computer scientists, administrative personnel, and doctors (in hospital and general practice) in the areas at present served by the five Scottish regional hospital boards. The system provides a screening and record-keeping service for general practitioners and effectively identifies patients with iatrogenic thyroid disease. The computer-assisted follow-up programme ensures continuity of care, automates all the procedures which do not require a decision by a doctor, and guarantees contact between general practitioner, laboratory, and patient at appropriate intervals.

The follow-up operations are controlled by a registry (*Fig.* 1) which maintains the follow-up file in the form of cumulative personal medical records for each patient using computer-assisted record-keeping techniques. These methods and the follow-up procedure have been described in detail elsewhere (Hedley, Scott, and Debenham, 1969; Hedley, Scott, Weir, and Crooks, 1970). The hospital clinician enters the euthyroid post-treatment patient on the register at the request of the general practitioner. The registry notifies the practitioner when a follow-up examination is due, processes the clinical information and blood sample which he returns, and finally reports the results in the form of a selective diagnosis. The secretarial functions of the automated registry include updating the patient's record in general practice and hospital, tracing non-responders, tabulating the reasons why patients and doctors discontinue their use of the system, and compilation of follow-up results including morbidity and mortality tables.

CONCLUSIONS

This new approach to aftercare circumvents many of the obstacles to effective follow-up. It leaves responsibility for patient care, outside hospital, with the general practitioner but provides him with a convenient and efficient method of carrying this out. Both the general practitioner and his hospital centre obtain accurate information for their medical records at regular intervals. The movement of patients and doctors is recorded, their files are constantly updated with changes of name and address, and the geographical problem of great distances between patient and specialist clinic no longer exists.

It may be claimed that the register link betwee general practice and hospital is an importar component of the efforts being made towards rational integration of these two parts of the healt service.

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'Diagnostic Procedures in the Management of Hypothyroidism', R. Hall (Newcastle upon Tyne).]

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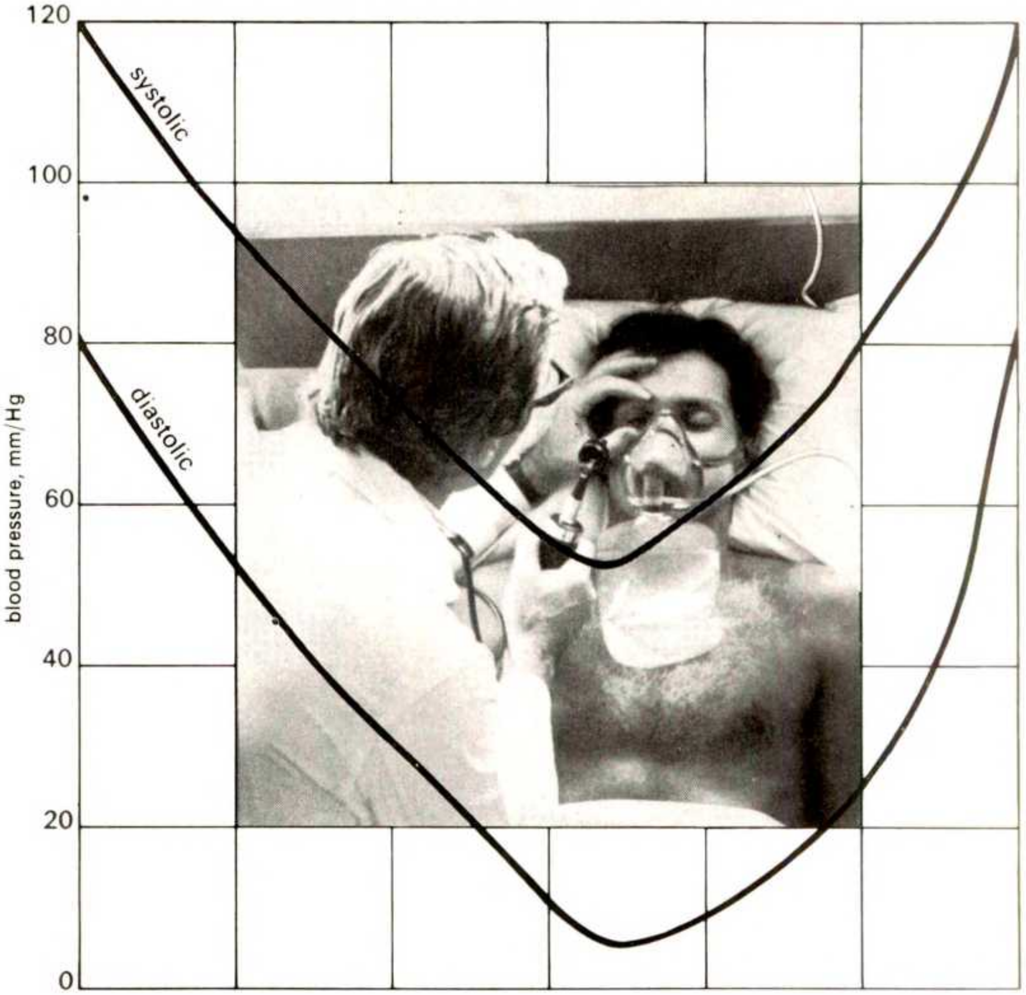

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SHORT PAPERS

OBSERVATIONS ON THE TREATMENT OF TRAUMATIC URETHRAL INJURIES AND THE VALUE OF THE FENESTRATED URETHRAL CATHETER

BY RICHARD TURNER-WARWICK

THE MIDDLESEX, ST. PETER'S, AND THE ROYAL NATIONAL ORTHOPAEDIC HOSPITALS, LONDON
AND THE INSTITUTE OF UROLOY

SUMMARY

A review of 250 traumatic urethral strictures in our series has provided the basis for a consideration of their management. Techniques that we have adopted or adapted for their resolution are outlined and the principles involved in reducing the effects of the initial injury are discussed. The value of the fenestrated shaft catheter in providing free drainage of periurethral exudates after urethral injury and repair is stressed.

DEVELOPMENTS in techniques of management have greatly improved the outlook for patients with traumatic urethral injury; although a stricture commonly results, its severity can be minimized by appropriate initial management and continent voiding can usually be restored by urethral reconstruction without the need for subsequent dilatations.

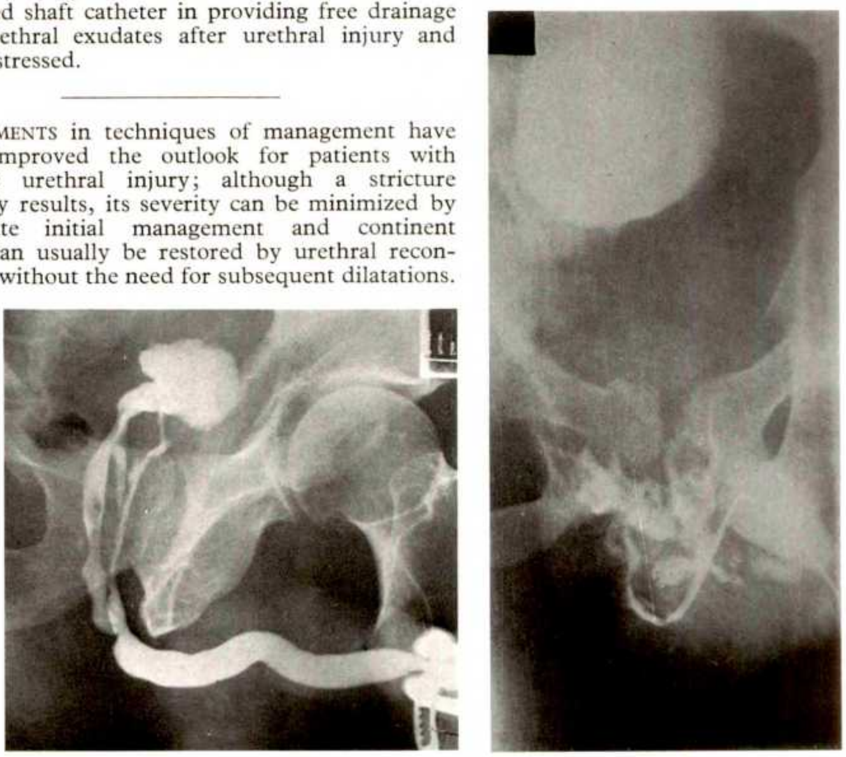
A B

FIG. 1.—A, Multiple false passages resulting from the treatment of a short traumatic bulbar stricture by repeated dilatation; such strictures are relatively easy to repair. B, Immediate intravenous pyelogram and synchronous retrograde urethrogram showing gross upward fracture-dislocation of the bladder and prostate with pelvic extravasation of urethrographic contrast; the 'pie in the sky' bladder.

Review of the treatment of 250 patients with strictures resulting from various types of traumatic injury has provided the basis for a consideration of the principles underlying their management and that of reducing the effects of the original injury.

PRINCIPLES OF SURGICAL REPAIR OF TRAUMATIC URETHRAL STRICTURES AND FISTULAE

Short traumatic strictures resulting from both straddle and pelvic fracture dislocation injuries are usually best treated by one-stage resection and reanastomosis (*Fig.* 1). Pedicle grafts using urothelial or skin islands provide useful one-stage techniques for slightly more extensive strictures (Turner-Warwick, 1972), but where the repair involves a trans-sphincter inlay or the surrounding tissues are grossly infected a two-stage scroto-urethral inlay is usually preferable (Turner-Warwick, 1968).

Catheter Drainage.—The larger indwelling urethral catheters (18F–22F) tend to obstruct the drainage of suture-line and rupture exudates which accumulate in the pericatheter urethral space and result in infection and fistula formation (*Fig.* 2 A); a small Gibbon catheter is an improvement since it allows some periurethral drainage (*Fig.* 2 B).

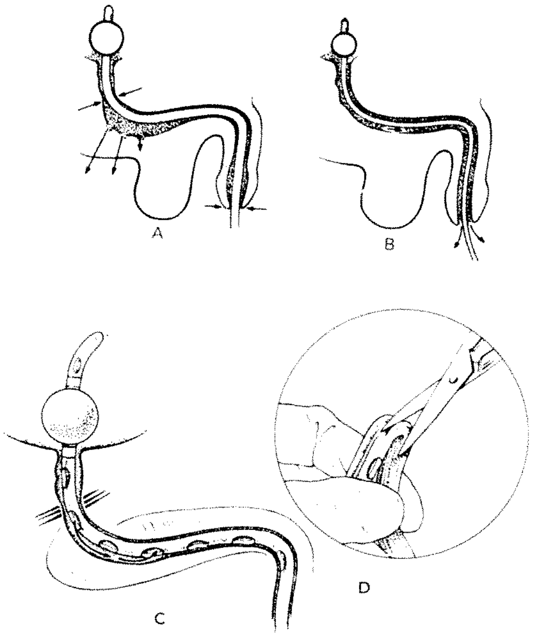

FIG. 2.—Urethral drainage and the indwelling urethral catheter. A, An indwelling urethral catheter of standard size impairs the drainage of the pericatheter space. B, Urethral drainage can occur around a small Gibbon catheter. C, A fenestrated catheter provides positive drainage and wash-out of the pericatheter space. D, Holes are easily cut in the shaft at levels appropriate to the drainage of the supramembranous and bulbar urethra; care must be taken to avoid the balloon-inflating channel. The fenestrated area of the catheter shaft must be pushed back into the bladder before any bladder wash-out is undertaken.

We use a specially fenestrated catheter to provide effective drainage of urethral exudates; this is particularly important in traumatic urethral injury and repair. The shaft of an appropriate catheter type and diameter is fenestrated in the area of the posterior bulbar urethra (*Fig.* 2 C); the pericatheter space is both drained and irrigated by urine, and there may be some additional siphonic suction if the catheter drainage connecting tube diameter is not too large to remain bubble free.

We routinely use this fenestrated catheter for all one-stage urethral reconstructions and for the closure of subsphincter inlay urethroplasty; in addition, it seems to provide a more effective drainage of a periurethral haematoma associated with traumatic urethral rupture than passive urethral drainage, and this is particularly important to the reduction of periurethral fibrosis which complicates subsequent urethral repair, especially in pelvic fracture injuries. We use a suprapubic catheter additionally when the bladder drainage is likely to be particularly critical or haemorrhagic. Effective bladder wash-out can only be achieved with a fenestrated catheter if it is pushed in so that all the holes lie within the bladder.

Omental Pedicle Graft.—Simple perineal bulbar and bulboprostatic anastomoses require no additional support, but the omentum is very useful for the more complex situations resulting from extensive injury and tissue loss. The omentum maintains its supple tissue consistency during and after the resolution of an inflammatory reaction and this, as well as its healing potential, makes an excellent flexible support for a bulboprostatic anastomosis inlaid through a rigid fibro-osseous tunnel, preventing it from becoming densely adherent to the wall and so risking both infection and re-stenosis.

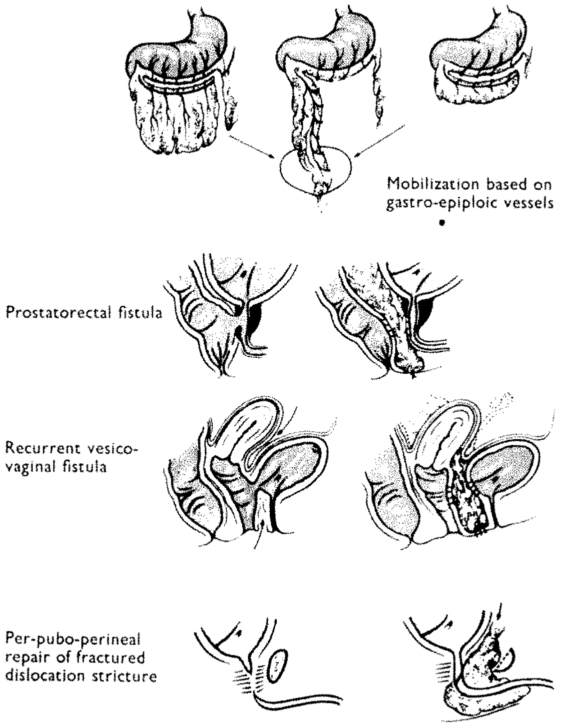
Mobilization based on gastro-epiploic vessels
Prostatorectal fistula
Recurrent vesico-vaginal fistula
Per-pubo-perineal repair of fractured dislocation stricture

FIG. 3.—The omental pedicle interposition graft is important to the resolution of many complex traumatic injuries. Formal mobilization based on the right gastro-epiploic vessels is usually required to enable it to reach the pelvis.

Only the lower fringe of the omentum will normally reach the pelvic cavity and definitive mobilization is usually necessary for its effective use in relation to the urethra (*Fig.* 3). The application of the omental interposition graft and the technique of its mobilization have been discussed elsewhere (Turner-Warwick, Wynne, and Handley Ashken, 1967; Turner-Warwick, 1972). It is particularly useful for rebuilding the septum in traumatic vesicovaginal and prostatorectal fistulae and for the repair of post-irradiation fistulae. Even large cloacal defects resulting from gross perineal tissue-loss injuries can be repaired with it, and less heroic replacements of the perineal tissues overlying an exposed urethra are relatively simple. It is important to anticipate the possibility that it may be necessary to use the omentum in a particular case, since a long median incision is required in order to mobilize the right gastro-epiploic arch from the stomach to the splenic pedicle.

CLOSED PERINEAL INJURIES

Closed urethral damage commonly results from fall-astride or straddle injuries, the bulbar urethra being crushed against the inferior margin of the pubis. A urethral stricture commonly develops and this is usually short and relatively easy to repair by one-stage reanastomosis (*Fig.* 4) (Turner-Warwick, 1974).

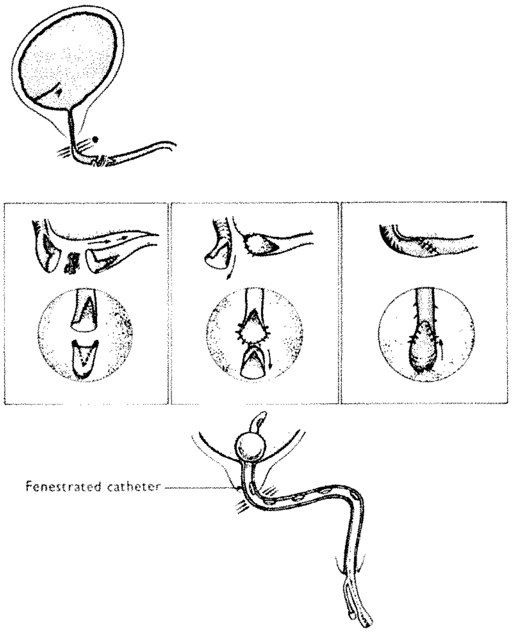

FIG. 4.—One-stage excision and reanastomosis of short bulbar urethral strictures following straddle injury; fenestrated catheter drainage. An antero-posterior overlap anastomosis reduces the risk of suture line cross-adhesion if its sides are spread apart and fixed laterally.

It is essentially the aetiology of a radiologically 'short' stricture which determines whether it should be treated by a reanastomotic or an inlay procedure. Mechanical trauma usually causes urethral scarring localized to the injury and the results of overlap reanastomosis are consequently good (*Fig.* 5).

The relatively poor reputation of resection and reanastomosis is the result of using it for apparently 'short' bulbar strictures due to urethritis; in these the damage caused by the original infection is characteristically much more extensive than the apparent stricture length on the urethrogram suggests and, because the urethra proximal and distal to it is abnormal, reanastomosis carries a high re-stricture rate.

Scarring resulting from traumatic bulbar urethral injury naturally compromises its mobilizable elasticity so that the length of stricture that can be easily resolved by an excision and overlap anastomosis is only about 1 cm. (*Fig.* 6). If the stricture much exceeds this length only a roof-to-roof approximation is possible and the anastomosis must be completed with an island skin-patch graft or a two-stage scroto-urethral inlay (Turner-Warwick, 1968, 1972).

Anastomotic Technique.—No special instruments are necessary for the reanastomosis of a mid-bulbar stricture. We prefer 0000 or 00000 atraumatic polyglycolic acid (Dexon) to catgut sutures for this with the knots lying in the lumen. A ring retractor with stay-suture knobs is generally helpful.

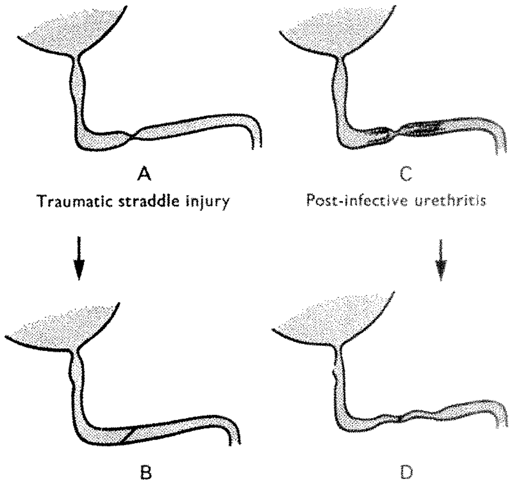

FIG. 5.—The urethra proximal and distal to a short traumatic stricture is usually normal (A) and the results of excision and reanastomosis are good (B). The urethra proximal and distal to an apparently short stricture resulting from urethritis is scarred (C) and reanastomosis results in recurrent stricture (D).

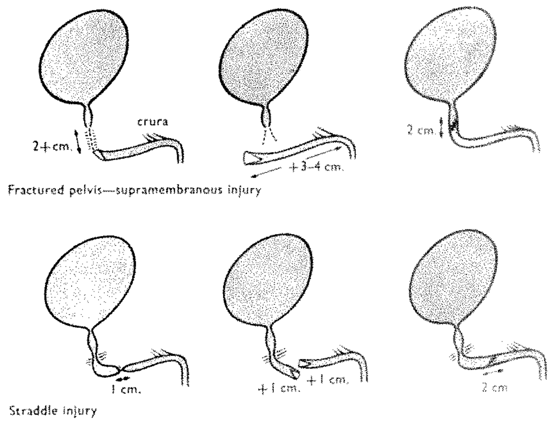

FIG. 6.—Bulbar urethral mobilization in relation to one-stage repair of traumatic bulbar and supramembranous urethral strictures.

THE IMMEDIATE MANAGEMENT OF CLOSED TRAUMATIC INJURIES OF THE BULBAR URETHRA

Urethral injury is usually indicated clinically by the appearance of blood at the meatus in association with a perineal haematoma or pelvic fracture. Depending upon the management envisaged it may be of importance not only to confirm the presence of a urethral injury but also to verify whether it is bulbar or supramembranous.

Diagnostic Radiography.—Retrograde urethrography will indicate the presence and the location of a urethral rupture but not usually whether it is complete or incomplete. Contrast media are, however, tissue irritants and excessive extravasation increases the local tissue damage. We have seen extensive tissue necrosis as a result of gross extravasation of viscid-based and also concentrated aqueous media, but this can be obviated by using a dilute aqueous solution and reducing the extent of the diagnostic extravasation to a minimum, either by limiting the volume of the retrograde injection or, better, by screening control.

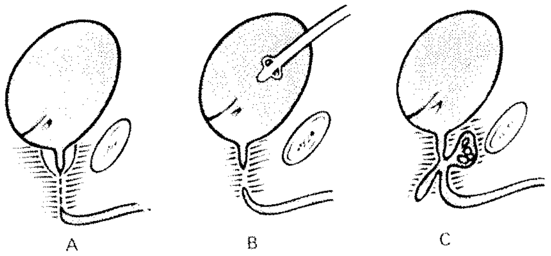

FIG. 7.—Severe fracture-dislocation in injuries may result in: (A) long strictures surrounded by dense haematoma-fibrosis; (B) complete loss of urethral continuity; (C) retropubic extravasation diverticula or fistulae which commonly contain calculi.

Urethral Catheterization.—Trial catheterization will indicate whether a rupture is partial or complete, but rough and inexpert attempts under less than ideal circumstances are rightly deprecated since it risks completion of a partial rupture and the introduction of infection. Of equal concern is that non-fenestrated catheters, once passed, are often left indwelling for a period of urinary drainage; this partially obstructs the urethral drainage of exudates from the periurethral trauma and may indeed risk extension of the effects of injury as a result of haematoma retention and infection. This risk is only partially reduced by the use of a fine (10F–14F) catheter (*Fig.* 2 B).

At the present time suprapubic catheter drainage of urine is the most generally accepted procedure for the immediate treatment of closed bulbar urethral injuries and any alternative must be carefully measured against this procedure, for the results are good and the subsequent repair of any bulbar stricture that occurs is relatively simple. Exudates can drain passively down the urethra, and while it is possible that this could be improved by positive fenestrated catheter drainage the advantages of avoiding further urethral damage by inexpert attempts at catheterization are generally overriding.

A total bulbar rupture almost inevitably results in the development of a stricture if it is treated by simple suprapubic catheterization. The immediate exploration and repair of the more severe closed bulbar injuries may have some advantages over suprapubic catheter drainage and delayed repair but is only advisable for specialist management. It is notoriously difficult to determine the limits of tissue viability in contused tissue and a recurrent stricture after a failed one-stage reanastomosis is more difficult to repair than one resulting from conservative treatment; an immediate roof-to-roof bulbar anastomosis with a scroto-urethral inlay, however, provides an equally satisfactory end result and may be more convenient than the alternative interim period of suprapubic catheter drainage. Marburger (1969) has a particular experience of immediate urethral exploration after tree-straddling ski-ing injuries.

URETHRAL INJURIES ASSOCIATED WITH PELVIC FRACTURE-DISLOCATION

The extent of the initial prostatic dislocation may be considered as minimal, moderate, or severe. A minimal supramembranous rupture usually compromises the intrinsic mechanism of the distal sphincter (the isolated loss of this may pass unnoticed, though it may later result in incontinence after prostatectomy); a short supramembranous stricture commonly develops but its appearance is sometimes delayed (Turner-Warwick, Arnold, and others, 1973).

A periurethral haematoma commonly accumulates in the floor of the pelvis at the apex of the prostate in patients with even a minimal fracture-dislocation; it is the organization of this that leads to the characteristic dense supramembranous periurethral fibrosis. The healing process in such a case may result in a further important complication which may compromise a simple perineal approach to the later repair. Urinary extravasation into a cavitating apical haematoma may create a urethral extravasation diverticulum or fistula and this may ultimately persist as an epithelized cavity or fistula in the dense fibrous tissue and calculi often form within it (*Fig.* 7).

Upward dislocation of the prostate results in a proportionally longer stricture through the dense fibrosis and sometimes a total loss of continuity if the false trans-passage is not maintained by dilatation. Distraction neuropathy resulting from dislocation may cause permanent impairment of potency and bladder dysfunction which compromises the bladder-neck–detrusor mechanism of urinary control (*Fig.* 10).

Reconstruction of Urethral Continuity.—We usually prefer to treat the established short supramembranous traumatic stricture by direct suture of the spatulated proximal end of the mobilized bulbar urethra to the prostatic urethra (*Fig.* 8) rather than by the indirect Solovow-Badenoch 'pull-through' procedure. Special instruments are helpful for high bulboprostatic anastomosis, in particular the fibrelight posterior urethral retractor and the three curves of posterior urethral needle for inserting 000 supramembranous Dexon sutures (Turner-Warwick, 1974).

Stricture Length in relation to Urethral Reanastomosis.—If the bulbar urethra is detached proximally at the level of the membranous urethra and mobilized to the penoscrotal junction it can be elongated some 3–4 cm. in the adult without undue tension. An oblique urethral suture line with about a 2-cm. overlap is advisable in order to avoid anastomotic narrowing, because the urethra is particularly prone to re-stenosis as a result of cross-adhesions of suture-line granulations. It follows that the length of a supramembranous stricture that can readily be resolved by direct bulboprostatic anastomosis without penile shortening or additional mobilization is in the region of 2–3 cm. Longer strictures can be resolved by approximating the penoscrotal junction to the apex of the prostate by mobilizing the suspensory attachment of the penis or resecting the pubis.

Synchronous Per-puboperineal Urethroplasty.—For the longer strictures and those associated with extensive fibro-osseous occlusion or extravasation diverticula we have used a synchronous approach from above and below (*Fig.* 9). The additional use of the omentum seems important to protect the urethroprostatic anastomosis if it lies in a fibro-osseous tunnel and also any exposed bone. A partial resection of the back of the pubis (*Fig.* 9) may obviate the need for a total pubic resection and this is technically facilitated by a Capener's bone gouge. The overall results of this combined approach with additional omental support have been remarkably good (Turner-Warwick, 1974).

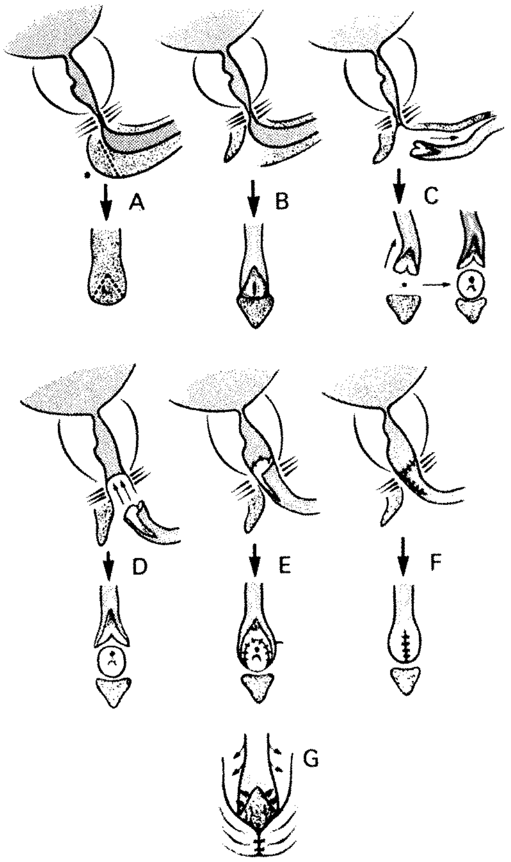

FIG. 8.—One-stage push-in bulboprostatic anastomosis. A, The posterior bulbar cavernous tissue lies behind the urethra. B, It is reflected as a posterior flap to facilitate subsequent closure; excess cavernous tissue at the anastomosis causes periurethral fibrosis. C, D, The bulbar urethra is mobilized to the penoscrotal junction and the stricture scarring excised to allow free passage of a finger to the prostatic urethra. E, F, The urethroprostatic sutures are inserted with posterior urethral needles using 000 absorbable sutures and fenestrated catheter drainage. G, Over-closure of the posterior cavernous tissue flap and additional lateral sutures are placed to 'push' the bulbar urethra towards the anastomosis and prevent tension due to erection.

Sphincter Function after Urethral Injury.—The restoration of urethral continuity often presents a formidable surgical problem but, assuming that it can be achieved, the functional result is dependent upon the survival of the bladder-neck sphincter mechanism because the composite distal sphincter mechanism (previously referred to as the 'external sphincter') is commonly ablated by the initial pubic arch injury (*Fig.* 10). An understanding of the elements of urinary control is important to the management of this type of stricture. In order to be continent of urine at rest the patient normally requires either an efficient bladder-neck mechanism or an efficient intrinsic mechanism of the distal group of muscles; the extrinsic muscles appear virtually incapable of maintaining resting urinary continence. The normal patient can interrupt his voiding stream by momentary contraction of the extrinsic muscles, the intrinsic mechanism then empties the proximal posterior urethra retrogradely, and the bladder neck closes as a result of detrusor inhibition (Caine and Edwards, 1958; Turner-Warwick, Whiteside, Worth, Milroy, and Bates, 1973) (*Fig.* 10 E).

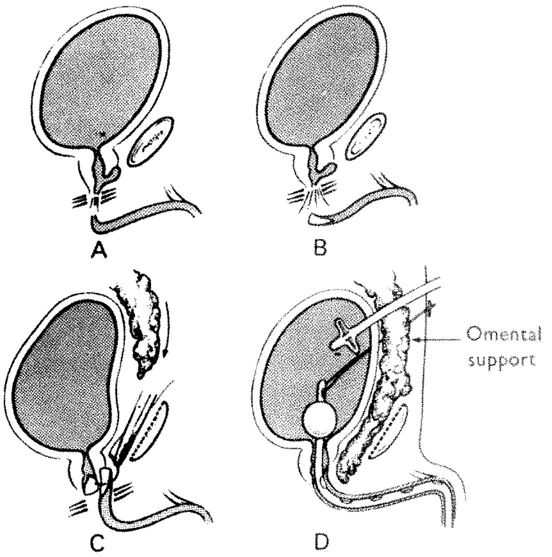

FIG. 9.—Synchronous per-puboperineal repair of traumatic urethral stricture. A, The bulbar urethra is mobilized in the perineum. B, The retropubic space is explored through a midline incision which can be extended upwards for omental mobilization. Access to the front of the prostate is facilitated by resection of the posterior part of the pubis. C, The mobilized bulbar urethra is passed up through a tunnel created in the fibro-osseous pelvic floor and sutured to the anteriorly opened prostatic urethra under direct vision from above using 000 absorbable sutures on conventional atraumatic needles. D, The tunnelled urethra and anastomosis are protected by a mobilized omental wrap. The bladder is drained by fenestrated urethral and suprapubic catheters.

A patient who is totally lacking in the elements of the distal urethral mechanism may nevertheless be continent on the basis of his detrusor–bladder-neck mechanism, for although he is unable to interrupt his voiding stream suddenly in the absence of the extrinsic urethral sphincter, he can interrupt it slowly as part of the voluntary inhibition of the detrusor contraction which results in the bladder-neck closure (*Fig.* 10 F).

It follows that preservation of the bladder-neck sphincter is vital to the functional result of supramembranous urethroplasty and every effort must be made to avoid impairing this both during the initial treatment and in the resolution of any subsequent stricture.

It is also of great importance to appreciate that global bladder hypertrophy is a natural result of outflow obstruction due to a long-standing urethral stricture; erroneous bladder-neck ablation based on the mistaken impression that the endoscopic appearances of trabeculation and bladder-neck hypertrophy represent dysynergic bladder-neck obstruction is an all too common surgical disaster that may compromise a successful functional result of a stricture repair (Turner-Warwick, Whiteside, and others, 1973).

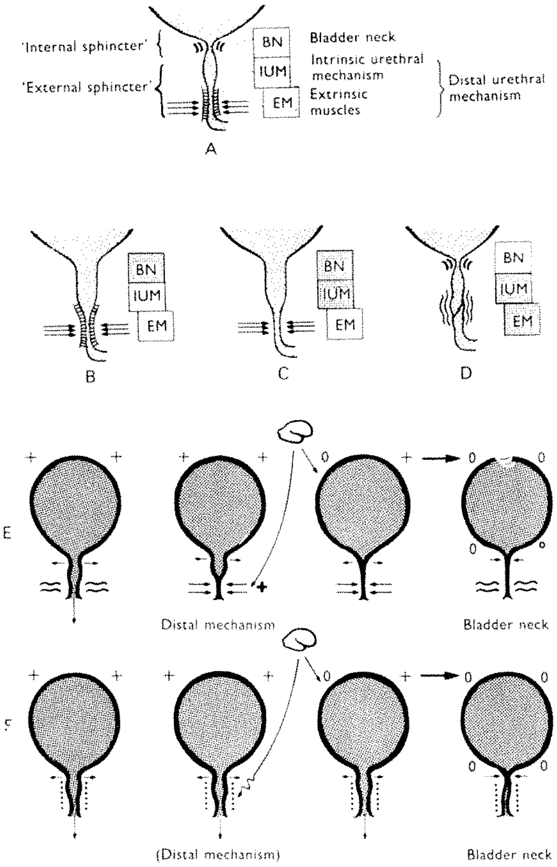

FIG. 10.—Isolated sphincter mechanisms after surgical procedures in the male, and the interruption of the voiding stream. A, Normal sphincter mechanisms. B, Continent after prostatectomy. C, Incontinent after prostatectomy. D, Urethroplasty for supramembranous stricture after fractured pelvis; continence dependent on detrusor–bladder-neck inhibition. E, Normally the mid-voiding stream can be voluntarily interrupted by the extrinsic distal sphincter with retrograde emptying of the urethra by the intrinsic distal mechanism and bladder-neck closure after detrusor inhibition. F, Loss of the distal mechanism. The mid-voiding stream can only be interrupted slowly by voluntary inhibition of the residual detrusor–bladder-neck opening mechanism.

THE IMMEDIATE MANAGEMENT OF FRACTURE-DISLOCATION INJURIES

The immediate concern in patients with fracture-dislocation is to preserve life; many are critically ill at the time of admission and the urological problem may be relatively low on the list of immediate priorities.

The whole of the urinary tract is at risk in such injuries; the urethra is damaged in a minority of cases and gross upward dislocation of the prostate occurs only in a few patients. The bladder may be additionally damaged.

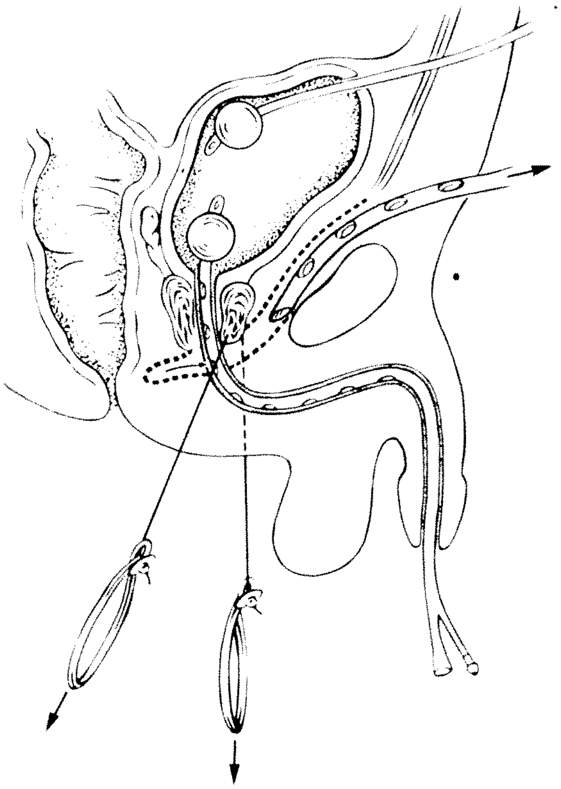

FIG. 11.—Operative treatment of fracture-dislocation of the prostate: Retropubic evacuation of haematoma; fenestrated urethral catheter for urethral alinement and apical drainage, additionally retained by suprapubic suspension stitch; elastic-band traction on apical prostatoperineal sling suture to maintain prostatic reduction; additional suprapubic catheter and retropubic suction drainage.

The initial problem is one of diagnosis. *Immediate intravenous pyelography* (I.I.V.P.) is of special value; not only may it exclude concomitant upper-tract complications but the position of the bladder shadow is often helpful in that it may be seen to be normally low lying, laterally compressed by the pelvic haematoma, or overtly dislocated upwards. A controlled dilute aqueous retrograde urethrogram will confirm or exclude a significant urethral injury but not its extent.

A high-riding dislocation of the prostate is relatively rare. It is, however, of great importance that this situation should not be missed, for it results in a formidable stricture problem if it remains unreduced. The diagnosis may be suspected by the absence of a normally placed prostate on rectal examination, although this may be difficult to determine as a result of the haematoma; the bladder shadow on the I.I.V.P. may show gross dislocation (*Fig.* 1), but a low-lying bladder does not exclude a significant distraction injury.

Treatment.—Treatment of patients with gross prostatic dislocation by simple suprapubic catheterization without drainage tends to result in a massive haematoma-fibrosis and a formidable stricture; even if the haematoma is evacuated as far as possible and drained retropubically a disproportionate apical periurethral fibrosis seems to result all too frequently.

The technique of maintaining the reduction of a prostatic dislocation by traction on a balloon catheter should probably be abandoned, for not only does an unfenestrated catheter shaft prevent the urethral drainage of the apical haematoma even when combined with a retropubic drainage but also it must carry an additional risk of injury to a surviving bladder-neck mechanism as a result of traction pressure (*Fig.* 10 D).

Primary prostato-urethral anastomosis through a retropubic approach is technically difficult and it is often virtually impossible to achieve a reliable sutured approximation of the prostatic apex to the shattered remnants of the pelvic floor. A transpubic resection and definitive reanastomosis offer a surgeon with proper experience of the technique a more rational approach for selected cases.

At the present time we would advocate a retropubic exploration of patients with a large pelvic haematoma, evacuating it and inserting a fenestrated 18F–20F Foley catheter through the urethra and into the bladder but only to provide urethral alinement and positive drainage of the apical haematoma (*Fig.* 11). (Accidental premature removal of this is prevented by a suprapubic retaining suture.) Any traction that may be required for the reposition of the prostate is applied to the apex of the prostate with a sling suture passed through the anterior commissure, each end being passed out into the perineum, lateral to the urethra, and each with a button stop and elastic band anchorage to the respective thigh. A retropubic suction drain and an additional suprapubic catheter are inserted to ensure efficient bladder drainage. A sling suture is a relatively simple procedure and may be helpful in reducing an apical urethral rupture completely even if the prostate is not much dislocated.

When the prostate is not dislocated a suprapubic catheter will provide effective bladder drainage, but even with additional retropubic drainage it does not always seem to resolve the apical haematoma effectively and the subsequent organization of this is largely responsible for the final periurethral fibrosis that commonly results. A simple indwelling urethral catheter makes the situation worse by obstructing the passive urethral drainage of exudates. The fenestrated catheter provides positive drainage to the periurethral space in this type of rupture and we hope that it will prove to reduce the extent of apical haematoma fibrosis.

It would also seem reasonable to use a fenestrated catheter for the management of a partial supramembranous urethral rupture when it can be passed into the bladder without difficulty, but free catheter drainage must of course be ensured. It is important to check that the catheter has in fact entered the bladder; a cystogram will confirm this and also exclude a concomitant bladder injury (the fenestrated shaft must be pushed fully into the bladder before contrast injection in order to avoid extravasation).

Traumatic urethral injury and extravasation of urine are major complications but do not require the most urgent immediate treatment; specialist management is indicated and premature attempts at trial catheterization in the admission room are generally inexcusable.

INTERNAL URETHRAL TRAUMA IN THE MALE

Only the occasional meatal stricture resulting from an indwelling catheter fails to respond to intermittent dilatation and subsequently requires a meatoplasty. Strictures in the membranous urethra following transurethral or open prostatectomy are usually better treated by dilatation since the bladder neck was ablated by the initial procedure and the apical damage which created the subsequent stricture usually impairs the intrinsic urethral mechanism and a transmembranous urethroplasty therefore carries a risk of incontinence. The characteristic strictures in the mid-anterior urethra resulting from instrumentation in children and adolescents present a relatively simple inlay repair problem (Turner-Warwick, 1968, 1974).

TRAUMATIC INJURY IN THE FEMALE

Traumatic injuries of the female urethra most commonly occur as a result of obstetric or gynaecological complications, and repair does not usually present a very difficult surgical problem (Turner-Warwick, 1970), but the functional result is of course dependent upon the survival of the sphincter mechanism.

Since females have in fact only a posterior urethra and both it and the pelvic floor are relatively elastic it is unusual for the urethra to be damaged in association with pelvic fractures although bladder injuries are not uncommon.

Acknowledgements.—I am most grateful to the many colleagues who have referred these interesting problems and to Miss Freda Wadsworth of the Institute of Urology for most helpful illustrations.

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THE OUTCOME OF TREATMENT AND CHANGES IN PRESENTATION OF PRIMARY HYPERPARATHYROIDISM

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SUMMARY

A review of 105 patients operated on over a 25-year period for primary hyperparathyroidism indicates that the diagnosis is now being made at an earlier stage of the disease. The incidence of bone disease is falling but renal symptoms remain the principal reason for presentation.

Hypertension in the presence of established disease persists after successful surgery and renal function frequently continues to deteriorate. Renal function is little affected in patients with minimal symptoms.

An accurate diagnosis can be made on the basis of persistent hypercalcaemia and elevated serum parathormone levels in peripheral or neck venous blood measured by sensitive immuno-assay.

Surgery is indicated as soon as the diagnosis is established with certainty even in the absence of any symptoms.

THE diagnosis of primary hyperparathyroidism is being made earlier in the course of the disease and neck exploration is often undertaken in patients with very few symptoms.

The management of patients with hypercalcaemia and primary hyperparathyroidism but with no symptoms is problematic. There is some doubt as to whether the neck should be explored at once on the basis of the biochemical evidence or else delayed until the onset of symptoms.

The answer to this question must be based in part on the results of surgery in patients with symptoms whose serum-calcium levels return permanently to normal after operation.

The mode of presentation and the outcome of surgery were examined in 105 consecutive patients with primary hyperparathyroidism treated in one unit during a 25-year period. Renal function was studied in 52 patients 2 or more years after successful parathyroid surgery.

RESULTS OF TREATMENT

Neck exploration was carried out in 105 patients with hypercalcaemia when the diagnosis of primary hyperparathyroidism was established. Eighty-two patients were female and 23 were male. Their ages ranged from 16 to 80 years but the majority of the patients were middle-aged females. Abnormal parathyroid tissue was removed at the first operation in 96 cases, with an immediate return of the serum-calcium levels to normal. A second operation was required in 4 patients before the calcium levels fell to normal. No abnormal parathyroid tissue was found in the remaining 5 cases and in 3 of these the serum calcium returned to normal. It is reasonable to suggest that the diagnosis was wrong in these patients. Hypercalcaemia persists in 2 patients and further exploration is planned for 1 of these. Treatment was thus successful in restoring the serum calcium to normal in 96 per cent of the patients.

Eighteen patients were found to have died at the time of the review. Eight patients had died from conditions unrelated to parathyroid disease but the rest had died from causes which could be related directly or indirectly to the complications of primary hyperparathyroidism. Four patients who all had hypertension before operation died from complications of hypertension. Three patients who had impaired renal function before surgery died subsequently of chronic renal failure. Two patients died in the immediate postoperative period in the early years of the series. Both had marked hypocalcaemia at the time of death which was probably related to gross metabolic imbalance. One patient died from a pulmonary embolus after a nephrolithotomy carried out shortly after a successful parathyroidectomy.

Fifty-two patients who had had an operation 2 or more years previously were examined in the review study. The most significant finding was that only 20 patients had no complaints when seen. Thirty-two patients had persistent urinary symptoms, ranging from mild dysuria to nocturia and recurrent ureteric colic. In 10 patients operations on the renal tract had been necessary following excision of parathyroid tumours. Intermittent symptoms of hypoparathyroidism were troublesome in 6 patients in this group.

Thirty-six of the 52 patients had repeated blood-pressure recordings above the normal range for their age and sex and 20 were on regular anti-hypertensive therapy (*Fig.* 1). Seventeen patients had become hypertensive since their neck exploration but the remainder were hypertensive when the diagnosis of parathyroid disease was made.

Fourteen patients had blood-urea levels elevated above 40 mg. per cent. In 9 of them the raised level had developed since the neck exploration.

The normal range of serum creatinine was taken to be 1·0–1·5 mg. per 100 ml. Eight patients had abnormally high levels and in 5 of these the increase had occurred since neck exploration.

Eight patients had a creatinine clearance of less than 80 ml. per minute at the time of review and 4 of these patients were being treated for chronic renal failure. It was not possible to estimate the extent of the deterioration in creatinine clearance.

Intravenous pyelograms were performed in all the patients at the review and changes were detected when comparisons were made with the preoperative pictures.

The incidence of hypertension, raised blood-urea, elevated serum creatinine, and abnormal creatinine

"Intravenous feeding of a fat-free preparation **for as short a time as 5 or 10 days** caused perceptible depletion of reserves of essential fatty acids. ....One case, maintained on fat-free intravenous feeding for 4.5 months, developed severe dermal lesions and the ratio of 20:3/20:4 in serum phospholipids reached 18, **the most extreme value thus far observed in animals or man.** Tissues from this case obtained at autopsy revealed the same abnormal pattern of fatty acids in triglycerides and phospholipids as was found in the serum lipids, confirming the extreme EFA deficiency." (American Journal of Clinical Nutrition (1972) Vol. 25 pp. 897–904).

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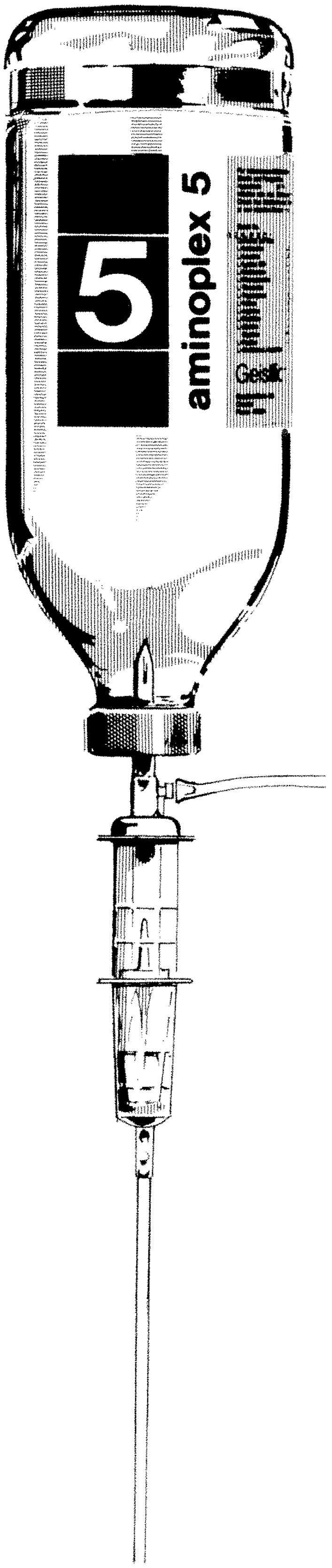

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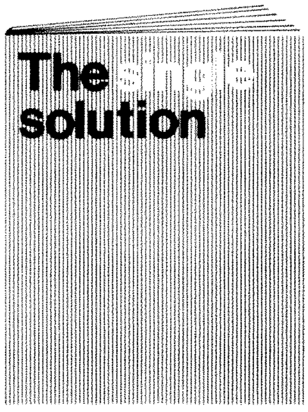

clearance was significantly less in the patients seen in the last 2 years compared with the first 20 years of the series.

The restoration of serum-calcium levels to normal is thus not the most important indication of a successful result of treatment. The persistence of symptoms and the decline of renal function are not related to the restoration of calcium homeostasis.

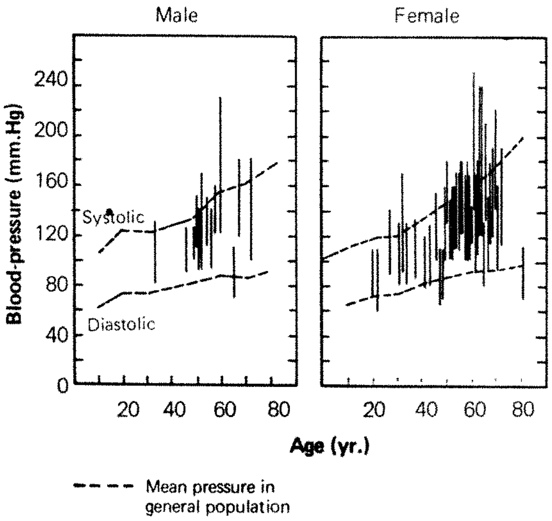

FIG. 1.—Blood-pressure in 52 patients 2 or more years after operation for primary hyperparathyroidism compared with the mean pressure in the general population. (*Reproduced from Britton, D. C., and others (1971), 'Lancet',* **2**, 74.)

PRESENTATION

The pattern of presentation during the past 25 years has changed significantly (*Fig.* 2). During the first 10 years all the patients were referred because of skeletal complications. In the second decade only 10 per cent were referred with bone disease and 80 per cent had urinary problems. The remaining 10 per cent had a mixture of symptoms including muscle weakness, dyspepsia, and mild dementia.

Forty-seven patients have been referred in the past 5 years, which is almost as many as were seen in the previous decade. The pattern of presentation has continued to change. The majority still have urinary symptoms (*Fig.* 2) but there has been a threefold increase in the number of patients with non-specific complaints. Nine of this group were totally asymptomatic, 4 were discovered as a result of the development of neonatal tetany in their newborn infants, and 5 were found as a result of random calcium estimations during investigation for unrelated complaints. Three patients were found to be hypercalcaemic in a survey of 500 patients 15 years after surgery for duodenal ulcer.

Preoperatively, 3 of the patients with non-specific complaints had slightly raised blood-urea levels, which have persisted at follow-up, but none of them has yet shown any sign of progressive renal dysfunction. Raised blood-urea levels fell to normal in 9 patients in the non-specific group and no patient in this group had a high serum-creatinine value.

CONFIRMING THE DIAGNOSIS

The biochemical diagnosis is becoming more and more important as the presenting symptoms are related less easily to the parathyroid glands.

The development of a sensitive radio-immunoassay of serum parathormone has been of value in the management of the last 14 cases in the present series.

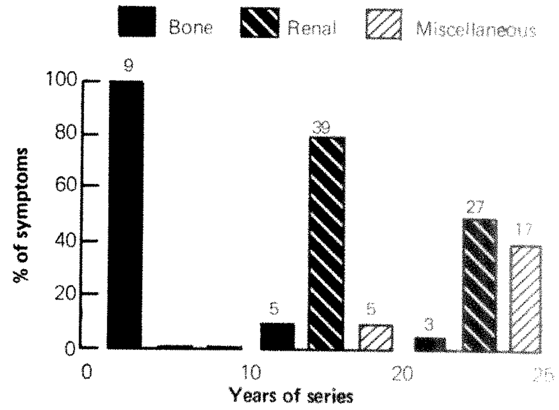

FIG. 2.—The changing pattern of presentation of primary hyperparathyroidism during 25 years.

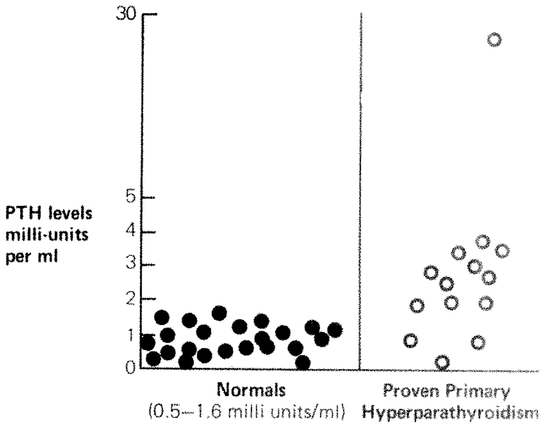

FIG. 3.—Serum-parathormone levels in primary hyperparathyroidism.

High peripheral blood-parathormone levels have been found preoperatively in 11 out of 14 cases with subsequently proved primary hyperparathyroidism. In 3 patients peripheral blood-levels were within normal limits (*Fig.* 3). Preoperative localization of a parathyroid tumour can be achieved by assaying blood samples taken from the veins of the neck under radiological control. Powell and others (1972) have reported a 56 per cent success rate in preoperative tumour localization. Using this method, localization has been attempted in 6 patients in this series and in all of them high levels of parathormone were found in the superior vena cava samples, thus confirming the presence of a tumour, but precise localization could only be predicted in 3 cases. Selective venous catheterization of the neck veins is of considerable value in localizing disease in patients who have had an initial unsuccessful exploration but it may also assist in the diagnosis of equivocal cases where hormone levels in the peripheral blood are in the normal range. An example of localization of a parathyroid adenoma in the right side of the neck is shown in *Fig.* 4.

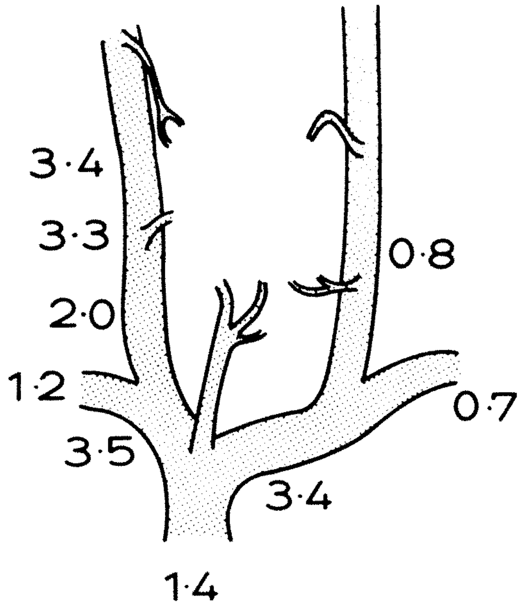

FIG. 4—Localization of a parathyroid adenoma in a patient with hypercalcaemia and few symptoms using parathormone content of selective venous samples from neck veins. (Normal PTH levels 0·5–1·6 milli-units per ml.)

Persistent hypercalcaemia is the keystone in the diagnosis of primary hyperparathyroidism in patients who are asymptomatic or who have presented atypically, but it is necessary to have some method of differentiating between hypercalcaemia due to primary hyperparathyroidism and hypercalcaemia due to other causes. The cortisone-suppression test and the selenium-methionine neck scan were used to assist in arriving at the diagnosis. The cortisone-suppression test depends upon the ability of 150 mg. of oral cortisone administered daily for 10 days to restore the serum-calcium level to normal in patients with conditions other than primary hyperparathyroidism. The hypercalcaemia of primary hyperparathyroidism is usually unaffected (Dent, 1956), but the effect of cortisone on the serum-calcium concentration in myelomatosis, secondary carcinomatosis, and the milk-alkali syndrome is inconsistent.

In practice the test has been used successfully to differentiate primary hyperparathyroidism in 23 cases. In 15 of these other stigmata of the condition had already been found, but in the other 8 successful neck exploration was carried out solely on the basis of persistent hypercalcaemia which was not suppressed by the administration of cortisone.

^{75}Se selenium-methionine neck scanning has not proved to be so reliable. It has been used in 43 patients and has localized the site of a parathyroid tumour correctly in 16 and incorrectly in 19; no localized uptake of selenium methionine was shown in the other 8 cases. The false-negative rate of 63 per cent in this series is considered to provide little assistance and this method of investigation has been abandoned.

DISCUSSION

This review indicates that more and more patients with few symptoms will be found to have evidence of primary hyperparathyroidism. Boonstra and Jackson (1971), in a survey of a general hospital adult population, found 50 patients with hypercalcaemia out of a total of 50,330 examined. This figure of 1 per 1000 examined in a hospital population has also been found by Haff, Black, and Ballinger (1970).

The management of patients found on routine biochemical screening to have hypercalcaemia and thus possible asymptomatic primary hyperparathyroidism poses a number of questions which are difficult to answer at the present time. Should surgery be carried out as soon as the biochemical abnormality is confirmed or should the patients be watched and operation delayed until symptoms develop or signs of other abnormalities can be detected? Dent (1962) has shown that some patients without bone diseases can continue for up to 40 years with hypercalcaemia before their renal function is disturbed. Purnell, Smith, Scholz, Elvesback, and Arnaud (1971) at the Mayo Clinic are engaged in a prospective study of patients with provisional hyperparathyroidism. This study may enable those patients with asymptomatic and uncomplicated hyperparathyroidism who will develop early complications to be detected and selected for surgery. It is clear that a number of patients will show the biochemical abnormality but will have no other manifestations of the disease for many years. Gough, Smith, and Bishop (1971) urge caution in exploring the neck of patients who have no symptoms or signs of disease apart from hypercalcaemia, owing to the complications associated with neck surgery.

Others, however, consider that the degree of renal impairment at surgery determines the ultimate prognosis (Britton, Thompson, Johnston, and Fleming, 1971; Chowdhury and Gray, 1973) and, because removal of parathyroid adenomas does not always cure the symptoms of the condition or allow renal function to return completely to normal, urge immediate neck exploration.

Analysis of the persistent symptomatology, renal function, and blood-pressure of the patients with classic primary hyperparathyroidism in this series who have been successfully treated shows that progressive renal deterioration and hypertension are relatively common sequelae of the disease. On this evidence it seems important to diagnose and treat primary hyperparathyroidism before renal dysfunction has developed; in effect this probably means before the classic symptoms of primary hyperparathyroidism have appeared.

There can be no clear-cut answer to the dilemma until a prospective trial of treatment has been carried out in patients with the asymptomatic form of the disease.

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THE CONTINENT ILEOSTOMY

BY A. CAMERON
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SUMMARY

In 1969 Professor Nils Kock of Göteborg published a description of a new kind of continent ileostomy. A pouch is formed of the terminal ileum. The pouch although small at first enlarges with time until its capacity is adequate to contain about one-third of the day's ileal output. The pouch is emptied several times a day by passing a catheter along a short efferent loop of ileum which is brought to the surface as an ileostomy stoma. The pouch is made in such a way that it does not develop expulsive contractions when it fills. It is therefore continent. By constructing a valve mechanism on the efferent loop continence is maintained under the stress of increased abdominal pressure as in coughing, laughing, etc. Since the pouch is continent the patient need wear no apparatus and the ileal stoma may be made flush with the skin.

This paper describes the author's experience with 6 patients in whom this type of ileostomy has been constructed. The results confirm the claim by Professor Kock that the technique is of value in selected patients.

A METHOD of constructing a continent ileostomy has been devised and described by Professor N. G. Kock of the University of Göteborg (Kock, 1969, 1971). In this procedure the terminal ileum is fashioned into a reservoir which lies within the abdomen and communicates via a short efferent loop of ileum with a stoma on the abdominal wall. The continuous discharge from the bowel above accumulates in the reservoir, which the patient then drains intermittently by catheterization of the stoma. Between catheterizations the reservoir is continent so that no external appliances need be worn. The advantages of such an arrangement over the conventional ileostomy are apparent.

In January, 1971, the author had the opportunity of observing Professor Kock's technique at first hand. This paper gives an account of the author's experiences with the technique in 6 patients and of the results obtained.

OPERATIVE TECHNIQUE

The technique employed differs in no essential way from that now advocated by Kock. Following total colectomy the terminal 45 cm. of ileum are folded as shown in *Fig.* 1 and the adjacent limbs, each 15 cm. long, are united along their anti-mesenteric borders by a continuous seromuscular suture of chromic catgut. The bowel is then laid open (*Fig.* 1 B), taking care to extend the incision into the afferent loop for about 3 cm. Another continuous catgut suture passing through all the layers completes the first suture line (*Fig.* 2 A).

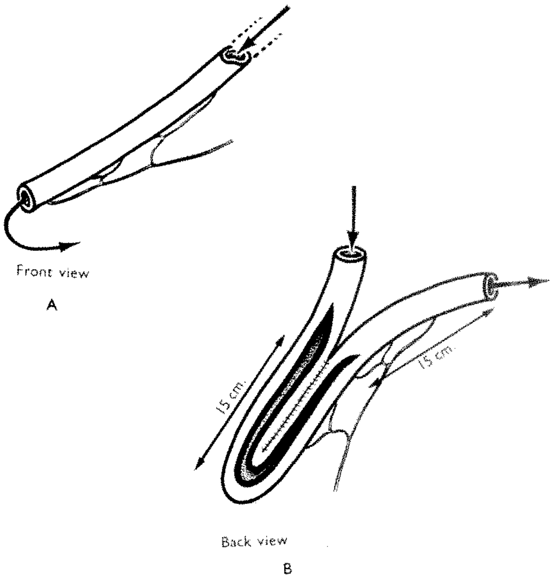

FIG. 1.—Diagram illustrating the procedure as seen by the assistant standing between the patient's legs, the patient being in the Lloyd-Davies position. In this position the assistant sees the left inferior aspect of the mesentery (A). When the bowel is folded in the direction indicated by the arrow, he then sees the right superior aspect of the mesentery (B).

A Babcock's tissue forceps is passed into the efferent loop, grasps the wall from within about 4 cm. from its junction with the reservoir, and intussuscepts it back into the reservoir. The intussusception is fixed in position by about eight black silk sutures passing through both layers of the intussusception from mucosa to mucosa. The placing of these sutures is facilitated by passing a firm plastic catheter through the efferent loop and intussusception to define the lumen. These sutures must be placed so that a nipple about 3 cm. long is fixed as a permanent projection into the reservoir. Care must be taken that these sutures do not occlude the blood-supply running in the mesentery to the efferent loop and that they effectively prevent lop-sided partial reduction of the intussusception—a complication which makes subsequent catheterization of the efferent loop impossible (*Fig.* 2 B).

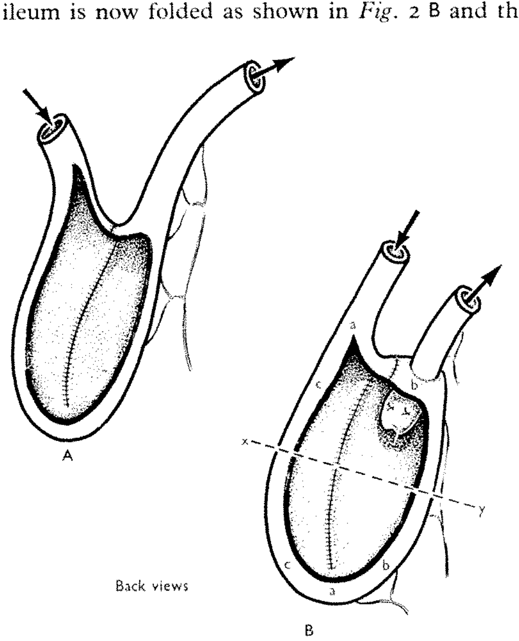

FIG. 2.—A, Both layers of the first suture line have been completed. B, The intussusception has been made and fixed with black-silk sutures. The pouch is to be folded along the line x–y so that c–c, a–a, and b–b are apposed (cf. *Fig.* 4).

The flat plate of bowel formed by the opened loops of ileum is now folded as shown in *Fig.* 2 B and the pouch is completed by continuous all-layer and seromuscular catgut stitches joining a–a, b–b, c–c, and so on. The prolongation of the original incision into the afferent loop ensures that the afferent and efferent loops are separated at their junction with the pouch by a short bridge (*Fig.* 3 A).

These steps have all been carried out from the upper right aspect of the mesentery (*Fig.* 1 B). From that aspect the pouch assumes a constricted bilobed appearance due to the pull of the mesentery (*Fig.* 3 A). If the pouch is now pushed through the mesentery and viewed from its left inferior aspect it assumes a bulbous shape which hangs snugly down towards the brim of the pelvis with the afferent loop entering it in a smooth curve and the efferent loop pointing towards the normal ileostomy site in the right iliac fossa (*Fig.* 3 B). The efferent loop is then brought through the abdominal wall at the lateral border of the rectus muscle in the usual way. Since the ileostomy is to be continent it need not project for more than 0·5 cm. or so and the opening may be made lower on the abdominal wall than usual so as to be more easily concealed.

The procedure described above is the present form of the operation and was carried out in *Cases* 5 and 6 (*Figs.* 4, 5; *Table I*). In *Cases* 3 and 4 an intussusception was made but it was not fixed with mucosal sutures and a rectus valve was made in addition. In this procedure an oblique tunnel is made through the rectus muscle and the efferent loop is brought through it so that some of the rectus fibres lie in front of the loop and some behind it. *Cases* 1 and 2 had a rectus valve made on the efferent loop but no intussusception. Since this form of rectus valve has proved less effective than the intussusception in maintaining stress continence it has now been abandoned (Kock, 1973).

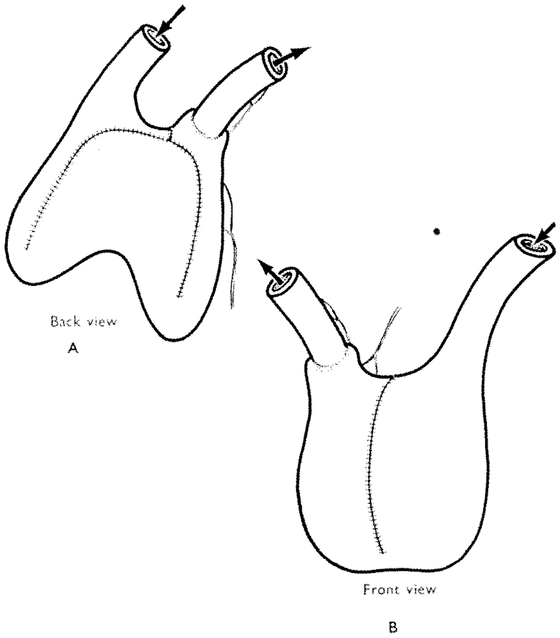

FIG. 3.—A, The completed pouch as seen from the right superior aspect of the mesentery. B, The pouch has been pushed through the mesentery and is now seen from the left inferior aspect of the mesentery (cf. *Fig.* 5).

After completion of the ileostomy but before the abdomen is closed a large-bore catheter (ileostomy catheter, AB Medena S, 434 00, Kungsbacka, Sweden) is passed into the reservoir. The afferent loop is clamped with a light occlusion clamp and the reservoir is distended with saline via the catheter to measure its initial volume (usually 50–80 ml.) and to check for anastomotic leakage. No saline should escape when the catheter is removed and light pressure is applied to the distended reservoir. Finally, the reservoir is again catheterized and drained and the catheter is fixed in a satisfactory position by means of a black-silk stitch to the skin. It is an advantage to mark the skin level on the catheter at this stage to remove doubts about its position in the postoperative period.

POSTOPERATIVE MANAGEMENT

The catheter is left in situ and allowed to drain continuously for 8–10 days. It should be washed out gently with small volumes of saline once or twice a day to prevent blockage. After this initial period it is occluded and drained 3-hourly for several days. At about 2 weeks it is removed and the pouch is catheterized 4-hourly thereafter, and as time passes the intervals can be lengthened gradually until the patient is catheterizing the pouch three or four times a day.

The stoma should be protected initially by a small square of petroleum jelly gauze.

SELECTION OF PATIENTS

The indications for operation in the 6 patients so far operated on are summarized in *Table I*.

The first patient was a woman aged 34 years suffering from polyposis coli complicated by the development of five separate carcinomas in the large bowel, one of which was in the rectum. The patient had hitherto refused colectomy because of her fear of a conventional ileostomy. Total proctocolectomy with the formation of a Kock's ileostomy was carried out as one procedure.

The third patient had had an emergency proctocolectomy with the formation of a conventional ileostomy for ulcerative colitis at the age of 78 years, 3 years previously. Her eyesight was poor owing to developing cataracts and she had rheumatoid arthritis in her hands. As a result of these disabilities she had never been able to apply the ileostomy apparatus herself. This was done by her daughter. The patient's frequent attempts to adjust the apparatus resulted in daily leakages and constant skin irritation. Prolapse of the ileostomy, which recurred after refashioning, resulted in a further decline in her well-being so that at the time of admission for conversion to a Kock ileostomy she was bedridden, incontinent, and required full-time nursing care by her daughter who had in consequence lost her job.

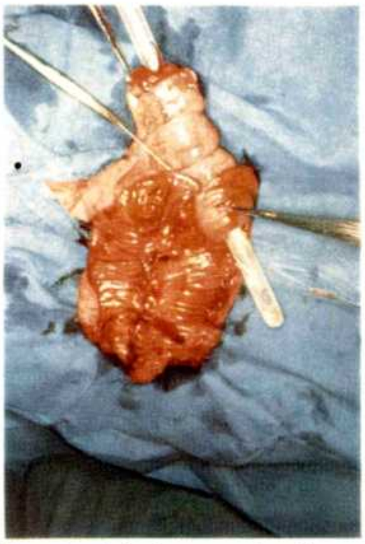

FIG. 4.—Formation of the intussusception. Photograph taken during operation showing the stage illustrated in *Fig.* 2 B.

Table I.—AGE, SEX, AND INDICATION FOR OPERATION IN THE PRESENT SERIES

CASE	AGE AND SEX	INDICATION
1	34 F.	Polyposis coli + carcinoma of rectum
2	59 F.	Ulcerative colitis
3	82 F.	Revision of conventional ileostomy
4	60 F.	Ulcerative colitis
5	65 M.	Ulcerative colitis
6	27 M.	Ulcerative colitis

In both of these patients the reservoir ileostomy offered a unique solution to a therapeutic impasse.

The remaining 4 patients were all suffering from chronic total ulcerative colitis. All 4 were in remission and were not receiving prednisone.

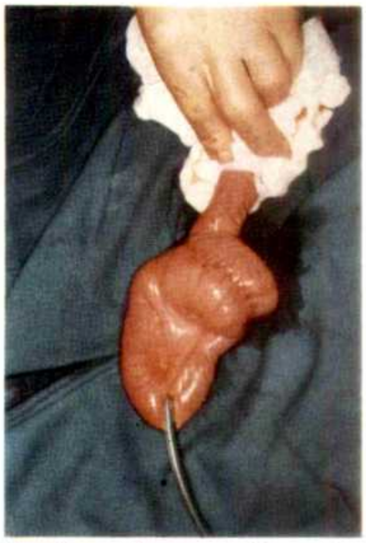

FIG. 5.—View of the completed pouch. Photograph taken during operation showing the stage illustrated in *Fig.* 3 B.

POSTOPERATIVE COMPLICATIONS

In *Cases* 1 and 3 a small abscess developed in the subcutaneous tissue close to the ileostomy about 2 weeks after operation. When this was incised and drained it was found to have a fistulous connexion with the efferent loop. In both cases the abscess healed and the fistula closed after drainage, without further treatment. Both of these cases had had a rectus valve constructed and it seemed likely that the fistula resulted from friction damage to the loop by compression between the indwelling catheter and the edge of the rectus sheath. The spontaneous healing of the fistula may perhaps be attributed to the absence of intraluminal pressure in the efferent loop and the fact that it does not usually contain faeces.

Case 6 developed abdominal distension with severe colicky pain and radiological evidence of intestinal obstruction associated with complete absence of ileostomy drainage 72 hours postoperatively. At laparotomy the small bowel was distended down to the pouch but no other abnormality was found. Twelve hours after operation the ileostomy started to drain satisfactorily. In retrospect this episode might have resolved on conservative treatment.

ASSESSMENT OF RESULTS

Clinical Assessment.—*Case* 5 died before leaving hospital from causes not connected with the ileostomy. *Case* 6 has been operated on too recently for the result to be assessed. The results in the first 4 patients are summarized in *Table II*.

Case 1, who had a rectus valve, has now had the ileostomy reservoir for 15 months. When she left hospital, 6 weeks after operation, she was passing the ileostomy catheter three times a day and was completely continent of faeces between catheterizations. The daily volume of effluent was about 300 ml. Since then the ileostomy has remained continent of faeces. As her appetite has increased with the improvement in her health she has found it necessary to pass the catheter four or five times each day. She does this when she feels that the reservoir is full, a sensation which she cannot further define. If this warning is ignored she will get transient, slight colicky pains and perhaps a slight leakage of gas from the stoma. She usually passes the catheter standing up and starts the reservoir emptying by coughing or straining. When the effluent is fluid the reservoir empties rapidly aided by pressure with the hand over the pouch, and the whole procedure is over in 5 minutes. When the effluent is thicker she washes the reservoir out with 50–100 ml. of tap water using a small funnel. The time taken is then 10–15 minutes. Between catheterizations she covers the stoma with a swab which is held in place by her tights. The skin around the ileostomy is unmarked. She has never been caused any embarrassment by the ileostomy and goes out and about with confidence. She feels no desire to have an ileostomy appliance and does not possess one.

Table II.—RESULTS OF OPERATION IN THE FIRST 4 PATIENTS IN THE PRESENT SERIES

CASE	DURATION (mth.)	CONTINENT	NO. OF CATHETERIZATIONS PER DAY	VOLUME OF POUCH AT 3 MONTHS (ml.)
1	15	Yes	3–4	150
2	14	No	—	200
3	7	Yes	2–3	250
4	5	Yes	3	150

Case 2, who had a rectus valve and no intussusception, never achieved complete continence of faeces. After catheterization of the reservoir the ileostomy would often remain continent for 3 or 4 hours and she might have a complete day without leakage. However, this would be unpredictable and quite large and troublesome leakages occurred on most days. These problems did not improve even when the pouch had had time to enlarge to a volume of 200 ml. She was accordingly fitted with an ileostomy bag and the ileostomy now functions in all respects like a conventional one. She will occasionally catheterize and empty the reservoir before going out socially, since this at least ensures that the ileostomy bag will remain empty for several hours. Fortunately in these early cases the patients were all given a short ileostomy spout placed in the conventional site so that management with an ileostomy bag is practicable. She has no skin problems.

The operation was most strikingly successful in *Case* 3, who was bedridden and incontinent with prolapse of a conventional ileostomy. She had a rectus valve and intussusception on the efferent loop. After formation of the reservoir ileostomy she remained completely continent of faeces, the catheter being passed every 8 hours and the average daily volume of effluent being about 400 ml. Her daughter was taught how to pass the catheter. The badly damaged skin around the ileostomy site rapidly healed and the burden of nursing care from this point of view was reduced to three 15-minute periods daily. The improvement in her physical condition was paralleled by a striking improvement in her mental state. She said that she felt clean again for the first time since her original proctocolectomy. She remained continent of faeces until her death 7 months later from bronchopneumonia complicating simple closure of a large perforated gastric ulcer.

Case 4 was discharged from hospital 3 weeks after a one-stage proctocolectomy with formation of a Kock ileostomy. She has now had the reservoir for 5 months. She passes the catheter two or three times a day and is completely continent of faeces between catheterizations. There is an occasional escape of gas but this has never been such as to cause her any social inconvenience. She has had only two episodes of leakage of faeces. One of these occurred after having had a traditionally large Christmas dinner when she forgot to pass the catheter for 10 hours. The other leakage occurred while she was suffering from a 24-hour attack of 'gastro-enteritis'. These episodes were insufficient to undermine her confidence and she has no desire to wear an ileostomy bag. The skin around the ileostomy has remained in perfect condition. She has now gone off on holiday to Majorca—perhaps as striking evidence of her sense of security as could well be devised.

Radiological Assessment.—Cine-cystography combined with simultaneous pressure recording as used in studying urinary-bladder dysfunction (Bates and Corney, 1971) has proved to be a most useful method of obtaining an objective assessment of the function of these reservoirs.

Such studies on these reservoirs have shown that as the reservoir fills the pressure in it rises slowly and steadily to 30–40 cm. of water. At about this pressure reflux occurs up the afferent loop. Although 'peristaltic' waves can be seen passing over the surface of the reservoir as it fills, these are not accompanied by any sudden increases in pressure within the pouch. The volume recorded in *Table II* is the volume held by the reservoir before reflux up the afferent loop occurs. After reflux has occurred pressure waves do occur in the pouch and these can be seen to coincide with the arrival of peristaltic waves from the afferent loop. These studies show also that the volume held by the pouch increases to about 200 ml. within 3 months of its formation.

If the catheter is removed when the pouch is full the mechanism of continence under stress can be examined by asking the patient to cough. Under these circumstances there is a sudden pressure wave in the reservoir owing to transmitted intra-abdominal pressure. It has been possible to demonstrate in this way that both the rectus valve and the intussusception can maintain continence.

Post-mortem Assessment.—The death of *Case* 3, 7 months after the formation of her ileostomy reservoir, provided an opportunity to study the appearance of a well-functioning reservoir at this interval. The reservoir formed an approximately spherical pouch some 10 cm. in diameter, with a volume on distension of 350 ml. The wall of the pouch was 2·5 mm. thick and was lined by a flattened mucosa (*Figs.* 6, 7). There was no evidence of muscular hypertrophy in the wall of the afferent loop.

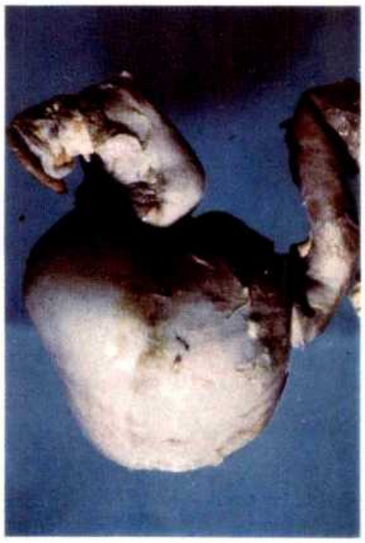

FIG. 6.—*Case* 3. Post-mortem appearance of the reservoir at 7 months.

The intussusception in this case had not been fixed internally with black silk sutures and it is evident that it has partially reduced. Microscopic examination showed a striking change in that the villi had disappeared and the mucosa consisted of parallel, straight, tubular glands lined with many mucus-secreting cells. It therefore resembled colonic mucosa.

DISCUSSION

An ileostomy reservoir which is to function satisfactorily in the way described above should have certain characteristics. It should be capable of accommodating about one-quarter of the daily ileostomy output without reflux. The valve mechanism on the efferent loop should be capable of withstanding the transient high intra-abdominal pressures transmitted to the reservoir on coughing, straining, etc. The reservoir itself should not respond to filling by developing co-ordinated expulsive contractions which would continually stress the efferent-loop valve mechanism. Catheterization of the efferent loop should be easy and therefore safe, and emptying of the reservoir should proceed fairly rapidly thereafter. Finally, continence must be able to be guaranteed so that the patient feels secure without any apparatus. Moreover, without such certainty some of the advantages of the continent ileostomy would be lost since the stoma could not then be made flush with the skin and could not be brought out low on the abdominal wall.

The results reported here suggest that the Kock ileostomy meets most of these requirements. The volume of ileostomy effluent varies considerably in different patients. However, a volume of about 500 ml. a day would be usual and volumes in excess of 1000 ml. a day probably indicate malfunction (Smiddy, Gregory, Smith, and Goligher, 1960). The reservoir volumes at 3 months (150–250 ml.) reported here would therefore be in the correct range to contain one-quarter to one-third of the daily effluent. It should be noted that these volumes were the volumes held by the reservoirs before reflux occurred. Kock, who measures the volume of the reservoir by distending it with a balloon until the patient feels slight discomfort, found volumes of about 500 ml. at 3 months in his patients (Kock, 1971).

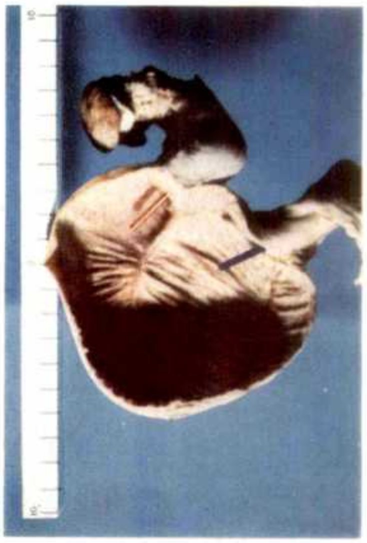

FIG. 7.—*Case* 3. Post-mortem appearance of the reservoir with the anterior half removed.

The radiographic studies in these cases showed that both the rectus valve and the intussusception were capable of maintaining continence when there was raised intra-abdominal pressure due to coughing and straining. However, Kock has found in his much larger series that the rectus valve is less reliable in this regard than the intussusception, which he now uses exclusively. The patient in the present series who failed to achieve continence had a rectus valve alone.

The radiographic studies in all these cases also confirmed that as the reservoir fills the pressure in it rises slowly and steadily to about 30 cm. of water with no sudden peaks due to expulsive contractions.

Catheterization of the efferent loop presents little difficulty when an intussusception only has been made and the technique is easily mastered by the patient. With a rectus valve catheterization may be more difficult owing to the oblique nature of the course through the rectus muscle.

Finally, only 1 patient out of the 4 assessed here at 3 months was incontinent of faeces. This patient had a rectus valve only. Kock (1971) achieved faecal continence in 22 out of 25 patients using a rectus valve in some and an earlier variety of the intussusception procedure in others. His own series now includes over 90 patients and he has found that using the technique of intussusception described here the proportion of patients with faecal continence is greatly increased as is the proportion who are also continent of gas (Kock, 1973). An overall assessment of the safety and reliability of the procedure must clearly await the publication of Kock's own results in this much larger series. However, the cases reported here confirm that this technique can produce highly satisfactory results in selected patients.

Acknowledgements.—I wish to express my gratitude to Professor Kock for introducing me to this procedure and teaching me the technique and for much helpful advice and criticism. I am also indebted to Mr. W. W. Slack for collaborating with me in the treatment of 2 of these patients.

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HIGHLY SELECTIVE VAGOTOMY WITHOUT A DRAINAGE PROCEDURE IN THE TREATMENT OF HAEMORRHAGE, PERFORATION, AND PYLORIC STENOSIS DUE TO PEPTIC ULCER

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SUMMARY

The good results of highly selective vagotomy (H.S.V.) in the elective surgical treatment of uncomplicated duodenal ulcer led to its use in the treatment of 30 patients who were suffering from complications of peptic ulcer, over a period of 21 months. In the emergency situation it is vital to select for H.S.V. patients who are fit enough to withstand a 1–2-hour operation.

Five out of a total of 9 patients with perforated duodenal ulcer were deemed to be suitable for H.S.V. In contrast, H.S.V. was used in the treatment of all 10 patients with haemorrhage (5 patients with duodenal ulcer and 5 with gastric ulcer), because definitive treatment for the ulcer is essential after haemorrhage has been arrested by direct suture.

Pyloric stenosis was diagnosed in 15 of 75 patients who came to elective surgery for duodenal ulcer. The diagnosis was made on clinical and radiological grounds and was confirmed at operation. Seven of the 15 patients had concomitant gastric ulceration. All 15 patients were treated by H.S.V. without a drainage procedure. The stenosis was simply dilated digitally. Seven patients who were followed up for at least a year underwent barium-meal examination, which showed that gastric emptying was normal in each case and that there was no sign of recurrent ulceration.

There was no operative mortality. None of the patients with haemorrhage bled again after operation. Only 1 of the 30 patients developed gastric retention, which was transient. Of the 14 patients who were reviewed more than 1 year after H.S.V., 11 had a perfect clinical result, 2 were very good, and 1 was 'fair' (Visick grade 3). The long-term prognosis should be the same as that of patients who have undergone elective H.S.V.

Granted a modicum of case selection, H.S.V. is a safe operation in the treatment of emergencies such as haemorrhage or perforation. In pyloric stenosis H.S.V. preserves and makes use of the stomach's compensatory mechanisms of hypertrophy and hyperperistalsis, whereas both gastrectomy and vagotomy with drainage destroy them. Vagotomy of the entire stomach makes necessary the addition of a drainage procedure. Vagotomy with drainage impairs the ability of the antrum to 'mill' food and to propel chyme onwards, and destroys or by-passes the pyloric sphincter. These surgical insults to normal gastric physiology harm the patient by producing dumping, diarrhoea, bilious vomiting, steatorrhoea, and gross elevation of serum gastrin. The main conclusion of this paper is that such harm can be avoided, because it is shown that even patients with pyloric stenosis can be treated by H.S.V. without a drainage procedure. The routine use of complete gastric vagotomy with a drainage procedure in the elective surgical treatment of duodenal ulcer is no longer justified.

Two hundred and fifty patients with duodenal or gastric ulceration have been treated by highly selective vagotomy without a drainage procedure (H.S.V.) (Johnston and Wilkinson, 1969, 1970) in Leeds in the past 4 years. Operative mortality was nil, only 1 patient required the addition of a drainage procedure, and none has developed a recurrent ulcer. H.S.V. was found to reduce acid output as effectively, for up to 2 years, as did truncal or selective vagotomy with drainage (T.V.+D., S.V.+D.) (Johnston, Wilkinson, Humphrey, Smith, Goligher, Kragelund, and Amdrup, 1973), while gastric emptying was much closer to the normal after H.S.V. than after T.V./S.V.+D. (Humphrey and Wilkinson, 1972; Wilkinson and Johnston, 1973). In consequence, side-effects such as dumping and diarrhoea were reduced significantly (Humphrey, Johnston, Walker, Pulvertaft, and Goligher, 1972; Johnston, Humphrey, Walker, Pulvertaft, and Goligher, 1972). The overall clinical results (Visick, 1948) as assessed at the Leeds Gastric

Follow-up Clinic 2 years after operation were much better after H.S.V. than after T.V./S.V.+D. (Johnston, Goligher, Pulvertaft, Walker, Amdrup, and Jensen, 1972).

This felicitous experience with the new operation encouraged us to use it in patients who were suffering from complications of peptic ulcer. H.S.V. has been used in the treatment of a few carefully selected patients with perforated duodenal ulcer. It has also found wide application in the treatment of patients with haemorrhage or pyloric stenosis. The operation can be done fairly quickly, usually within 90–120 minutes.

PERFORATION

Patients.—Five slim men with perforated duodenal ulcer who were less than 60 years of age were treated by H.S.V. Further details are given in *Table I*. They were selected for H.S.V. out of a total of 9 patients who came to emergency operation for perforated duodenal ulcer in the same period. Three of the remaining 4 patients were treated by simple suture of the perforation, and 1 by truncal vagotomy and pyloroplasty. H.S.V. was used, first, if definitive surgery to cure the ulcer was indicated because of recurrent pain, previous haemorrhage, or perforation, and, secondly, if the patient was thought to be fit enough to withstand an operation which takes from 1 to 2 hours to perform. Thus, H.S.V. is usually contra-indicated in patients over 60 years of age, in the obese, and in those with a history of cardiac or respiratory disease. In addition, patients should arrive in the operating theatre within 8 hours of perforation, and soiling of the peritoneal cavity should not be gross.

Table I.—CLINICAL DETAILS OF THE PATIENTS WITH PERFORATED DUODENAL ULCER TREATED BY H.S.V.

CASE	AGE AND SEX	WEIGHT (kg.)	LENGTH OF ULCER HISTORY (yr.)	LENGTH OF STOMACH LEFT INNERVATED (cm.)	OPERATING TIME (min.)	ACID OUTPUT 1 WEEK AFTER H.S.V.				CLINICAL RESULT	
						B.A.O. (mEq./hr.)	*M.A.O.pg** (mEq./hr.)	*Insulin Response*		Length of Follow-up (mth.)	Visick Grade
								+ ve/ − ve†	P.A.O.I‡ (mEq./hr.)		
1. J. G.	59 M.	51	25	7·0	83	0·2	22·8	− ve	0·9	20	1
2. S. W.	31 M.	52	3	6·8	70	0·0	27·8	− ve	0·0	16	2
3. D. J.	39 M.	60	4	6·6	105	0·1	24·3	− ve	0·0	16	1
4. F. R.	48 M.	61	10	7·5	150	0·0	21·0	− ve	0·1	15	3§
5. J. C.	24 M.	70	5	8·0	Not recorded	3·6	51·5	− ve	0·8	3	Brief follow-up
Mean	40·20	58·8	9·4	7·18	105	0·78	29·48	− ve	0·36	4	

* M.A.O.pg, Maximum acid output to a dose of pentagastrin of 10 μg. per kg. intramuscularly.
† Insulin test was judged positive or negative by Hollander's (1948) criteria.
‡ P.A.O.I is the peak 30-minute acid output × 2, minus the basal acid output. Dose of insulin was 0·2 U per kg. intravenously.
§ Patient's symptoms of epigastric discomfort probably attributable to incisional hernia.

Operative Procedure.—A midline epigastric incision was used. The diagnosis having been confirmed, peritoneal toilet was performed, the perforation closed, and H.S.V. performed as expeditiously as possible.

Postoperative Progress.—Recovery was uneventful in each of the 5 patients although 1 developed a wound infection. Gastric retention did not occur. The insulin test (Hollander, 1948) was negative in each case. The mean length of stay in hospital after operation was 9·6 days (range, 8–13 days).

Clinical Result.—Three patients were reviewed in the Gastric Follow-up Clinic 1 year after operation. One had a perfect result (Visick grade 1), 1 was nearly perfect (Visick grade 2), and 1 was graded Visick 3 on account of symptoms attributable to an incisional hernia, which has since been repaired. The 2 remaining patients are in excellent health, 3 and 6 months respectively after operation.

HAEMORRHAGE

Patients.—All 10 patients were suffering from moderate to severe haemorrhage, which either did not stop or recurred after the patient's admission to hospital. The volume of blood transfused preoperatively ranged from 6 to 9 pints, with a mean of 7·2 pints. Five of the patients had chronic duodenal ulceration, 4 had chronic gastric ulceration, and 1 had two acute gastric ulcers. Further details are given in *Table II*. These 10 patients form a *consecutive* series of patients with upper gastro-intestinal bleeding who were operated upon as emergencies by one of us (D. J.) in the past 2 years. Four of the 10 patients were relatively high-risk cases (*Table II*): *Case* 2 was 71 years old and obese, *Case* 5 had recently undergone her second mitral valvotomy, *Case* 6 had cirrhosis of the liver and carcinomatosis, and *Case* 10 was 61 years old and obese, and her systolic blood-pressure was 50 mm. Hg at the time of admission to hospital.

Preoperative Management.—Patients were admitted under the care of a physician, who then asked the surgeon for an opinion. This request was usually made soon after the patient's admission to hospital. A barium-meal examination was performed in the department of radiology as a matter of urgency, if the patient was well enough. Gastroscopy was used, not routinely but in an attempt to gain additional information when the diagnosis was obscure. Patients over the age of 50 who had bled severely (requiring transfusion of more than 4 pints of blood in 24 hours) and who were known to have a chronic gastric or duodenal ulcer were usually operated upon as soon as they had been adequately transfused, without being given a chance to bleed again. Younger patients were accorded the privilege of having a second bleed.

Operative Procedure.—To save time a midline incision was used. Access to a gastric ulcer was obtained by means of a longitudinal gastrotomy, which was placed carefully along the greater curvature if the ulcer was within 8 cm. of the pylorus in order to avoid damage to the nerve-supply of the antral 'pump'. A duodenal ulcer was approached by a 5-cm. longitudinal incision in the anterior wall of the duodenum which reached the pyloric ring but did not transect it. This incision gave adequate access to the ulcer in 4 of the 5 patients with duodenal ulcer. The fifth patient (*Case* 10, *Table II*) was obese and had a particularly deep penetrating ulcer, access to which was obtained only when a 10-cm.-long gastropyloroduodenotomy had been performed. All these incisions, including the last one, were closed as they had been made, longitudinally. Edge-to-edge apposition without inversion was the aim. When the diagnosis was in doubt and no lesion could be seen or felt at the time of operation a long gastrotomy was performed and the whole of the gastric mucosa was inspected. If this search proved unrewarding a duodenotomy was done but the pylorus was not divided. When the ulcer was found its base was underrun with several deeply placed 0 Mersilene sutures. The entire epithelial margin of a gastric ulcer was excised and sent for histological examination. The mucosal defect in the stomach or duodenum was closed with interrupted catgut sutures. The gastrotomy or duodenotomy was then closed with

Table II.—CLINICAL DETAILS OF THE 10 PATIENTS WITH ACUTE HAEMORRHAGE WHO WERE TREATED BY H.S.V. PLUS SUTURE OF THE ULCER

CASE	AGE AND SEX	WEIGHT (kg.)	LENGTH OF ULCER HISTORY	NO. OF PINTS OF BLOOD TRANSFUSED	SITE OF ULCER	LENGTH OF STOMACH LEFT INNERVATED (cm.)	OPERATING TIME (min.)	ACID OUTPUT 1 WEEK AFTER H.S.V.				POSTOPERATIVE		CLINICAL RESULT	
								B.A.O. (mEq./hr.)	M.A.O.pg (mEq./hr.)	*Insulin Response* +ve/−ve	*Insulin Response* P.A.O.I (mEq./hr.)	Stay in Hospital (d.)	Complications	Length of Follow-up (mth.)	Visick Grade
1. M. D.	63 M.	71	1 wk.	8	2 acute G.U.s, upper third	6·5	80	0·0	—	−ve	0·0	18	Gastrostomy tube leak → peritonitis	24	1
2. W. T.	71 M.	63	3 wk.	6	G.U., distal third	7	105	1·1	17·9	Not done (age >70)	—	10	Partial wound dehiscence → hernia	15	1
3. W. R.	36 M.	64	4 wk.	8	G.U., middle third	8	Not recorded	0·0	17·0	−ve	0·1	20	? Pulmonary embolus	7	1
4. I. B.*	58 F.	57	?	6	G.U., middle third	?	?	0·3	5·9	−ve	0·0	13	None	7	2
5. J. H.	56 F.	49	1 wk.	6	G.U., middle third	8	90	—	—	Not done (mitral stenosis)	—	17	None	6	2
6. C. C.	55 M.	57	1 yr.	8	D.U.	5·8	115	1·3	—	−ve	0·2	28	Wound abscess	4	—†
7. K. W.	17 M.	46	3 yr.	9	D.U.	5·4	120	2·0	—	−ve	0·6	13	None	15	1
8. A. B.	42 M.	68	12 yr.	7	D.U.	10	Not recorded	0·0	23·1	Early +ve‡	0·7	9	None	6	1
9. W. L.	59 M.	82	0	8	D.U.	6	150	0·8	24·5	−ve	0·0	14	None	3	—
10. E. H.	61 F.	63	17 yr.	6	D.U.	12	135	2·2	16·4	−ve	0·0	19	Duodenal fistula,§ wound infection	1	—
Mean ±1 S.E.	51·80 5·00	62·00 3·33	Range, 0–17 yr.	7·2 0·36	5 G.U. 5 D.U.	7·6 0·7	113·6 8·6	0·84 0·27	17·45 2·69		0·20 0·11	16·1 1·8		8·8 ±2·2 3 for >1 yr.	5 Visick 1 2 Visick 2

* Some of the details for *Case* 4 are lacking because her case notes have been lost.
† Died of carcinomatosis.
‡ Positive in first hour.
§ The discharge from the duodenal fistula was scanty and the fistula closed within 2 days (*see* text).

continuous catgut reinforced by seromuscular sutures of interrupted catgut in the stomach and by interrupted fine silk in the duodenum, without inversion. The operation was completed by the performance of H.S.V., which was done as quickly as possible, usually in 30 or 40 minutes.

Postoperative Progress.—None of the patients re-bled either in hospital or later and none developed gastric retention. All eventually made a good recovery, although convalescence was marred in several by a minor degree of chest infection. The worst complication occurred in the patient in whom a gastroduodenotomy had been closed longitudinally rather than as a pyloroplasty. She developed a duodenal fistula on the ninth postoperative day but fortunately this closed spontaneously within 2 days.

Clinical Result.—At the Gastric Follow-up Clinic each of the 3 patients who were reviewed 1 year after operation was considered to have achieved a perfect (Visick grade 1) clinical result. Three patients were reviewed 6 months after operation: 1 had a perfect result and 2 had very good results (Visick grade 2).

PYLORIC STENOSIS

Definition.—The diagnosis of pyloric stenosis was based on the presence of one or more of the following features: a history of copious and repeated vomiting (particularly if the vomitus contained food which had been eaten on the previous day), the finding of a succussion splash 3 hours or more after the last meal, gastric 'resting juice' of more than 250 ml. and containing food residues after an overnight fast, and finally the demonstration of the typical radiological features of pyloric stenosis. In all except 1 of the 15 patients the diagnosis was confirmed at laparotomy, when the pyloroduodenal channel was found not to admit the distal interphalangeal joint of the index finger or a No. 14 Hegar's dilator (Kirk, 1970).

Patients.—Fifteen patients (20 per cent of *all* the patients coming to elective surgery for duodenal ulcer in the past 21 months) were found to have pyloric stenosis. All 15 cases were treated by H.S.V. plus digital dilatation. The stenosis was of varying degree. In some patients spasm and oedema probably contributed to the gastric obstruction because simple rest in bed before operation, supplemented if necessary by once-daily gastric lavage, led to the cessation of vomiting and disappearance of the succussion splash. It then became possible to re-hydrate the patient by the oral route. Five of the 15 cases could be classified on these grounds as having mild pyloric stenosis. At the other end of the spectrum none of the 15 patients could be regarded as having late neglected pyloric stenosis because none had visible gastric peristalsis, a palpable stomach, or gross dehydration associated with severe uraemia or tetany. Nevertheless, the fact that no fewer than 7 of the 15 patients had concomitant gastric ulceration is suggestive of a moderately severe degree of gastric obstruction. In addition, a tight unyielding fibrous stricture was found in most patients at the time of operation (*Table III*).

The 15 patients consisted of 9 men and 6 women whose mean age was 54 years. This is 14 years older than the mean age of patients coming to surgery for duodenal ulcer (D.U.) *without* pyloric stenosis. Their mean weight was 56 kg., which is 7 kg. less than that of the average D.U. patient coming to operation. Their mean loss of weight before operation was 6 kg. (*Table III*). Most of these patients had suffered from the pain of their ulcer for many years, the mean length of history being 21 years, compared with 10 years in the average D.U. patient coming to surgery.

Operative Procedure.—

1. *Highly Selective Vagotomy.*—H.S.V. is a delightfully easy operation in these patients, both on account of their lean build and because the nerves of Latarjet are prominent. It is important to leave a generous length of stomach innervated, first, because the stomach is usually dilated so that the *proportion* which is left innervated may be little greater than usual, and, secondly, because in the absence of a drainage procedure gastric emptying depends upon the vigour of antral peristalsis. Hence the necessity of preserving the motor nerve-supply to the antral 'pump' is obvious. The mean length of pre-pyloric stomach left innervated was 8·2 cm., compared with 6·5 cm. in patients with uncomplicated duodenal ulcer.

2. *Dilatation of the Stenosis.*—A small gastrotomy is made in the denervated portion of the stomach and the index finger is inserted. In 50 patients with D.U. *without* the clinical or radiological features of pyloric stenosis we have found that the pylorus and duodenum will admit the distal interphalangeal joint of the index finger and at least a No. 14 Hegar's dilator. This is in accord with Kirk's observations (Kirk, 1970). By these criteria 14 of the 15 patients had stenosis, which was usually post-pyloric rather than truly 'pyloric'. The fifteenth patient had a widely patent pyloric channel, on one side of which there was an active gastric ulcer and on the other an active duodenal ulcer. The spasm and oedema produced by these ulcers had presumably caused functional obstruction to gastric emptying. In most patients the degree of stenosis was so severe (*Table III*) that only very narrow Hegar's dilators could be passed. The stenosis was gently but firmly dilated with the tip of the index finger, and the 'sphincter' gradually stretched until it admitted both the distal and the proximal interphalangeal joints. Since the stricture was fibrous and unyielding this dilatation was usually felt to rupture scar tissue and indeed in 4 patients it produced frank perforation of the anterior duodenal wall. These perforations were closed transversely with interrupted catgut sutures. In no instance was the pyloric ring or the distal antrum disrupted.

3. *Management of Concomitant Gastric Ulcer.*—This was treated in the manner which we have described previously (Johnston, Humphrey, Smith, and Wilkinson, 1972). The ulcer was excised by a transgastric approach and confirmation that it was benign was obtained by frozen-section examination. The mucosal defect was closed with catgut sutures. When the ulcer is within 8 cm. of the pylorus, as was the case in 5 of the 7 patients, there is no need to separate the nerves of Latarjet from the base of the ulcer. When the gastric ulcer is proximal to the incisura, however, as it was in 2 patients, a tedious dissection through oedematous fibrosed tissues in the ulcer base may be required. On the other hand, since the alkaline zone of the stomach has been shown to extend from the pylorus proximally as far as the

Table III.—CLINICAL DETAILS OF THE 15 PATIENTS WITH

CASE	AGE AND SEX	WEIGHT (kg.)	WEIGHT-LOSS BEFORE OPERATION (kg.)	LENGTH OF ULCER HISTORY (yr.)	VOMITING*	SUCCUSSION SPLASH	BARIUM-MEAL REPORT	FINDINGS AT OPERA	
								Degree of Stenosis*	Di
1. J. B.	43 F.	37	6	15	+ +	+	D.U., P.S., dilated stomach	Severe; No. 6 Hegar	D.U
2. S. H.	50 F.	43	7	16	+ +	[illegible]	D.U., P.S., much resting juice	Severe; No. 6 Hegar	D.U
3. E. A.	56 M.	56	4	25	+	[illegible]	Deformed cap. No P.S.	Severe; No. 6 Hegar	D.U
4. T. K.	52 M.	60	18	20	+ +	+	D.U., P.S., much resting juice, slow emptying	Severe; No. 6 Hegar	D.U
5. R. McK.	54 M.	73	1	35	+ +	[illegible]	D.U., P.S., food residues	Severe; No. 8 Hegar	D.U
6. M. W.	54 F.	56	9	10	+ +	[illegible]	Delayed emptying food residues + P.S.	Severe; No. 5 Hegar	D.U
7. G. M.	68 M.	60	0	40		[illegible]	Not done (previous barium-meal showed D.U.)	Severe; No. 6 Hegar	D.U
8. J. McC.	42 M.	46	13	15	+	[illegible]	Delayed emptying, D.U., P.S.	Mild; No. 12 Hegar	D.U
9. T. G.	63 M.	61	3	30	+ +	[illegible]	Grossly deformed duodenal cap	Severe; tiny orifice in fibrous ring	D.U
10. G. I.	54 F.	58	4	32	Occasional vomiting	[illegible]	Deformed duodenal cap	Severe; No. 5 Hegar	D.U
11. E. W.	74 M.	57	14	20	+ +	+	Dilated stomach, minimal emptying	Moderate; No. 11 Hegar	D.U
12. P. D.	71 M	58	6	6	+ +	[illegible]	Pyloric ulcer, delayed emptying	None; No. 16 Hegar	D.U
13. W. A.	56 F.	61	3	40	+	[illegible]	D.U., P.S., delayed emptying	Severe; No. 8 Hegar	D.U
14. D. F.	37 M.	48	6	10	+ +	[illegible]	D.U., dilated stomach, delayed emptying, multiple antral ulcers	Moderate; No. 11 Hegar	D.U
15. J. J.	40 F.	59	0	0·25	+	[illegible]	D.U., G.U., P.S.	Severe; No. 8 Hegar	D.U
Mean	54·27	55·53	6·27	20·95		11 + ve			8 D.U
± 1 S.E.	2·88	2·27	1·36	3·19		4 − ve			7 D.U

* + + signifies repeated and copious vomiting. † Mean reduction in B.A.O. was 83·6 per cent. ‡ Mean reduction in M.A.O. was 55·4 per c

proximal margin of the gastric ulcer (Oi, Oshida, and Sugimura, 1959) it is probably unnecessary to lay bare the lesser curve as low down as the incisura. It may be sufficient to begin the dissection at the *upper* margin of the gastric ulcer. This certainly renders the operation much easier technically, reduces the risk of damage to the nerves of Latarjet, and makes H.S.V. more acceptable as a routine procedure for gastric ulcer. A 'proximal H.S.V.' of this type was used in 1 case in this series. Despite the fact that 13 cm. of stomach were left innervated the insulin test performed 1 week after operation was negative.

Postoperative Progress.—No patient developed gastric retention in the postoperative period. All 15 patients made a good recovery, although wound infection and chest infection were both fairly common (*Table III*).

One patient (*Case* 6, *Table III*) was readmitted to hospital 3 months after operation with a complaint that she was vomiting food almost every day. She could eat only small meals and had failed to gain weight. Barium-meal examination showed that gastric emptying was slow, although there was no sign of recurrent ulceration. She was treated conservatively, first with a liquid diet, then with 'sloppy' foods. She gradually regained the ability to eat solids without vomiting. A barium-meal examination 7 months after operation showed that gastric emptying was within normal limits and that there was no sign of duodenal or of gastric ulceration.

The remaining 14 patients have no symptoms or signs of gastric retention. Barium-meal examination was performed in the 7 patients who had been followed up for 1 year. In each case gastric emptying was reported to be normal, and although deformity of the duodenal cap remained there was no sign of recurrent ulceration.

Clinical Result.—Seven patients were reviewed at the Gastric Follow-up Clinic 1 year after operation.

WHO WERE TREATED BY H.S.V. PLUS DILATATION

OF CH TED	EFFECT OF H.S.V. ON ACID OUTPUT						POSTOPERATIVE COMPLICATIONS	POSTOPERATIVE STAY IN HOSPITAL (d.)	CLINICAL RESULT	
	B.A.O.† (mEq./hr.)		*M.A.O.pg*‡ (mEq./hr.)		*Insulin Test*				Length of Follow-up (mth.)	Visick Grade
	Pre	Post	Pre	Post	+ve/−ve	P.A.O. I (mEq./hr.)				
	1·8	0·0	27·9	21·2	−ve	0·0	None	12	6	1
	1·5	0·2	42·3	18·8	−ve	0·0	None	8	12	1
	2·3	0·1	22·8	10·3	−ve	0·0	Wound infection + dehiscence	20	12	1
	7·8	0·0	70·5	6·4	−ve	0·0	Chest infection	16	15	2
	19·7	5·9	76·1	33·8	−ve	0·0	None	13	10	Lost
	1·9	—	23·9	—	Not performed		None	15	9	3
	3·9	0·3	21·2	17·6	Late + §	2·0	Chest infection	12	2	—
	6·0	0·5	41·0	8·5	−ve	0·0	None	9	6	1
	—	0·0	—	17·4	Not performed		?Myocardial infarct	16	12	1
	0·5	0·5	14·5	9·2	−ve	0·0	None	8	12	1
	4·0	0·1	56·9	11·0	Not performed		None	12	12	1
	3·4	0·4	48·0	26·3	−ve	0·0	None	17	16	1
	7·5	0·5	46·3	12·2	Late +	3·3	None	14	1	—
	11·0	0·0	38·7	18·9	−ve	0·0	None	9	1	—
	—	3·5	—	15·4	−ve	0·0	None	11	1	—
	5·49 1·45	0·86	40·78 5·26	16·20 2·01		0·44		12·8 0·9	8·47 ± 1·34 7 > 1 yr.	

§, Positive in the second hour.

Six were judged to have achieved a perfect (Visick grade 1) clinical result, and one had a very good (Visick grade 2) result. Of the remaining patients, 1 has been lost to follow-up, 1 is the patient with transient gastric retention who now has a 'fair' (Visick grade 3) result, and the remaining patients are known to be progressing well on shorter periods of follow-up.

DISCUSSION

The absence of operative mortality in this series of 30 patients with severe complications of peptic ulcer who were treated by H.S.V. is gratifying, particularly because the patients with haemorrhage and with pyloric stenosis were *consecutive* patients suffering from these complications, while the 5 patients with perforation were selected out of a total of only 9. Two hundred and fifty patients have been treated by H.S.V. in Leeds in the past 4 years without mortality. H.S.V. is thus an extremely safe operation. This safety may be due in part to the absence of an anastomosis and in part to the postoperative convalescence which is usually uneventful. Indeed, provided that haemostasis is perfect and wound closure secure there is little to go wrong, apart from the general complications of anaesthesia and surgery. There is no problem with a 'loop' or stoma, as in gastro-enterostomy or Polya gastrectomy, no duodenal stump to leak, and the disturbances of motility which occasionally delay convalescence after truncal vagotomy with a drainage procedure have not been encountered. After H.S.V. patients are routinely managed without either a nasogastric tube or an intravenous drip. Nursing is thereby simplified and the patients are free to move around and to walk about the ward.

The main aim in the treatment of emergencies such as haemorrhage and perforation is, of course, to save life. The quality of that life is a secondary, if important, consideration. The surgeon must exercise judgement both in deciding whether or not, and when, to operate, and then in choosing which operation to perform. In the treatment of perforated duodenal ulcer simple suture is the simplest and safest method. Definitive procedures such as vagotomy with drainage or H.S.V. should be used only in carefully selected patients, who are *relatively* young and fit, not shocked, and in need of cure of a troublesome chronic ulcer. The surgeon obviously should choose a procedure with which he is familiar. We would merely suggest that if definitive surgery *is* indicated, H.S.V. in the hands of those who use it frequently will not carry a higher mortality than does vagotomy with drainage and it will yield better clinical results.

If H.S.V. has only a limited place in the surgical treatment of perforated ulcer it would seem to merit much wider application in the treatment of haemorrhage, if only because definitive surgery is indicated in all patients coming to surgery for haemorrhage whereas the same is not true for perforation. In the treatment of bleeding *duodenal* ulcer, vagotomy with underrunning of the ulcer has been shown to be safer than partial gastrectomy (Carruthers, Giles, Clark, and Goligher, 1967; Farris and Smith, 1967; Williams, 1969; Schiller, Truelove, and Williams, 1970). But which type of vagotomy? The choice would appear to lie between truncal vagotomy with drainage and H.S.V. H.S.V. takes about 30 minutes longer to perform than does truncal vagotomy with a drainage procedure, and for this reason should probably not be used in patients with massive haemorrhage who have a low blood-pressure immediately before or during operation, in patients over the age of 70, or in those who have severe cardiac or respiratory disability. The presence of obesity is also a relative contra-indication to H.S.V. In case of doubt it is advisable to ask the anaesthetist if he thinks that an additional 30 minutes' operating would entail an added risk to life.

In 4 out of 5 cases of bleeding duodenal ulcer, duodenotomy without transgression of the pylorus gave adequate access to the ulcer. In the fifth case it was necessary to perform a wide gastroduodenotomy. All these incisions were sutured longitudinally, without pyloroplasty. The technical difficulties (and dangers) of attempting to reconstitute a divided pylorus in the presence of oedema and fibrosis could, however, be formidable in some patients with duodenal ulcer. Leakage and stenosis are two of the potential hazards.

Haemorrhage from a *gastric* ulcer is a different problem which many surgeons still treat by gastric resection, reserving vagotomy, drainage, and suture of the ulcer for use in special circumstances such as an ulcer near the cardia or a poor-risk patient. It is therefore interesting to note that Schiller and others (1970) found that the operative mortality was nil in 15 patients with gastric ulcer who were treated by vagotomy and drainage, whereas it was 10 per cent in 81 patients who were treated by Billroth-I gastrectomy, and 19 per cent in 27 patients who were treated by Polya gastrectomy. Again, Williams (1969), in a review article, stated that the post-operative mortality for bleeding gastric ulcer treated by gastrectomy was 25 per cent, compared with 9 per cent after vagotomy with pyloroplasty. These figures must be viewed with caution since the comparisons are not of controlled series, but they do suggest that vagotomy with drainage is safer than gastrectomy. In Leeds H.S.V. has yielded good clinical results in the *elective* treatment of gastric ulcer for up to 3 years (Johnston and others, 1972) and fears that gastric emptying would be delayed have not been confirmed. Whether the incidence of recurrent ulceration will be as low after H.S.V. as after Billroth I-gastrectomy remains to be established. Of the technical considerations in the performance of H.S.V. for gastric ulcer, the most important is that the ulcer should be excised to exclude the possibility of malignancy. The approach to the ulcer should be from inside the stomach to reduce the chance of damage to the nerves of Latarjet. The most novel and exciting consideration, however, is that a *very proximal* H.S.V. (above the ulcer) may suffice to denervate the entire acid-secreting portion of the stomach (Oi and others, 1959).

Fifteen patients with pyloric stenosis were treated by H.S.V. plus pyloric 'sphincter stretch'. Only 1 patient subsequently developed gastric retention, which was transient, and barium-meal examination in the 7 patients who were followed up for at least 1 year showed that gastric emptying was satisfactory. Although the pattern of emptying of barium does not necessarily reflect the pattern of emptying of a normal meal the radiological findings are fully supported by the clinical results, because none of the patients complains of vomiting and 6 out of 7 patients who were reviewed at the Gastric Follow-up Clinic 1 year after operation were judged to have a perfect clinical result. The obvious objection to the use of simple dilatation for pyloric stenosis is that re-stenosis will take place as the ulcer heals, but this does not seem to have occurred. If gastric retention has not developed within 6–12 months of operation it is unlikely to do so subsequently.

As mentioned earlier, 5 of the 15 patients had quite a mild degree of stenosis which was made worse by the oedema and spasm associated with an active ulcer. There is no doubt, however, that the stenosis was moderate to severe in 10 patients; severe enough, indeed, to cause hypertrophy and dilatation of the stomach and to produce secondary gastric ulceration in no fewer than 7 of the 10 patients. So tight was the stenosis in 4 patients that gentle dilatation with one finger produced actual perforation of the anterior duodenal wall. Our preliminary experience would thus suggest that pyloric stenosis of this degree can be treated successfully without the need for a drainage procedure or for gastric resection. None of the patients, however, exhibited the severe dehydration, tetany, or the vast atonic stomach which characterize late, neglected pyloric stenosis. Patients with such very advanced pyloric stenosis would be unsuitable for treatment by H.S.V. plus sphincter stretch.

The finding of satisfactory gastric emptying after H.S.V. for pyloric stenosis is relevant to the surgical management of patients with duodenal ulcer who do *not* have pyloric stenosis, because it implies that none of them need have a drainage procedure added. This in turn means that there is no need to expose patients with uncomplicated duodenal ulcer to the *relatively* high incidence (compared with that which follows H.S.V.) of diarrhoea, early dumping, and bile vomiting which follows truncal or selective vagotomy with a drainage procedure. Indeed, by extending the use of H.S.V. to patients with haemorrhage, perforation, and pyloric stenosis we have been able to treat 100 consecutive patients with duodenal ulcer in the past 2 years without the addition of a drainage procedure. Presumably H.S.V. plus dilatation provides effective treatment for pyloric stenosis because, by preserving the nerves to the antrum, it preserves and uses the compensatory mechanisms of hypertrophy and hyperperistalsis which the stomach has developed in an attempt to overcome the obstruction at its outlet. The conventional operations such as gastrectomy or vagotomy with drainage accord these compensatory mechanisms no such respect.

Acknowledgements.—It is a pleasure to thank our colleagues Dr. F. R. Ellis and Dr. W. D. A. Smith of the Department of Anaesthetics, The General Infirmary, Leeds, for their help with these cases. We are indebted to Dr. K. C. Simpkins who performed most of the follow-up barium-meal examinations. Professor J. C. Goligher and Dr. B. E. Walker kindly permitted us to include data from the Leeds Gastric Follow-up Clinic. We would also like to thank Mrs. Elaine Nutter who typed the manuscript.

Dr. P. J. Lyndon and Dr. R. B. Smith were supported by grants from the Board of Governors of the United Leeds Hospitals.

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A REVIEW OF 15 YEARS' EXPERIENCE IN THE USE OF SCLEROTHERAPY IN THE CONTROL OF ACUTE HAEMORRHAGE FROM OESOPHAGEAL VARICES

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SUMMARY

The results of 15 years of sclerotherapy for acute variceal haemorrhage are reviewed retrospectively. One hundred and seventeen patients with portal hypertension received a total of 217 injections. Haemorrhage was controlled in 93 per cent of admissions. The mortality per injection was under 12 per cent, and the total admission mortality was 18 per cent. Even where a subsequent shunt was impracticable, sclerotherapy provided useful palliation with few serious complications.

IT is generally agreed that some form of portal systemic shunt is the most effective means of preventing haemorrhage from oesophageal varices in a patient with portal hypertension. Unfortunately a shunt is not always possible or even desirable; for example, in patients under the age of 10 years with portal vein thrombosis where a shunt is impracticable, and in the acute bleeding episode in patients with cirrhosis, of whom only a few with good liver function are suitable for emergency or urgent portacaval shunt. Indeed, the majority of these patients with cirrhosis who survive the acute haemorrhage never become acceptable for a shunt because of advanced years or poor liver function. Even in the best surgical circles a small percentage of 'post-shunt bleeders' are found, particularly in patients with portal vein thrombosis —these present yet a further problem. It is in all these situations that we find sclerosing injections particularly useful. It is not suggested that this form of therapy is an alternative to a shunt; it is merely a further weapon in our therapeutic armoury. Although this form of treatment was first described by Crafoord and Frenckner in 1939 and was introduced to the British Isles in 1955 by Macbeth it has not been universally accepted. The technique described here has been used in Belfast, with few modifications, since 1958.

METHODS

On admission the patient is resuscitated with fresh blood and a Sengstaken tube is passed to limit blood-loss. In addition, neomycin, *Lactobacillus*, and lactulose are introduced into the bowel via the Sengstaken tube to reduce the risk of portal systemic encephalopathy. Injection therapy is delayed for some hours, thus allowing this régime to take effect and the patient to become haemodynamically stable.

In adults a 50-mm. Negus rigid oesophagoscope with proximal fibre lighting is passed under general anaesthesia. In children the largest instrument which can be passed with safety is used. A rigid wide-bore instrument is required to distend the varices prior to injection and to compress them following injection. Initially the oesophagoscope is passed right down to the cardia and this controls bleeding in virtually every patient. In our experience it is extremely rare to find bleeding originating in varices below the cardia. The instrument is then withdrawn a few centimetres, allowing the varices to bulge into the lumen (*Fig.* 1A). Using a Macbeth needle, 2–3 ml. of ethylolamine oleate (Varistab) are injected into each varix; up to 15–25 ml. of sclerosant are used at each session. The aim is to perform an intravascular injection, though undoubtedly some sclerosant goes outside the vein wall. Bleeding from each injection site is immediately controlled, either by pressure from a small swab or by advancing the oesophagoscope over the puncture wound (*Fig.* 1B). Following injection a Sengstaken tube is usually inserted to produce tamponade for a few hours and thus aid the initiation of vascular sclerosis.

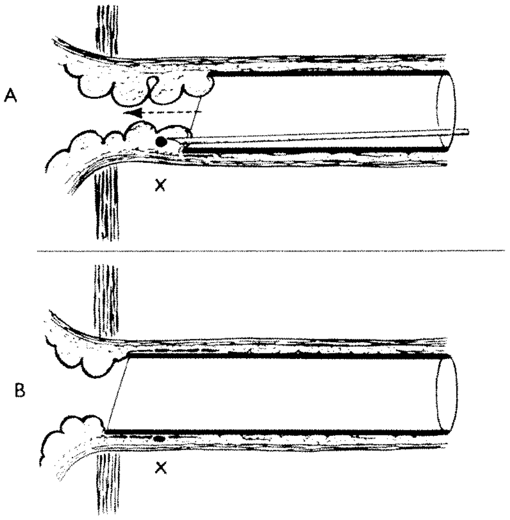

FIG. 1.—A, Showing varices bulging into the lumen of the oesophagoscope, thus facilitating injection at point X. B, The oesophagoscope is advanced over the puncture wound X to control bleeding.

PRESENT SERIES

Patients reviewed.—During the 15-year period from 1958 to 1972, 117 patients received a total of 217 injections. In 87 patients the portal hypertension was due to intrahepatic block, chiefly cirrhosis. In 29 patients the obstruction was extrahepatic. One patient in the series had no demonstrable obstruction to the portal venous system (*Table I*). There was a predominance of females in all groups in the series. The ages ranged from 9 to 82 years in the intrahepatic group and from 6 months to 52 years in the extrahepatic group (*Table II*).

Control of Haemorrhage.—The 117 patients had 194 admissions when injection was carried out for acute variceal haemorrhage. Bleeding was controlled in 177 instances, giving a 93 per cent control rate. One injection was sufficient in 158 instances, but occasionally more than one injection was required (*Table III*). It should be pointed out that injection therapy was used only for episodes of acute bleeding and not prophylactically, as recently described by Pinel, Richard, Dentan, Troutoux, and Leger (1971).

Table I.—PATIENTS WITH ACUTE HAEMORRHAGE FROM OESOPHAGEAL VARICES TREATED BY INJECTION, 1958–72

OBSTRUCTION	NO. OF PATIENTS	NO. OF INJECTIONS
Intrahepatic	87	134
Extrahepatic	29	82
None	1	1
Total	117	217

Table II.—AGE AND SEX OF THE PATIENTS IN THE PRESENT SERIES

OBSTRUCTION	AGE AND SEX	AGE RANGE (yr.)	MEAN (yr.)
Intrahepatic	51 F. 36 M.	9–82	56
Extrahepatic	20 F. 9 M.	½–52	20
None	1 F.	58	58

Table III.—RESULTS OF TREATMENT BY SCHLEROTHERAPY OF 194 ADMISSIONS FOR VARICEAL BLEEDING

NO. OF INJECTIONS	BLEEDING CONTROLLED	BLEEDING UNCONTROLLED
1	158	15
2	18	1
3	1	1
Total	177*	17

* Ninety-three per cent control rate.

Hospital Mortality.—In the 15 years under review there were 35 hospital deaths during 194 admissions. Nineteen deaths occurred even after bleeding had been controlled; 10 of these patients died as a result of hepatic coma, 6 from unrelated pathology, and 3 following elective portacaval shunt during the same hospital admission. Sixteen deaths occurred where bleeding was not controlled; 10 from continuing haemorrhage and 6 following further emergency operations, one of which was for a coexisting bleeding duodenal ulcer. This gives a total admission mortality of 18 per cent, but the mortality per injection was under 12 per cent. We would emphasize that injection therapy is used routinely for all admissions with acute variceal bleeding and there is no selection of patients. Only patients *in extremis* who do not live long enough to reach the operating theatre are excluded.

Long-term Effectiveness of Sclerotherapy.—Injection therapy reduces the frequency and severity of haemorrhage and occasionally permanent sclerosis occurs. At subsequent oesophagoscopy the varices are of smaller calibre and sometimes they are no longer visible (Johnston and Rodgers, 1964). For example, 1 boy with portal vein thrombosis required seven series of injections for acute haemorrhage between the ages of 15 and 20. Since then he has been free from bleeding for almost 10 years and now has no evidence of varices. In patients coming to autopsy after injection therapy histological examination of the submucous veins of the oesophagus has shown organized intraluminal thrombosis, intimal thickening, and perivenous fibrosis to be the basis of haemorrhage control (Hunt, Johnston, and Rodgers, 1969).

Where a shunt is impossible and sclerotherapy has to be relied upon as the definitive treatment, significant control can be obtained. Thus, in the patients with cirrhosis the average period of relief from bleeding using injection therapy only was 10 months, and the maximum period of freedom in any one patient was 5½ years. In the extrahepatic group the average period of relief was 2½ years, and the longest period of freedom from haemorrhage was almost 15 years. The patient with no demonstrable block has not bled since being injected 8 years ago (*Table IV*).

Table IV.—Freedom from Haemorrhage following Injection

Obstruction	Average Relief	Maximum Relief
Intrahepatic	10 mth.	5½ yr.
Extrahepatic	30 mth.	15 yr.
None	8 yr.	8 yr.

Of course, where feasible some form of portal systemic shunt is performed as an elective procedure at a later date. We now feel that it is best to discharge the patient from hospital for a month or two to recuperate before performing the shunt. In this series only 28 of the patients with cirrhosis were subsequently considered fit for a shunt, and in the extrahepatic group only 10 patients had an elective shunt. The small number in the extrahepatic group is explained by the fact that some were 'post-splenectomy bleeders', some had previously failed shunts, and some are still too young for a splenorenal shunt.

Complications.—The procedure is remarkably free of complications, although it is not unusual for the patient to have a mild tachycardia, slight pyrexia, and sometimes retrosternal discomfort for 24–48 hours after injection. This is presumably due to oesophagitis and peri-oesophagitis from the irritant effect of the sclerosant. On 3 occasions the inflammatory reaction in the oesophagus was severe enough to cause delayed necrosis of the oesophageal wall with leakage. This occurred 5–10 days after the injection. Two of the patients were 11-year-old girls with portal vein thrombosis and severe thrombocytopenia. In both cases excess sclerosant was probably used in an effort to obtain haemostasis. One patient required a colonic replacement of the oesophagus but later developed an anastomotic leak and died. The other patient developed an empyema which required drainage. She subsequently had a splenorenal shunt and is now well and free from bleeding 7 years later. The other delayed perforation occurred in a 59-year-old male with alcoholic cirrhosis, causing death 19 days after injection. One other young girl with an extrahepatic block developed a temporary oesophageal stricture after receiving twelve injections in 9½ years (the largest number in this series). The stricture responded to one oesophageal dilatation and she has been free of dysphagia and bleeding for the past 4 years.

Follow-up.—Our follow-up extends from 3 months to almost 15 years from the first injection. In the cirrhotic group 36 patients survive, and 25 of the 29 patients with extrahepatic block are still alive. Three patients in the cirrhotic group have been lost to follow-up and are presumed dead.

DISCUSSION

In most reported series acute haemorrhage from oesophageal varices carries a mortality of around 50 per cent for the first hospital admission. This figure has not improved in the past 20–25 years and is unlikely to do so unless an effort is made to concentrate these patients in centres experienced in their therapy. The first priority is control of bleeding, and although a Sengstaken tube does this adequately initially, 40 per cent of patients re-bleed on release of the tamponade (Rothwell-Jackson and Hunt, 1968). Systemic vasopressin gives only temporary relief and is not without risk (Sherlock, 1967), and direct infusion of the drug into the superior mesenteric artery fares no better (Murry-Lyon, Pugh, Nunnerley, Laws, Dawson, and Williams, 1973). The Boerema-Crile operation of transthoracic ligation of the varices carries a mortality of 30–40 per cent when performed as an emergency procedure (Hunt, 1967), and has only a temporary effect. An emergency shunt is unlikely to save more than 50 per cent of cases unless patients are carefully selected (Edmondson, Jackson, Juler, Digel, and Perrin, 1971). Sclerotherapy carries a lower morbidity and mortality than any of these more usually accepted emergency measures and deserves to be more widely adopted. Without any patient selection the admission mortality is reduced to under 20 per cent.

CONCLUSION

Sclerotherapy is not advocated as a substitute for portal systemic shunt operations. However, in patients where a shunt is untenable it is a useful means of obtaining an appreciable survival rate, and carries a lower morbidity and mortality than the more usually adopted procedures.

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[Although not presented here, the following papers were also read:—

'Prolactin in Breast Cancer', R. Buchan, R. G. Wilson, M. M. Roberts, A. P. M. Forrest (Edinburgh), and A. Boyes and K. Griffiths (Cardiff).

'The Management of Pulmonary Embolism', G. E. Mavor (Aberdeen).]

SHORT PAPERS FOR THE MOYNIHAN PRIZE AND MEDAL

[The prize was won jointly by A. Cuschieri (Liverpool) and D. C. Carter, D. Bhana, S. M. M. Karim, and A. P. Canesan (Edinburgh and Uganda).]

URINARY HYDROXYPROLINE EXCRETION IN EARLY AND ADVANCED BREAST CANCER—A SEQUENTIAL STUDY

BY A. CUSCHIERI

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SUMMARY

A sequential study of urinary hydroxyproline was performed in 47 patients with cancer of the breast. The results have shown that hydroxyproline excretion in the urine provides a sensitive index of the early development of secondary deposits in bone from primary breast cancer. Elevation of the urinary excretion of hydroxyproline may predate by several months the radiological demonstration of osseous deposits. Sequential estimations have shown that the elevated urinary hydroxyproline excretion is persistent in patients who subsequently develop deposits in bone.

MOST of the hydroxyproline (OH.P) in the urine originates from bone (Dull and Henneman, 1963; Klein, Lafferty, Pearson, and Curtiss, 1964) and the urinary excretion of this imino acid is mainly derived from the degradation of newly synthetized (soluble) collagen (Lindsedt and Prockop, 1961; Prockop, 1964; Kivirikko, Laitinen, and Lamberg, 1965). Only 5–10 per cent of the OH.P released into the circulation is excreted in the urine, the rest being oxidized to CO_2 and H_2O. Therefore, relatively large changes in the degradation of collagen are required to alter the rate of urinary excretion of OH.P which nevertheless has been found to be a useful index in a number of clinical situations. Hydroxyproline excretion is increased in several disorders of bone and several reports have indicated that it is more sensitive than other biochemical tests in conditions such as acromegaly, hyperthyroidism, and hyperparathyroidism (Jasin, Fink, Wise, and Ziff, 1962; Keiser, Gill, Sjoerdsma, and Bartter, 1964; Kivirikko, Laitinen, Aer, and Halme, 1965). Subsequent studies have shown an increased hydroxyprolinuria in patients with radiologically demonstrable metastases in bone from a variety of malignant neoplasms including carcinoma of the breast (Bonadonna, Merlino, Laird Myers, and Sonnenberg, 1966; Hosley, Taft, Oslen, Gates, and Beebe, 1966; Leroy, Carbone, and Sjoerdsma, 1966). Guzzo, Pachas, Pinals, and Krant (1969) showed that increased OH.P excretion is a more sensitive index of bone metastases than hypercalciuria. They also reported 5 patients with breast cancer and 5 patients with bronchial neoplasms in whom elevated urinary OH.P excretion predated by several months the demonstration of osseous deposits by radiography. The present study was designed to investigate the urinary excretion of OH.P in cases of breast cancer in order to assess its value as an early index of the development of osseous deposits.

MATERIAL AND METHODS

The study was performed in 18 normal females (aged 25–60 years) and 49 patients with breast cancer (aged 33–74 years). The breast cancer cases included 12 patients with radiologically demonstrable osseous deposits (group 1), 10 patients with soft-tissue deposits (group 2), 18 patients who remained free of secondary deposits throughout the period of the study (6 months to 4 years) (group 3), and 9 patients who were initially free of secondary deposits on clinical and radiological investigation but who subsequently developed osseous deposits (group 4).

All the breast cancer patients were reviewed clinically at frequent intervals and those in groups 3 and 4 had sequential urinary OH.P and creatinine excretion studies together with repeated limited skeletal surveys.

Twenty-four-hour OH.P excretion was measured in all the subjects whilst on a gelatin-free diet for 4 days. They were instructed to omit all meats, tinned fish, ice-cream, sweets, synthetic cream, jelly, lemon/orange pie fillings, cake decorations, and chocolate from their diet. Two 24-hour urine specimens were then collected on days 3 and 4 whilst still on the gelatin-free diet, using boric acid (8·0 g. per container) as a preservative. The urinary OH.P (free and total) was measured by a modification of Grant's technique (Grant, 1964). The test involves the oxidation of OH.P to pyrrole compounds which can then be used to form a specific colour reaction with *p*-dimethylaminobenzaldehyde.

The urinary creatinine was measured (standard Technicon Autoanalyser method) in order to correct for errors in the urine collection, especially in patients in whom the test was performed on an out-patient basis. Other biochemical estimations performed included serum alkaline phosphatase and fasting serum calcium (Technicon Autoanalyser).

Total OH.P and creatinine were expressed as absolute values and as an index, total OH.P/creatinine × 100, as suggested by Guzzo and others (1969).

Statistical Methods.—Student's *t*-tests for paired and unpaired data were used as appropriate. Analysis of variance was also performed on the sequential data on OH.P excretion.

RESULTS

Control Subjects.—The urinary OH.P excretion of 18 normal female adults is shown in *Table I*. No significant difference was noted between the first and the second 24-hour collections for either free or total OH.P (*Table II*). The urinary excretion of OH.P is influenced by age, and *Fig.* 1 shows the mean and S.D. of the various age-groups. It is obvious that in comparative studies the age-group of the patients and the controls should be similar.

Table I.—URINARY OH.P EXCRETION IN 18 NORMAL FEMALE SUBJECTS AGED 25–60 YEARS

	FREE OH.P (mg. per 24 hr.)	TOTAL OH.P (mg. per 24 hr.)	OH.P/CREATININE INDEX
Mean	1·87	16·6	1·73
S.D.	1·07	5·0	0·49
S.E.	0·25	1·2	0·12

Breast Cancer Patients.—The initial values for the breast cancer cases are shown in *Table III*. The total OH.P excretion and the OH.P/creatinine ratio in patients with radiologically demonstrable osseous metastases were significantly elevated when compared with the controls ($P < 0·001$). In fact the OH.P excretion was elevated in all but one of the patients in this group and the urinary OH.P excretion was a more sensitive index of osseous deposits than either the fasting serum-calcium level or serum alkaline phosphatase activity (*Fig.* 2).

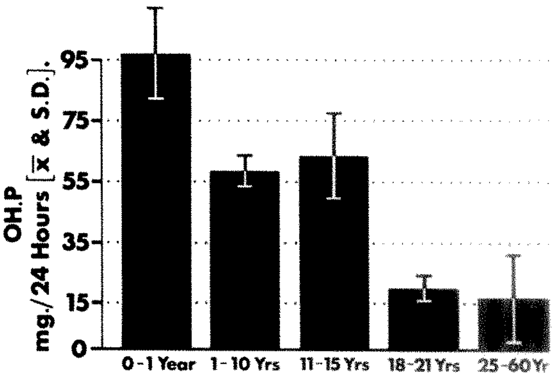

FIG. 1.—Urinary excretion of OH.P with age. Compiled from the data of Jasin and others (1962), Kivirikko and Laitinen (1965), Laitinen, Nikkila, and Kivirikko (1966), and Cuschieri and Felgate (1972).

Table II.—DIFFERENCE IN THE URINARY OH.P CONTENT BETWEEN THE FIRST AND SECOND 24-HOUR COLLECTIONS OF 17 PAIRS OF RESULTS FROM NORMAL FEMALE SUBJECTS AGED 25–60 YEARS

	FREE OH.P	TOTAL OH.P	OH.P/CREATININE INDEX
Mean difference	−0·28	0·5	0·16
S.E. of mean difference	0·14	1·0	0·11
t	1·964	0·482	1·498
P	>0·05	>0·06	>0·1

Table III.—INITIAL URINARY OH.P EXCRETION AND OH.P/CREATININE INDEX IN THE BREAST CANCER CASES STUDIED

GROUP	TOTAL OH.P (mg. per 24 hr.)	OH.P/CREATININE INDEX
1	46·0 ± 3·0*	4·70 ± 0·38*
2	26·9 ± 2·30*	2·40 ± 0·39
3	16·9 ± 2·30	2·13 ± 0·15
4	33·05 ± 6·32*	4·26 ± 0·37*

* Significant difference ($P < 0·05$) from values in a normal female population of a similar age range.

Results are expressed as mean and standard error.

In cases with soft-tissue deposits only, as assessed by clinical and radiological investigation (group 2), the urinary total OH.P excretion was significantly raised when compared with the controls ($P < 0·01$). In the patients who remained free of secondary deposits throughout the period of study the urinary excretion of OH.P fell within the normal range, whereas it was significantly elevated ($P < 0·001$) in the patients who subsequently developed radiologically demonstrable metastases between 3 and 12 months later ($P < 0·001$).

Sequential Studies.—The sequential estimations for urinary total OH.P and OH.P/creatinine index in patients who have remained free of secondary deposits to date are shown in *Table IV*. They have remained within the normal range although the total OH.P excretion has shown a significant elevation from the initial value when analysed by Student's *t*-test for paired data ($P < 0{\cdot}05$). However, analyses of variance indicated no significant change between the initial values and those at the end of 9–12 months for total OH.P excretion (F ratio = 0·633, $P > 0{\cdot}2$) and the OH.P/creatinine index (F ratio = 0·221, $P > 0{\cdot}2$).

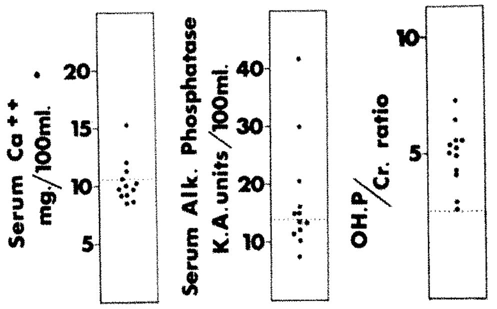

FIG. 2.—Serum-calcium and alkaline phosphatase levels and OH.P/creatinine index in 12 patients with carcinoma of the breast and osseous involvement on radiographic survey. The dotted line indicates the upper limit of the normal range.

Table IV.—SEQUENTIAL ESTIMATION OF URINARY OH.P EXCRETION AND OH.P/CREATININE INDEX (3–4 MONTHLY) IN 12 PATIENTS WHO HAVE REMAINED FREE OF SECONDARY DEPOSITS

	SEQUENTIAL ESTIMATIONS				
	1	2	3	4	*P*
Total OH.P (mg. per 24 hr.)	16·92 ± 2·27	18·28 ± 1·69	20·72 ± 2·92	20·92 ± 2·68	<0·05
OH.P/creatinine index	2·13 ± 0·15	2·06 ± 0·15	2·21 ± 0·22	2·29 ± 0·31	>0·20

Results are expressed as mean and standard error.

Table V.—SEQUENTIAL ESTIMATION OF URINARY OH.P EXCRETION AND OH.P/CREATININE INDEX (3–4 MONTHLY) IN 8 PATIENTS WHO SUBSEQUENTLY DEVELOPED RADIOLOGICALLY DEMONSTRABLE OSSEOUS METASTASES

	SEQUENTIAL ESTIMATIONS				
	1	2	3	4	*P*
Total OH.P (mg. per 24 hr.)	33·05 ± 6·32	38·21 ± 5·54	42·56 ± 7·31	42·26 ± 6·35	<0·01
OH.P/creatinine index	4·26 ± 0·37	4·49 ± 0·39	4·75 ± 0·55	4·59 ± 0·45	<0·05

Results are expressed as mean and standard error.

The sequential data for urinary OH.P excretion in patients who subsequently developed osseous deposits are shown in *Table V*. Both the total OH.P excretion and the OH.P/creatinine index have remained persistently elevated above normal and have increased significantly with time.

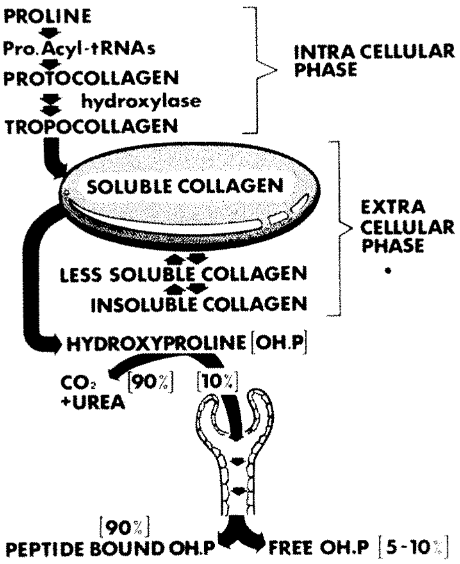

FIG. 3.—Biosynthesis and degradation of collagen.

DISCUSSION

The urinary excretion of OH.P is increased in patients with breast cancer who have radiologically demonstrable osseous deposits. Moreover, the urinary OH.P excretion was persistently elevated several months before the radiological demonstration of involvement of bone by tumour in 9 patients of the present series. It appears, therefore, that OH.P excretion is a sensitive index of secondary deposits in bone and together with radio-isotope scintiscanning is useful in accurate staging of breast cancer. The reason for increased excretion of this imino acid in the presence of secondary deposits is closely linked with the accepted scheme for the metabolism of collagen (*Fig*. 3). It appears that cells that synthesize collagen first assemble polypeptides called protocollagen which have the identical amino-acid composition of collagen except that they contain proline and lysine instead of hydroxyproline and hydroxylysine (Lukens, 1965; Juva and Prockop, 1965). An enzyme, protocollagen hydroxylase, then converts the proline and lysine to the hydroxyl compounds with the formation of tropocollagen (Kivirikko and Prockop, 1967). Thus the OH.P in the urine does not originate from OH.P peptides in precursors of collagen but results from the degradation of both newly synthetized (soluble) and to a lesser extent insoluble collagen (Prockop, 1964).

The factors known to influence OH.P excretion include age (Ziff, Kibrick, Dresner, and Cribetz, 1965), sex, growth hormone (Avioli and Prockop, 1967), and thyroid hormone (Kivirikko, Koivusalo, Laitinen, and Lamberg, 1964). The administration of moderate doses of cortisone does not affect the OH.P excretion in human subjects (Benoit, Theil, and Watten, 1963), and excretion levels in Cushing's syndrome are within the normal range (Klein and others, 1964). The administration of oestrogens to patients has been reported to decrease the urinary excretion of OH.P (Katz and Kappas, 1965). Increased OH.P excretion has been reported in various diseases affecting bone, such as Paget's disease, fibrous dysplasia, and rickets (Dull and Henneman, 1963; Crabbe and Isselbacher, 1965).

Changes in OH.P excretion are therefore not specific to a particular disease process and the finding of an elevated excretion of this imino acid in patients with breast cancer does not necessarily indicate the presence of osseous deposits. It is evident that other causes of increased hydroxyprolinuria have to be excluded on clinical and biochemical grounds. Nevertheless, it appears to be more sensitive than radiography in the detection of osseous deposits. In this respect it has been estimated by Borak (1942) that approximately 30 per cent of the bone matrix has to be destroyed before metastases become radiologically demonstrable. Our work supports Galasko's (1971) findings using radio-isotope bone scans that a significant percentage of patients with breast cancer have occult deposits in bone at the time of their initial presentation and that there is a need for reappraisal of staging in carcinoma of the breast.

Acknowledgements.—This work was carried out in association with the Department of Chemical Pathology, University of Liverpool, where the biochemical studies were performed. The author would like to thank Dr. W. Taylor, Head of the Department of Chemical Pathology, and Dr. Felgate for their close co-operation in this work.

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CARDIAC SEQUELAE OF HAEMORRHAGIC SHOCK

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SUMMARY

Using selective cardiac catheterization and a ^{133}Xe wash-out technique, myocardial blood-flow and oxygen utilization were studied in greyhounds during and following brief and prolonged haemorrhagic hypotension. The progressive fall in myocardial oxygen extraction as the shock period was prolonged and the subsequent failure of myocardial oxygen consumption to rise during re-infusion suggested the presence of a metabolic defect in the myocardial cell.

The use of a special 'elemental' diet was shown to eliminate the intestinal blood-loss typical of canine haemorrhagic shock models; despite this the apparent myocardial cellular metabolic defect persisted.

In addition, a myocardial depressant factor which depressed myocardial function *in vitro* was isolated from ultrafiltrates of post-shock plasma.

THE extent to which myocardial dysfunction contributes to death after experimental haemorrhagic shock remains uncertain. While many studies (Crowell and Guyton, 1961, 1962; Gomez and Hamilton, 1964; Siegel and Downing, 1970) have implicated the presence of overt cardiac failure, other investigators doubt whether a functional and metabolic defect occurs such that death inevitably ensues (Simeone, 1961; Weidner, Albrecht, and Clowes, 1964).

Variations in the experimental model such as the duration and severity of hypotension and the adequacy of fluid replacement during resuscitation contribute to conflicting opinion. Also many experimental studies have been performed in spontaneously breathing anaesthetized animals in which varying degrees of hypoxaemia may occur, particularly if subjected to major cardiac or thoracic surgical procedures. A particular problem in the canine haemorrhagic shock model is the occurrence of an overt haemorrhagic enteritis with secondary intraluminal blood-loss which may be massive and obscure the response to re-infusion, thus complicating the evaluation of the resuscitation phase.

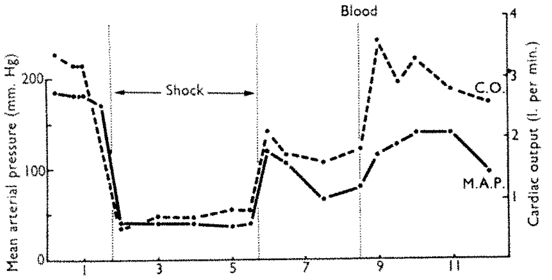

FIG. 1.—The changes in mean arterial pressure (M.A.P.) and cardiac output (C.O.) of a typical animal before, during, and after prolonged haemorrhagic hypotension (3½ hours).

The aim of the present study was therefore to evaluate the nature and severity of myocardial dysfunction following canine haemorrhagic shock using a model in which surgical manipulation was minimal, hypoxaemia did not occur, and normal blood-volumes were maintained during resuscitation, and also to assess the importance of intestinal necrosis in myocardial dysfunction. In addition, the suggestion by Lefer (1970) that cardiac failure in canine haemorrhagic shock may be due to the presence in the post-shock plasm of a circulating peptide, myocardial depressant factor (M.D.F.), which has been shown to produce depression of myocardial function both *in vitro* and *in vivo*, has been investigated further.

MATERIAL AND METHODS

Twelve anaesthetized ventilated greyhounds (weight range 23–32 kg.) were subjected to an arterial haemorrhage into a reservoir until the mean arterial pressure was 35–40 mm. Hg (Heimbach, Fisher, Hutton, McArdle, and Ledingham, 1973). In 6 animals the duration of hypotension was 210 minutes, at the end of which time the residual shed blood was re-infused. In the remaining 6 animals re-infusion was commenced after only 60 minutes. Both groups of animals were then observed for a further 4 hours.

In an attempt to eliminate the problem of intestinal blood-loss another 6 animals were fed on a special 'elemental' diet, similar to that devised by Bounous, Sutherland, McArdle, and Gurd (1967), which consisted of amino acids, carbohydrates, and fat with added salts and vitamins; the dogs were then subjected to a similar 3½-hour shock protocol.

Throughout the period of investigation recordings were made of arterial and right atrial pressure and cardiac output. Myocardial blood-flow (M.B.F.) was measured using a ^{133}Xe-clearance technique (Ross, Ueda, Lichtlen, and Rees, 1964), the xenon being injected directly into the left circumflex coronary artery via a catheter previously placed in position under fluoroscopic control. In addition, arterial, coronary sinus, and mixed venous blood-samples were withdrawn at frequent intervals for the measurement of blood-gases and other biochemical data. The oxygen content of the blood was then calculated in the following manner:—

Blood-oxygen content (ml. per 100 ml.)
= Hb (g.); measured by the cyanmethaemoglobin technique × 1·39 × percentage saturation/100 + P_{O_2} (mm. Hg) × 0·0031 (Bunsen coefficient).

It has been shown previously that within the range 7–24 ml. of oxygen per 100 ml. of blood there is a close relationship between this indirect method of measurement of oxygen content and the direct method of Van Slyke (Ledingham, McBride, Parratt, and Vance, 1970).

The following information was then obtained by calculation:—

Myocardial oxygen availability (ml. per 100 g. per min.)
= M.B.F. (ml. per 100 g. per min.) × the arterial oxygen content (ml. per 100 ml.)/100,

Myocardial oxygen extraction (per cent)
= [Coronary arterial-venous oxygen content difference (ml. per 100 ml.)/arterial oxygen content (ml. per 100 ml.)] × 100,

Myocardial oxygen consumption (ml. per 100 g. per min.)
= M.B.F. (ml. per 100 g. per min.) × [arterial oxygen content (ml. per 100 ml.) − coronary sinus oxygen content (ml. per 100 ml.)]/100.

Arterial blood samples (50 ml.) were removed prior to haemorrhage (control) and at the conclusion of each experiment (post-hypotension). Ultrafiltrates were then prepared and assayed using a guinea-pig atrial preparation (Fisher, Heimbach, McArdle, Maddern, Hutcheson, and Ledingham, 1973).

In addition, ultrafiltrates were evaporated to dryness, dissolved in a small amount of distilled water, and applied to Biogel P2 (200–400 mesh) gel chromatography columns (90 × 1·5 cm.). The columns were eluted with distilled water at room temperature and a flow-rate of 1·5–2 ml. per minute, and 3-ml. aliquots were collected and read at 230 nm. in a Unicam SP 1800 spectrophotometer. The resultant peaks were lyophylized and taken up in the original volume of Krebs-Henseleit buffer and assayed on the guinea-pig atrial preparation. Human albumin, polymyxin B (molecular weight = 1150), and tryptophan (molecular weight = 204) were used to calibrate each column.

RESULTS

The required degree of hypotension was achieved with the loss of 50 ± 3 ml. per kg. of body-weight (mean ± S.E.M.) over a 30-minute period. In the animals subjected to prolonged hypotension (3½ hours) the spontaneous re-uptake of shed blood was 39 ± 3 per cent.

The typical response to re-infusion in 1 animal subjected to prolonged (3½ hours) hypotension is shown in *Fig.* 1. The fall in mean arterial pressure and cardiac output during shock was only partly corrected upon re-infusion of the shed blood alone. Massive supplementary infusions of blood and colloid were then necessary to prevent progressive deterioration and death.

During the immediate post-infusion period there was evidence of incomplete return of normal cardiac function. Rapid re-infusion of the residual shed blood often led to disproportionately large increases in right atrial pressure, although if the rate of infusion was limited by alterations in right atrial pressure the heart was able to cope with the fluid load. Assessment of this period was further complicated by the presence of intestinal blood-loss, which at times was massive, which is a striking feature of severe and prolonged canine haemorrhagic shock.

Table I.—HAEMODYNAMIC DATA FOR ANIMALS SUBJECTED TO PROLONGED AND BRIEF HYPOTENSION

	PROLONGED HYPOTENSION (3½ hr.)					BRIEF HYPOTENSION (1 hr.)			
	C	S_1	S_2	R_1	R_2	C	S_1	R_1	R_2
Mean arterial pressure (mm. Hg)	158 ± 8	37 ± 1	37 ± 2	87 ± 7	97 ± 6	147 ± 9	39 ± 2	127 ± 9	120 ± 22
Cardiac output (l. per min.)	3·9 ± 0·4	0·9 ± 0·2	1·0 ± 0·1	2·5 ± 0·3	3·1 ± 0·3	4·1 ± 0·5	0·9 ± 0·3	3·7 ± 0·5	4·0 ± 0·6
Myocardial blood-flow (ml. per 100 g. per min.)	116 ± 11	37 ± 1	37 ± 1	73 ± 7	82 ± 4	122 ± 9	39 ± 1	96 ± 11	90 ± 20

Data expressed as mean ± S.E.M. C, Control period. S_1, Early shock. S_2, Late shock. R_1, Early resuscitation. R_2, Late resuscitation.

Table II.—MYOCARDIAL OXYGEN USAGE DATA FOR ANIMALS SUBJECTED TO PROLONGED AND BRIEF HYPOTENSION

	PROLONGED HYPERTENSION (3½ hr.)					BRIEF HYPERTENSION (1 hr.)			
	C	S_1	S_2	R_1	R_2	C	S_1	R_1	R_2
Myocardial oxygen availability (ml. per 100 g. per min.)	23·7 ± 2·0	7·5 ± 0·3	7·7 ± 0·3	14·0 ± 1·6	16·3 ± 0·6	28·3 ± 3·5	9·9 ± 1·2	19·3 ± 2·4	14·5 ± 2·4
Myocardial oxygen extraction (per cent)	48 ± 3	74 ± 5	56 ± 6	33 ± 5	33 ± 5	53 ± 10	73 ± 8	52 ± 5	57 ± 3
Myocardial oxygen consumption (ml. per 100 g. per min.)	11·1 ± 0·7	5·5 ± 0·4	4·2 ± 0·5	4·5 ± 0·6	5·3 ± 0·9	13·8 ± 1·4	6·9 ± 0·7	9·8 ± 0·8	8·2 ± 1·5

See Table I for key to abbreviations.

The haemodynamic data following both brief (1 hour) and prolonged (3½ hours) hypotension are shown in *Table I.*

With the onset of hypotension there was a significant increase in heart-rate ($P < 0{\cdot}001$) and the stroke volume fell by 80 per cent. In resuscitation despite re-infusion of the residual shed blood along with additional fluid the mean arterial pressure remained significantly below control values ($P < 0{\cdot}001$) although the right atrial pressures were normal. By the end of the resuscitation, however, cardiac output and myocardial blood-flow had returned to levels not significantly different from the control values. Random left ventricular end diastolic pressures were normal. In contrast, after only 1 hour's hypotension re-infusion of the residual shed blood rapidly restored these parameters to within normal limits.

With the onset of hypotension there was a slight fall in arterial oxygen tension which quickly corrected itself in resuscitation. In the presence of an unchanged minute ventilation and inspired oxygen concentration this indicates that significant alveolar hypoventilation did not occur. Arterial *p*H fell substantially early in shock to a mean of 7·18 ± 0·02 units but did not deteriorate further even after 3½ hours' hypotension. The *p*H remained low during early resuscitation but by the end of the experiment had returned to control values without the addition of alkaline fluids. These changes in *p*H were predominantly related to a gross metabolic acidosis, the mean base excess falling to − 15 ± 1 mEq./l. during hypotension.

The changes in myocardial oxygen usage following both brief and prolonged hypotension are shown in *Table II.* The changes in myocardial oxygen availability reflect the changes in myocardial blood-flow, there being no significant change in arterial oxygen content between the control and resuscitation phases. Concomitant with the fall in myocardial blood-flow in shock there was a significant rise in myocardial oxygen extraction ($P < 0{\cdot}001$). However, as the period of hypotension was prolonged myocardial oxygen extraction fell despite no further alteration in myocardial oxygen availability. In addition, myocardial oxygen consumption which fell by 65 per cent in shock failed to rise significantly above shock levels in resuscitation, thereby suggesting the presence of a metabolic defect in the myocardial cell. By contrast, in the animals subjected to only brief hypotension myocardial oxygen extraction and consumption rapidly returned to normal values, thus showing that the changes seen after prolonged hypotension are not solely related to a non-specific deterioration in the preparation used.

'Elemental' Diet.—A number of important differences emerged in the group of animals fed on the 'elemental' diet and then subjected to prolonged shock.

In the initial or control group of animals subjected to prolonged hypotension the early period of resuscitation was bedevilled by the occurrence of multiple arrhythmias associated with profound falls in the mean arterial pressure and cardiac output.

A–V junctional rhythms predominated although supraventricular tachycardias with left bundle branch block and atrial fibrillation also occurred. By contrast arrhythmias in the 'elemental' diet-fed animals were transient and not associated with hypotension.

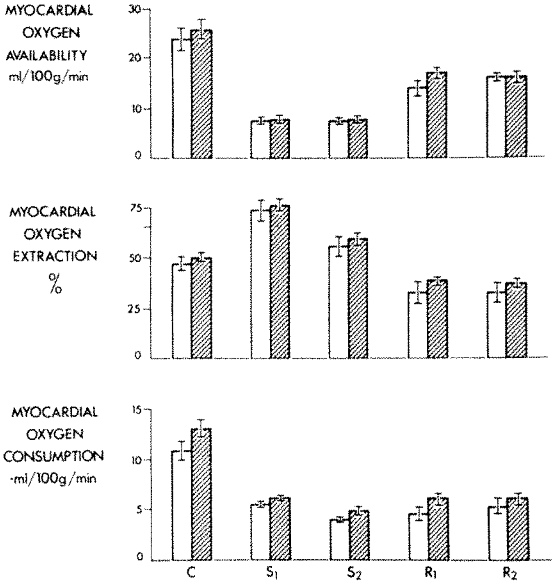

FIG. 2.—Myocardial oxygen availability, extraction, and consumption following prolonged haemorrhagic hypotension (3½ hours) in control (open columns) and 'elemental'-diet-fed (shaded columns) animals (mean ± S.E.M.).

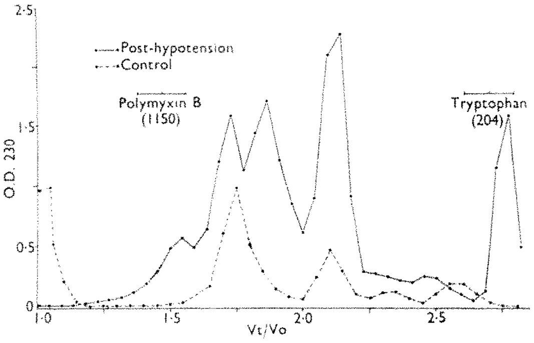

FIG. 4.—Elution curves of 5-ml. samples of ultrafiltrates from an animal before and after 3½ hours' hypotension following application to a Biogel P_2 column. Vt/Vo, Total eluted volume/void volume of column. The positions of the peaks of the markers of known molecular weight are shown.

The spontaneous re-uptake of shed blood during shock was only 16 ± 3 per cent in the 'elemental'-diet-fed animals as opposed to 39 ± 3 per cent in the control animals. In addition, 'elemental'-diet-fed animals required only a mean additional 12 ml. per kg. of body-weight of whole blood or colloid to maintain their haemodynamic parameters in resuscitation, as opposed to a mean additional 56 ml. per kg. of body-weight required by the control animals.

The explanation for these findings was seen on post-mortem examination of the gut, which in the 'elemental'-diet-fed animals was macroscopically normal, in contrast to the gross haemorrhagic enteritis in the control animals.

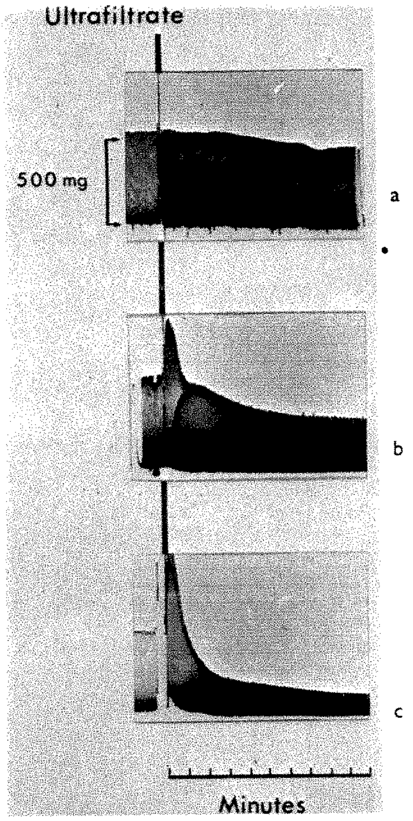

FIG. 3.—Typical tracings of guinea-pig atrial activity following the addition of ultrafiltrates from (a) control pre-shock, (b) brief hypotension (1 hour), and (c) prolonged hypotension (3½ hours) plasma.

However, in spite of the improved stability in the immediate post-infusion period and the elimination of the need for massive quantities of additional fluid in resuscitation there was no significant improvement in myocardial oxygen extraction or myocardial oxygen consumption, as seen in *Fig*. 2. It is therefore unlikely that the defect in myocardial oxygen usage seen in resuscitation is related to the presence of intestinal mucosal necrosis with secondary intraluminal blood-loss.

M.D.F.—Typical tracings produced by ultrafiltrates obtained from individual animals during the control period and following brief and prolonged hypotension in undieted animals are shown in *Fig*. 3. Following the addition of ultrafiltrates the initial increase in developed tension is the result of temporary exposure of the atrium on emptying the organ bath.

Control samples produced 15 ± 2 per cent (mean ± S.E.M.) depression. Following 1 hour of hypotension depression had increased significantly ($P < 0{\cdot}001$) to 45 ± 4 per cent, and after 3½ hours' hypotension had increased significantly further ($P < 0{\cdot}005$) to 77 ± 9 per cent.

Following 3½ hours' hypotension there was no significant difference in percentage depression between the control dogs and those fed on the special elemental diet (73 ± 4 per cent).

Typical elution patterns of ultrafiltrates obtained in the control period and after 3½ hours' hypotension are shown in *Fig.* 4. Significant depression was found to occur in the fourth peak ($Vt/Vo = 2{\cdot}1$) after 3½ hours' hypotension. In 4 dogs this peak produced a mean depression of 54 ± 10 per cent. This peak would correspond to a substance with a molecular weight of 500–700. The remaining peaks produced little depressant activity.

DISCUSSION

These studies have shown that following severe and prolonged canine haemorrhagic shock, progressive cardiac failure need not occur. Indeed, with careful and appropriate fluid replacement cardiac output may return to within normal limits.

Nevertheless, the progressive decrease in myocardial oxygen extraction and consumption with prolongation of hypotension and in the presence of an unchanged myocardial oxygen availability would suggest a metabolic defect in the myocardial cell. A similar deterioration in myocardial performance has been noted by others (Crowell and Guyton, 1961, 1962; Gomez and Hamilton, 1964; Regan, La Force, Teres, Block, and Hellems, 1965).

The defect in oxygen utilization is unlikely to be related to an increase in preferential blood-flow through the myocardium, as nutritive flow (as measured by the xenon-flow technique) does not change as the period of hypotension is prolonged. Alternatively the decrease in oxygen extraction might be due to a transfer to anaerobic pathways in the myocardial cell. However, previous studies from this laboratory (Heimbach and others, 1973) and others (Edwards, Siegel, and Bing, 1954; Lundsgaard-Hansen, 1966) have shown that this does not occur. Furthermore, in resuscitation myocardial oxygen consumption fails to rise despite an increased myocardial oxygen availability, and this would further support the concept that the defect lies in the inability of the myocardial cell itself to extract oxygen.

The assessment of the resuscitation period following severe canine haemorrhagic shock is complicated by the presence of intestinal necrosis with secondary intraluminal blood-loss and the consequent instability of the model. It has been shown that this problem can be eliminated by the simple expedient of pretreating the animal with a special elemental diet.

Despite the improved stability of the model and the elimination of the need for massive quantities of fluid in resuscitation there was no significant improvement in myocardial extraction or consumption, suggesting that the defect in myocardial cellular metabolism is not related to the presence of toxic substances released from the 'shocked' gut.

The presence in the post-shock plasma of a circulating substance of low molecular weight which can produce depression of myocardial contractility *in vitro* is intriguing. It is interesting to note that it appears in association with the deterioration in cardiac function and its appearance may contribute to the development of the myocardial metabolic cellular defect. As there is no significant difference in the degree of depression obtained with ultrafiltrates from animals with or without intestinal necrosis it is unlikely that this depressant factor is related to the toxic breakdown substances produced in the 'shocked' intestine. Partial purification by gel chromatography would suggest that the active component is a single compound with a molecular weight of 500–700.

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EARLY CHANGES IN THE POST-PHLEBITIC LIMB: THEIR CLINICAL SIGNIFICANCE

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SUMMARY

The long-term results of treatment of the established post-phlebitic syndrome by compression sclerotherapy or by ligation of incompetent perforating veins were unsatisfactory in approximately 40 per cent of patients. Changes in superficial venous pressure during exercise occurred when the deep veins were recanalized and the perforating veins became incompetent. These pressure changes could be used to select patients likely to develop the full syndrome. It is suggested that development of an intractable syndrome might be prevented if ligation of incompetent perforating and deep veins is performed before tissue changes become established.

DEEP-VEIN thrombosis is an important cause of disability and death. The patient may die from pulmonary embolism or may develop the post-phlebitic syndrome which represents one of the common and intractable problems in surgery.

When thrombosed veins recanalize the valves are destroyed (Edwards and Edwards, 1937) and become incompetent, causing sustained high pressure in the leg veins (Beecher, 1937; Linton and Hardy, 1948). The patients complain of pain in the leg, swelling, eczema, pigmentation, and ulceration. Several workers have stressed that incompetent perforating veins are responsible for these clinical features (Homans, 1917; Linton, 1938; Cockett and Elgan Jones, 1953; Fegan, 1967). This concept has been the basis for treating these patients by ligation of incompetent perforating veins (Cockett and Elgan Jones, 1953) or by compression sclerotherapy (Fegan, 1963).

In this paper we report the results of a study which had two aims: first, to compare the effectiveness of subfascial ligation and compression sclerotherapy in treating patients with the post-phlebitic syndrome, and secondly to define criteria which could be used to select patients likely to develop severe disease so that treatment could be instituted at an early stage before an intractable syndrome develops.

MATERIAL AND METHODS

The present study was conducted in two parts.

1. Assessment of Treatment.—

Patients.—Eighty patients were studied; their age, sex, and presenting clinical features are shown in *Table I*. Incompetent perforating veins (*Fig.* 1) were located by ascending phlebography (Kakkar, 1972). The patients were also examined for incompetence of the saphenofemoral or saphenopopliteal valves. Patients who had ulceration or marked oedema were admitted to hospital. The ulcers were healed and the oedema was controlled before commencing the selected treatment. Envelopes were prepared, sealed, and numbered in sequence, each containing one of two treatment schedules in random order. As each patient was admitted to the trial his treatment was selected by opening the next envelope.

Compression Sclerotherapy.—The technique of sclerotherapy employed was that described by Fegan (1967); 0·5–1·0 ml. of sodium tetradecyl (S.T.D.) was injected through a 21-gauge needle into each of the sites which had been shown by phlebography to be that of an incompetent perforating vein. In patients with saphenofemoral or saphenopopliteal incompetence the saphenous vein was ligated at its junction with the main vein before commencing compression sclerotherapy.

Table I.—AGE, SEX, AND PRESENTING CLINICAL FEATURES IN 80 PATIENTS WITH THE POST-PHLEBITIC SYNDROME

	TREATMENT	
	Compression Sclerotherapy	Ligation of Incompetent Perforating Veins
No. of patients	43	37
Age		
Range (yr.)	28–70	34–68
Mean	42	47
Male : female ratio	10 : 33	14 : 23
Previous surgery	11	8
Clinical features		
Aching pain	34	29
Ankle oedema	20	15
Eczema	24	17
Pigmentation	36	29
Induration	33	25
Varicose veins	19	12
Ulcers	31	24
Saphenofemoral or saphenopopliteal incompetence	11	6

Ligation of Incompetent Veins.—Patients in this group were admitted to hospital. The sites where phlebography had shown perforating veins were explored under general anaesthesia and the veins were ligated subfascially. If a tortuous vein was found during dissection it was ligated and excised. Incompetence at the saphenofemoral or saphenopopliteal junction was dealt with in exactly the same manner as described above.

Aftercare and Follow-up.—Patients in both groups were seen in the Varicose Veins Clinic at regular intervals. Aftercare was similar in both groups; all the patients wore elastic stockings for a period of at least 3 months.

2. Assessment of Early Changes.—

Patients.—Thirty patients who had developed acute extensive deep-vein thrombosis which had been treated by us during the preceding 4 years were investigated. In each case phlebograms had been performed to confirm the diagnosis and had been repeated to assess the final outcome. The patients had been treated with heparin for 7 days followed by oral anticoagulants for 6–9 months. In 16 patients the tibial, popliteal, and femoral veins had been involved while in 14 cases the thrombus had extended into the iliac segment as well (*Table II*).

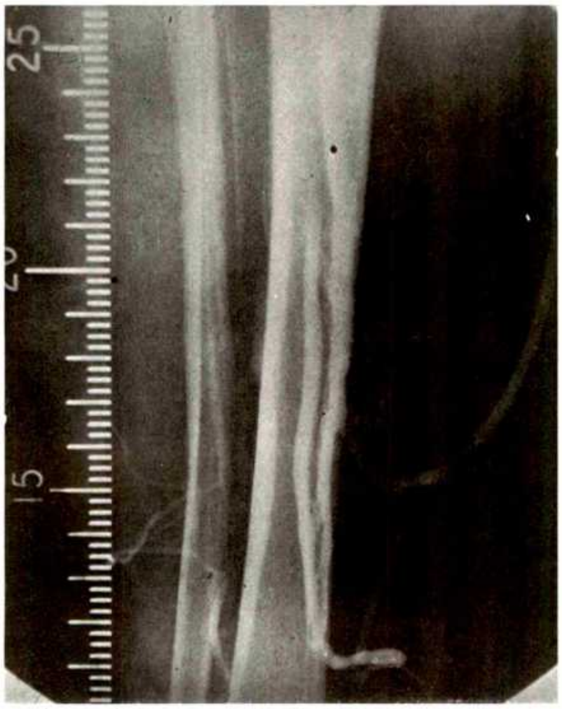

FIG. 1.—Phlebogram showing the tibial vein and two incompetent perforating veins. A radio-opaque ruler marks the distance in centimetres from the tip of the lateral malleolus.

Table II.—TIME INTERVAL BETWEEN EPISODE OF DEEP-VEIN THROMBOSIS AND THE PRESENT INVESTIGATION

Time after Deep-vein Thrombosis (mth.)	*No. of Patients*
6	8
12	14
24	4
36	2
48	2

In 20 patients the normal limb was also investigated on the present occasion. A total of 50 legs were therefore examined and the following investigations were performed.

Ascending Functional Cine-phlebography.—Patency of the deep veins, sites of incompetent perforating veins, and the function of their valves were studied. The technique of phlebography employed has already been described in detail (Kakkar, Howe, Laws, and Flanc, 1969).

Pressure Studies.—Pressure in the superficial veins was recorded in each patient. A scalp vein infusion needle attached to a flexible polyethylene tube was introduced into a vein on the dorsum of the foot. The cannula was connected to a Bell & Howell pressure transducer, type 4-327-L221, with a recording range of 0–75 cm. Hg, connected to a Devices pen recorder. The patients were examined in a standing position. The pressure was allowed to stabilize while the patient stood 'at ease'. He was then instructed to walk 'in place' for a period of 30 seconds and at the end of this time he stood 'at ease' until the pressure stabilized again. This was repeated three times.

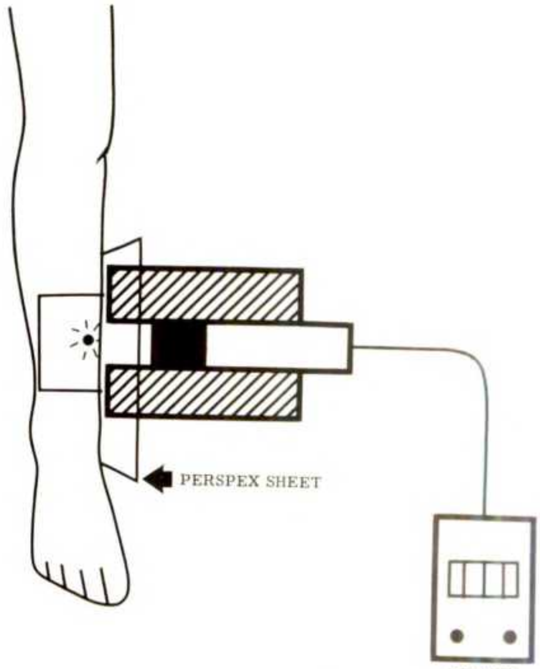

FIG. 2.—^{24}Na clearance was measured from a site approximately 5 cm. above the medial malleolus. The ^{24}Na depot was maintained in constant relation to the collimator by the Perspex sheets shown.

The following pressure measurements were analysed in each tracing: pressure in an upright position at rest (resting pressure); pressure immediately after a period of walking 'in place' (end exercise pressure); time taken for the pressure to return to the resting level after exercise (return time).

Sodium (^{24}Na) *Clearance.*—Venous flow-rate and capillary permeability were assessed by measuring ^{24}Na clearance from the subcutaneous tissues in the ankle region. The investigations were performed in a room where the temperature was maintained at between 25 and 27° C. The patient rested in a horizontal position on a couch for 15 minutes before the examination began. A site approximately 5 cm. above the medial malleolus was marked with a skin pencil and 0·05 ml. of isotonic saline containing 2·5 μc. of ^{24}Na was injected into the subcutaneous tissue, using a fine-bore (25G) needle. Ten minutes after the injection the patient was allowed to stand up and the radioactivity directly over the injected site was recorded (*Fig.* 2). The radioactivity was measured with a scintillation counter, the counts being recorded for a 10-second period in each minute for 5 minutes. The patient was then allowed to walk 'in place' for exactly 50 seconds and at the end of this period the radioactivity was recorded again in the same manner. This was repeated four times so that the patient was exercised for a total of 5 minutes. Great care was taken to ensure that all readings were obtained from the same area by placing the limb in exactly the same position in relation to the scintillation probe on each occasion.

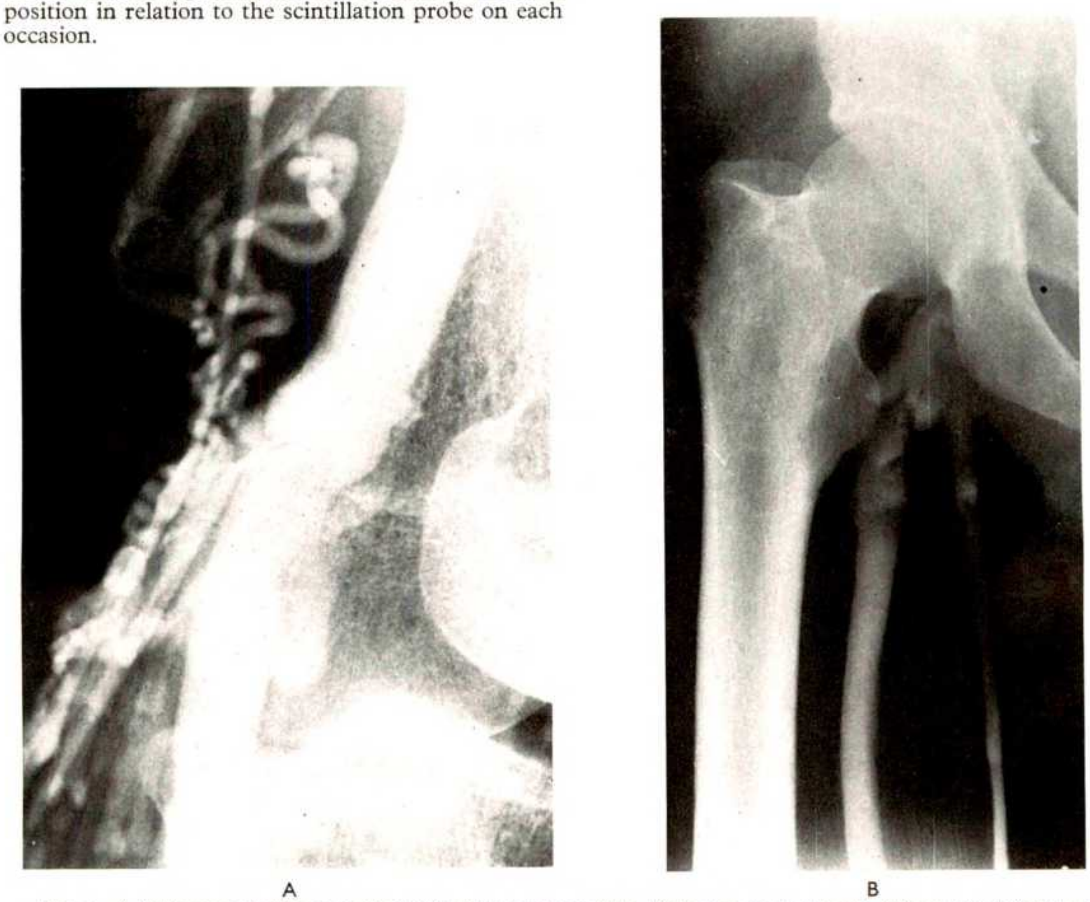

FIG. 3.—A, Phlebogram showing the popliteal vein and a competent valve. Both cusps are clearly seen. These opened with the onward flow of blood and closed during the Valsalva manœuvre. B, Phlebogram showing the femoral and long saphenous veins. Both cusps are clearly seen. The valve was found to be competent.

Electron Microscopy.—The ultrastructure of the subdermal capillaries, venules, and superficial veins was examined in 7 early post-phlebitic limbs and 3 normal limbs. The biopsies of subdermal tissue and subcutaneous veins were obtained under local or general anaesthesia. The tissues were fixed in isotonic 1 per cent osmium tetroxide and after standard processing sections were cut on an LKB ultratome. These sections were examined with an AEI electron microscope.

RESULTS

1. Assessment of Treatment.—Of the 80 patients treated, 5 died from various causes and another 8 failed to attend the clinic or moved to other areas. These patients were excluded from further consideration. This left 67 patients for analysis and all have been followed up for a period of at least 3 years. Of these, 38 patients had compression sclerotherapy and in the remaining 29 patients the incompetent perforating veins were ligated.

Table III.—RESULTS OF COMPRESSION SCLEROTHERAPY AND LIGATION OF INCOMPETENT PERFORATING VEINS (I.P.V.) ASSESSED AT 3 MONTHS, AND 1 AND 3 YEARS

DURATION OF FOLLOW-UP	COMPRESSION SCLEROTHERAPY (38 Patients)				LIGATION OF I.P.V.'s (29 Patients)			
	Satisfactory		*Un-satisfactory*		*Satisfactory*		*Un-satisfactory*	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
3 months	37	88	7	12	22	75	7	25
1 year	25	62	13	38	20	70	9	30
3 years	21	57	17	43	18	65	11	35

The results were recorded as satisfactory when the patient remained asymptomatic throughout the period of follow-up and did not develop further skin changes, and if the stasis ulcer which had been present before treatment remained healed. All other patients were classified as having unsatisfactory results.

Three months after completion of treatment 31 patients (88 per cent) in the compression sclerotherapy group and 22 (75 per cent) in the ligation group had satisfactory results. However, an increasing number of patients developed a recurrence of symptoms or ulceration during the follow-up period (*Table III*). At the end of 3 years 43 per cent of patients in the compression sclerotherapy group and 35 per cent in the ligation group had unsatisfactory results.

In normal limbs the mean return time was 45 seconds. In patients who had blocked deep veins but competent perforators the return time was also 45 seconds. However, in patients with recanalized or blocked veins but with incompetent perforators the return time was considerably less (*Table IV*, *Fig.* 5).

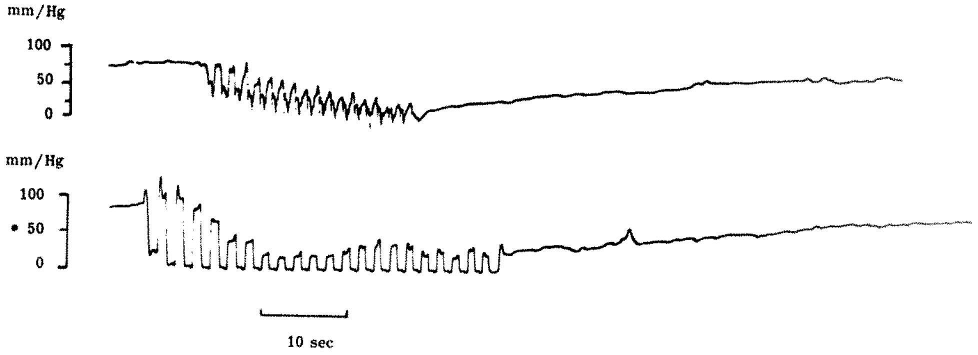

FIG. 4.—Pressure tracing in the normal (*above*) and early post-phlebitic limb (*below*) of the same patient. The resting pressure in the normal limb is 75 mm. Hg; during exercise the pressure fell to 20 mm. Hg and returned to the resting level in 45 seconds. A similar pattern is seen in the other limb. Phlebography in this limb showed blocked femoral and competent perforating veins.

Table IV.—PHLEBOGRAPHIC FINDINGS AND SUPERFICIAL VENOUS PRESSURE IN 20 NORMAL AND 30 POST-PHLEBITIC LIMBS

PHLEBOGRAPHIC FINDINGS	NO. OF LIMBS	MEAN RESTING PRESSURE (mm. Hg)	MEAN END EXERCISE PRESSURE (mm. Hg)	MEAN RETURN TIME (sec.)
Normal limbs	20	85 (75–95)	16 (5–25)	45 (24–80)
Deep veins blocked, perforating veins competent	16	80 (75–85)	20 (15–25)	45 (25–60)
Deep veins blocked, perforating veins incompetent	8	80 (75–90)	25 (20–30)	15 (10–18)
Deep veins incompetent, perforating veins incompetent	6	80 (75–95)	56 (50–80)	8 (0–18)

Figures in parentheses represent the range.

2. Assessment of Early Changes.—In the second part of the study 50 limbs were examined.

Phlebography.—It was possible to classify the state of the deep veins into four groups on the basis of the phlebographic findings (*Table IV*). The function of the valves in the venous system was also assessed. A valve was considered to be competent when both cusps were seen to open and close with onward flow of blood and no retrograde flow occurred (*Fig.* 3). In normal limbs the tibial and popliteal valves were invariably found to be competent. However, the upper femoral valves could not be seen consistently. Six patients had recanalized veins and in none of these could valves be demonstrated.

Pressure Studies.—There was no difference in the resting pressure between normal limbs and those with blocked or recanalized deep veins (*Table IV*). The end exercise pressure in normal limbs and in those with blocked veins was also similar (*Fig.* 4), but was considerably higher in those with recanalized veins (*Table IV*).

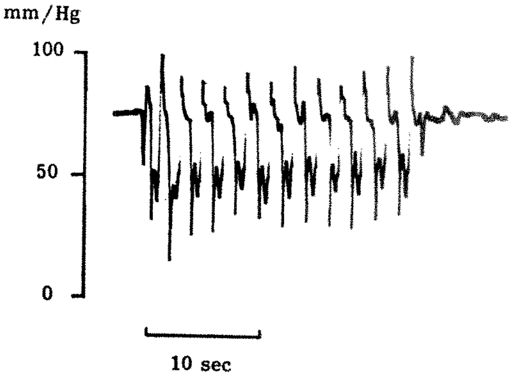

FIG. 5.—Pressure tracings in an early post-phlebitic limb. The resting pressure is 80 mm. Hg; after exercise the pressure immediately returned to the resting level. Phlebography in this limb showed recanalized deep veins and incompetent perforating veins.

^{24}Na *Clearance*.—The counts recorded during rest and during exercise were analysed by a Digital Equipment Corporation PDP-8 computer and clearance slopes were obtained (*Fig.* 6). In normal limbs the mean clearance rate per minute at rest was 0·73 per cent and during exercise this increased to 2·6 per cent per minute. In patients with blocked or recanalized veins the mean clearance rate at rest was 0·59 per cent per minute and during exercise 1·7 per cent per minute. Comparing these two groups, the clearance rates at rest were similar (*Fig.* 7) but during exercise clearance was more rapid in normal limbs than in those with blocked or recanalized veins; this difference was statistically significant ($P < 0{\cdot}02$).

Electron Microscopy.—The structure of the capillaries and subcutaneous veins was studied. The tissues obtained from the normal limbs showed that the capillaries consisted of a single layer of epithelial cells and occasional pericytes surrounded by a basement membrane. The endothelial cell cytoplasm was flattened and fenestrations were observed in some areas. In the venules of approximately 50–80 μ in diameter the endothelial cells were surrounded by a complete layer of pericytes, a basement membrane, and a connective-tissue sheath made up of bundles of collagenous fibrils and veil cells.

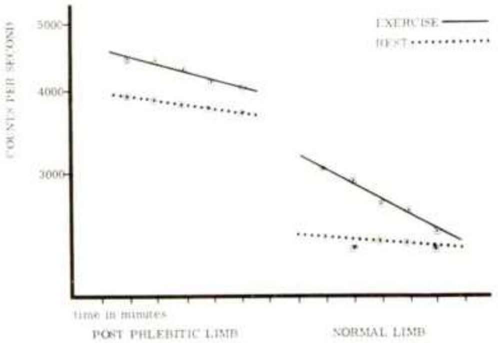

FIG. 6.—Sodium clearance from the subcutaneous tissue in the normal limb and early post-phlebitic limb of the same patient. The clearance rate on exercise in the normal limb is 5·0 per cent per minute and in the post-phlebitic limb 2·8 per cent per minute.

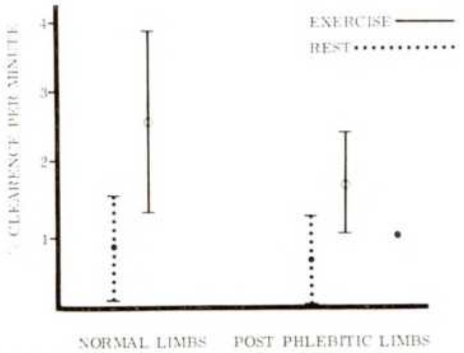

FIG. 7.—The mean and standard deviation of sodium clearance in 20 normal and 22 post-phlebitic limbs. The exercise clearance is significantly reduced in the post-phlebitic group ($P < 0{\cdot}02$).

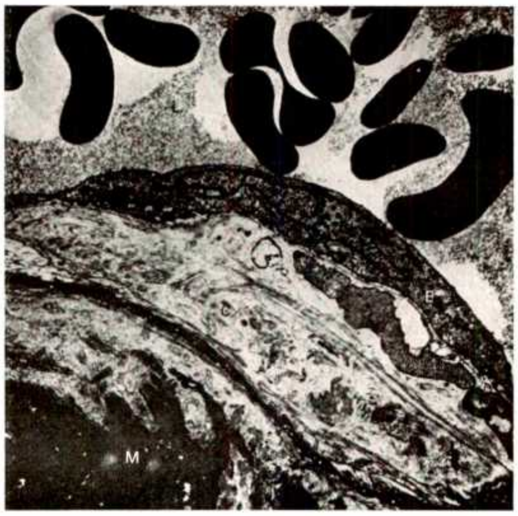

FIG. 8.—Electron micrograph of a subdermal vein obtained from a normal limb. In the lumen (L) many red-blood cells are seen. The epithelial cell (E) is flattened and has a regular surface. The basement membrane has a uniform surface. A layer of collagenous fibrils (C) underlying the basement membrane is seen. A muscle cell (M) is also present. (× 8250.)

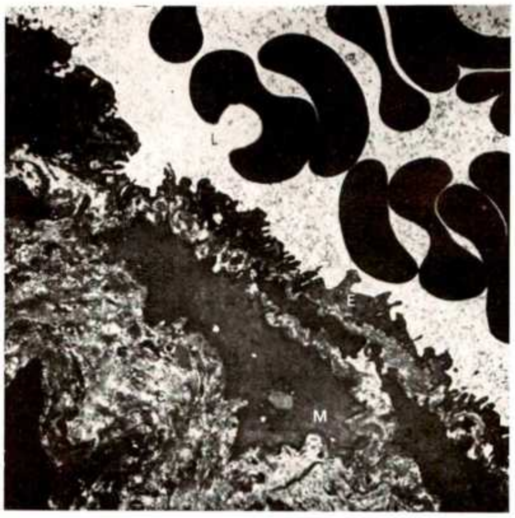

FIG. 9.—Electron micrograph of a subdermal vein obtained from a post-phlebitic limb. In the lumen (L) red-blood cells are again seen. The epithelial cells (E) are disorganized and have multiple cytoplasmic projections into the lumen. The basement membrane is thickened in some areas. The smooth muscle cells (M) and the collagenous fibrils (C) show similar changes. (× 8250.)

Sections of capillaries and venules from post-phlebitic limbs showed that the endothelial cells were often swollen and contained large vacuoles and cytoplasmic projections into the lumen of the vessel. The basement membrane was thickened in places but this change was not uniformly observed (*Figs.* 8, 9).

DISCUSSION

The management of patients with the post-phlebitic syndrome presents a major clinical problem. Treatment of incompetent perforating veins fails to produce satisfactory results in all patients. This study has shown that when localized perforating veins are blocked by ligation or by compression sclerotherapy, long-term satisfactory results are obtained in only 60 per cent of patients.

These findings raise two important questions: why does treatment fail in approximately 40 per cent of patients, and, secondly, what can be done to improve these results? Failure of treatment may be due to several factors. It is possible that some of the incompetent perforating veins were missed during treatment in this study. However, this is unlikely since our findings (Kakkar, Howe, and Flanc, 1969) and those of others (Townsend, Jones, and Williams, 1967) have shown that phlebography is an accurate method of localizing these veins.

Another possibility is that in patients where treatment fails incompetence of the deep venous system plays a major role in the production of symptoms rather than the incompetent perforating veins. If this is true it is not surprising that treatment directed towards dealing with incompetent perforating veins alone fails in a high proportion of patients.

Thirdly, it is possible that irreversible tissue changes may have already occurred in some patients and correction of the haemodynamic abnormality at this stage fails to improve their symptoms.

What can be done to improve the results? Several workers (Bauer, 1948; Linton and Hardy, 1948) have stressed the importance of deep venous incompetence. Procedures suggested to deal with this abnormality include popliteal vein resection (Bauer, 1948), ligation of the superficial femoral vein distal to the junction with the deep femoral vein (Linton and Hardy, 1948), venous by-pass grafting (Hardin, 1962), or the formation of an artificial popliteal valve by transposition of the gracilis tendon (Psathakis, 1966). Although these methods have been claimed by their proponents to be successful they have not met with general acceptance and their multiplicity in itself suggests that the results do not justify their use in patients with the post-phlebitic syndrome.

Another approach would be to select at an early stage the patients who are likely to develop a severe degree of the post-phlebitic syndrome and to initiate treatment before secondary tissue changes developed. In order to select these patients we have assessed the value of pressure measurements in the superficial veins and ^{24}Na clearance to determine the venous flow-rate and capillary permeability. These factors have been investigated because it is believed that sustained venous hypertension (De Camp, Schramel, Ray, Feibleman, Ward, and Ochsner, 1951) and abnormal capillary permeability and venous flow-rate (Fontaine, 1957) are basic mechanisms involved in the pathogenesis of the post-phlebitic syndrome. ^{24}Na-clearance studies showed that although there were differences between normal and early post-phlebitic limbs during exercise, suggesting an impaired capillary permeability and blood-flow in the latter, a considerable overlap was observed when individual patients in each group were compared. The degree of scatter observed in our studies was similar to that reported by McInally, Campbell, Robertson, and Douglas (1952). It is therefore unlikely that this investigation would in itself be useful in patient selection.

The measurement of pressure in the superficial veins was found to be the most useful indicator of future trouble. In patients with blocked veins and competent perforators as shown by phlebography, the pressure pattern was similar to that found in normal limbs, suggesting that venous return is maintained via a competent collateral circulation. Patients with blocked deep and incompetent perforating veins had a pressure pattern which differed from the normal but the differences were not clear-cut. However, those with recanalized deep veins and incompetent perforating veins had a high end exercise pressure and a very short return time. This change is similar to that seen in patients with a well-established post-phlebitic syndrome (Warren, White, and Belcher, 1949; De Camp and others, 1961; Arnoldi, 1966). It can therefore be argued that the development of an intractable syndrome can be prevented if ligation of incompetent perforating and deep veins is performed at the time that these pressure changes occur.

Acknowledgements.—We wish to thank Professor J. G. Murray and Mr. C. T. Howe for their help and encouragement and for allowing us to study their patients; Pfizer Ltd. (U.K.) for financing a research fellowship for T. P. C.; Dr. Ferrigan, Department of Pathology, Pfizer Ltd., Sandwich, Kent, for help in preparing and examining electron microscopic sections; Dr. M. B. Clarke for computer assistance; Mr. K. Eley for technical help; Mr. Redman, Royal College of Surgeons of England, for the photographs; and Mrs. Margaret Shelton for secretarial help.

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THE INTESTINAL COMPLICATIONS OF RADIOTHERAPY

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SUMMARY

The clinical features of 38 patients with intestinal complications after radiotherapy are recorded. Intestinal complications are commonly progressive and in this series led to the death of 14 patients (37 per cent). Nine of these patients had no sign of recurrent tumour. 'Spontaneous' necrosis of the irradiated bowel and necrosis of intestinal anastomoses after surgical operation carried a particularly high mortality. Only 3 patients (8 per cent) became completely asymptomatic after treatment of their bowel disease. Apparently localized radiation lesions in the small bowel were sometimes associated with severe malabsorption. Radiographs showed distinctive radiological patterns in the small bowel. A combined radiotherapy/surgical follow-up clinic is advocated.

DIARRHOEA and systemic upset commonly occur during or shortly after pelvic radiotherapy. These acute symptoms usually subside but they may sometimes be replaced by symptoms of chronic intestinal damage. These intestinal complications of radiotherapy have received little attention in the British literature although sporadic reports have appeared in North America and the Continent (Graham and Villalba, 1963; Calame and Wallach, 1967; Smith, Douglas, McLean, Ruckley, and Bruce, 1968; DeCosse, Rhodes, Wentz, Reagan, Dworden, and Holden, 1969; Lindahl, 1970; Yuen and Boyes, 1970). This paper presents the clinical features of 38 patients with chronic radiation damage to the bowel who attended St. Thomas's Hospital, London, between 1961 and 1971 inclusive.

Table I.—ORIGINAL DISEASES TREATED BY RADIOTHERAPY AND THE INCIDENCE OF INTESTINAL COMPLICATIONS AT ST. THOMAS'S HOSPITAL DURING THE YEARS 1961–71

ORIGINAL DISEASE TREATED BY RADICAL RADIOTHERAPY	NO. OF PATIENTS DEVELOPING INTESTINAL COMPLICATIONS	INCIDENCE OF INTESTINAL COMPLICATIONS (per cent)
Carcinoma of cervix	17	7
Carcinoma of bladder	13	9
Carcinoma of endometrium	2	2
Carcinoma of ovary	2	4
Carcinoma of prostate	2	4
Seminoma of testis	1	—
Menorrhagia	1	—

CLINICAL FINDINGS

There were 26 women and 12 men in the series, their ages ranging from 39 to 76 years at the time of presentation with intestinal symptoms. All except 1 patient had received radiotherapy for malignant disease (*Table I*). Eleven patients (29 per cent) had received what would now be regarded as a high or in some cases very high dose of radiation during the development of a new dose fractionation technique for use with hyperbaric oxygen. Twenty-five patients had large-bowel complications (*Table II*) and 21 had small-bowel complications (*Table III*). Seventy per cent had more than one complication. The incidence of pre-radiotherapy operations or pelvic sepsis was 32 per cent. This incidence was the same in the group of patients with large-bowel complications and in the group with small-bowel complications.

Table II.—LARGE-BOWEL COMPLICATIONS OF RADIOTHERAPY IN 25 PATIENTS

Complication	*No. of Patients*
Proctocolitis	18
Stricture	
Colorectal	13
Anal	4
Rectal ulcer	7
'Spontaneous' necrosis	3
Fistula	3

Table III.—SMALL-BOWEL COMPLICATIONS OF RADIOTHERAPY IN 21 PATIENTS

Complication	*No. of Patients*
Stricture	11
Malabsorption	9
'Spontaneous' necrosis	6
Fistula	2
Impaired healing	6

Table IV.—TIME INTERVALS BETWEEN COMPLETION OF RADIOTHERAPY AND THE DEVELOPMENT OF SYMPTOMS OF LARGE-BOWEL COMPLICATIONS

COMPLICATION	NO. OF PATIENTS	TIME INTERVALS			
		<6 mth.	<1 yr.	1–5 yr.	>5 yr.
Proctocolitis or rectal ulcer	25	13	8	3	1
Colorectal stricture	13	5	5	2	1
Anal stricture or spontaneous necrosis or fistula	10	0	3	4	3

Five of the patients (13 per cent) had clinical evidence of arteriosclerosis.

There was a latent interval between completion of radiotherapy and the development of intestinal complications (*Tables IV, V*). Proctocolitis, rectal ulcers, and steatorrhoea tended to occur earlier than large- and small-bowel stricture formation. Perforations, fistulae, and anal strictures were relatively late complications. Commonly, one intestinal complication was the precursor of another and the disease was often progressive. Proctocolitis preceded the development of colorectal strictures by up to a year and antedated anal strictures by up to 4½ years. Colorectal stricture was associated with subsequent perforation of the rectum in one patient and with the later development of a rectovesical fistula in another. Abdominal pains had been present for between 1 week and 20 months before the emergency admission of 4 of the 6 patients with spontaneous necrosis of the small bowel. Large-bowel complications had caused severe symptoms in the other 2 patients with small-bowel necrosis and may have masked small-bowel symptoms.

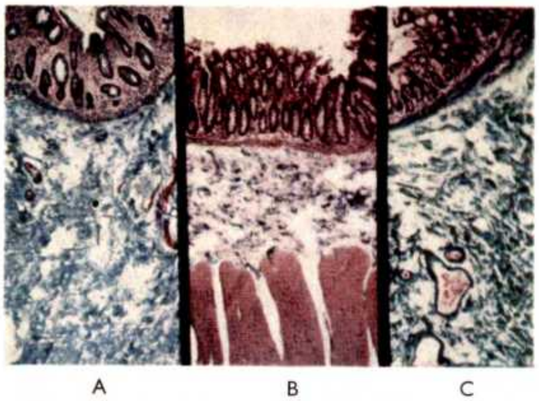

FIG. 1.—Photomicrograph showing greatly increased submucosal fibrous tissue in a section of colon damaged by radiation (A) contrasted with the normal appearance of colon (B) and the appearance of ischaemic colitis (C). (× 10.)

Table V.—TIME INTERVALS BETWEEN COMPLETION OF RADIOTHERAPY AND THE DEVELOPMENT OF SYMPTOMS OF SMALL-BOWEL COMPLICATIONS

COMPLICATION	NO. OF PATIENTS	TIME INTERVALS			
		<6 mth.	<1 yr.	1–5 yr.	>5 yr.
Steatorrhoea	6	3	2	0	1
Stricture	11	6	2	3	0
Spontaneous necrosis or fistula	8	1	2	3	2

Table VI.—MALABSORPTION FOLLOWING PELVIC RADIOTHERAPY

Malabsorption or Deficiency	*Manifestation*	*No. of Patients*
Fat	Steatorrhoea	6*
Vitamin B_{12}	Impaired Schilling test	5†
Calcium	Tetany (1 patient)	2‡

* Range, 11·8–39 g. per 24 hours.

† Range, 0·3–2·9 per cent per 24 hours.

‡ In one patient the level in the serum was 5·7 mg. per 100 ml. and that in the urine 34 mg. per 24 hours; in the other patient the level in the serum was 8·4 mg. per 100 ml and that in the urine 10 mg. per 24 hr.

Patients with large-bowel complications presented with rectal bleeding, alteration of bowel habit, and the passage of mucus per rectum. Colicky lower abdominal pain was associated with stricture formation, and pain on defaecation was associated with rectal ulcers and anal strictures. Perforation of the rectum caused a pelvic abscess in 2 patients and generalized peritonitis in a third. A rectovaginal fistula was the presenting complaint in another patient.

Symptoms of small-bowel complications included alteration in bowel habit and colicky abdominal pains. Three patients developed intestinal obstruction from small-bowel strictures, and 'spontaneous' necrosis of the bowel occurred in 6 patients, 2 of whom presented with generalized peritonitis and 2 with a pelvic abscess. The necrotic bowel was adherent to the uterus and side wall of the pelvis in the remaining 2 cases and perforation had not occurred.

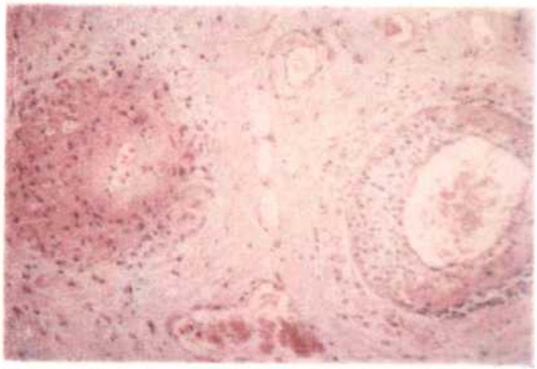

FIG. 2.—Photomicrograph showing the arterial sclerosis typical of radiation damage. (× 40.)

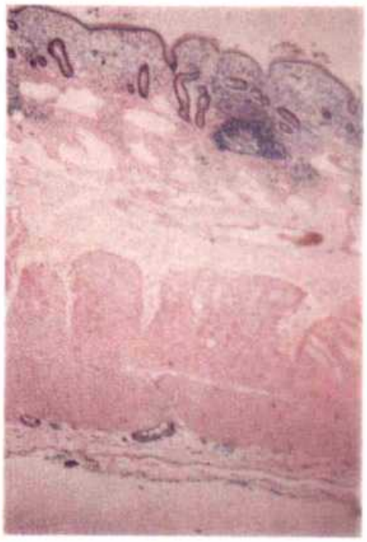

FIG. 3.—Photomicrograph showing submucosal lymphatic ectasia in the ileum of a patient with post-radiotherapy malabsorption. There is also loss of villi with simplification of the epithelium. (× 10.)

Small-bowel anastomoses failed to heal after surgical operations in 6 patients. In 5 of these patients there had been no symptoms to indicate that the intestine had been damaged by radiotherapy. One such postoperative patient developed an ileovaginal fistula and the others presented with peritonitis and faecal fistula. Further resection of bowel was undertaken in 4 cases, but the new anastomoses also became necrotic and the patients died.

Evidence of malabsorption of fat, vitamin B_{12}, and calcium was found (*Table VI*). The faecal fat (39 g. per 24 hours) exceeded the daily intake (30 g. per 24 hours) in 1 out of 6 patients with steatorrhoea, causing a 'fat-losing enteropathy'. The Schilling test indicated defective vitamin B_{12} absorption in 5 patients. One of the 2 patients with calcium deficiency presented with tetany 2 months after the resection of a small-bowel stricture.

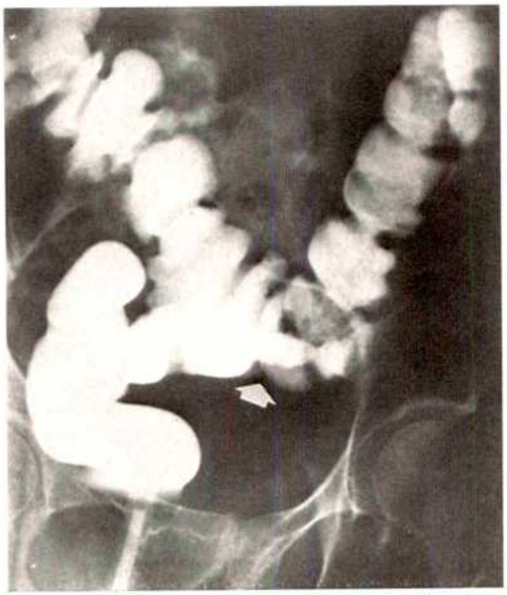

FIG. 4.—Barium-enema film showing the smooth and concentric outline of a post-irradiation stricture of the sigmoid colon (arrowed).

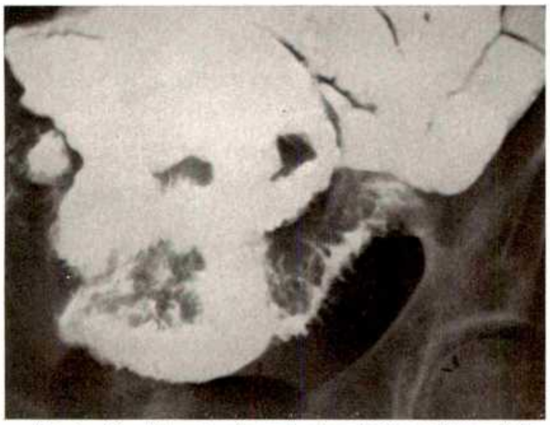

FIG. 6.—Small-bowel radiograph of a radiation stricture of the terminal ileum showing abnormal spiky appearance with narrowing and irregularity of the lumen.

The intestinal complications of radiotherapy caused the death of 14 patients (37 per cent), 9 of whom had no sign of recurrent tumour (*Table VII*). Spontaneous necrosis of the irradiated bowel or necrosis of an intestinal anastomosis accounts for 11 of the deaths. Only 3 patients (8 per cent) became completely asymptomatic after treatment of their bowel disease.

HISTOLOGY

The histological changes in the intestine after radiotherapy were first described by Warren and Friedman (1941). Such changes were found in all of the operative specimens obtained in the present series. Of particular interest was the increase in amount and density of the submucosal fibrous tissue (*Fig.* 1), well-developed arterial sclerosis (*Fig.* 2), and marked lymphatic ectasia which was present in 11 specimens (*Fig.* 3).

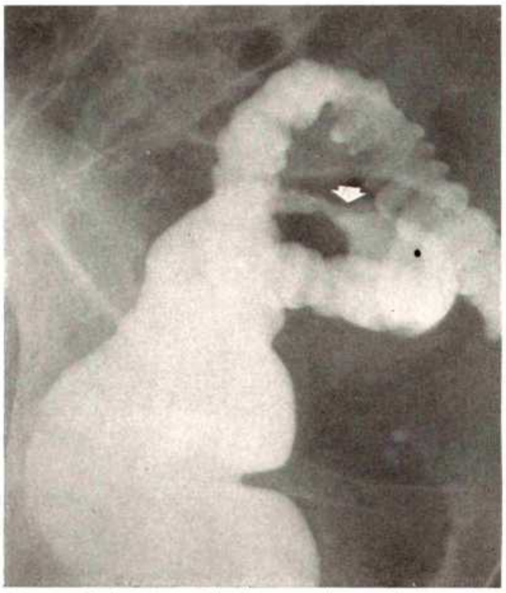

FIG. 5.—Barium-enema film demonstrating a radiation stricture of the colon (arrowed). There is irregularity and shouldering suggestive of malignancy.

Table VII.—CAUSE OF DEATH IN 14 PATIENTS WITH INTESTINAL COMPLICATIONS OF RADIOTHERAPY*

Complication	*No. of Patients*	*Cause of Death*
Necrosis of intestinal anastomosis or 'spontaneous' necrosis of intestine	11	Peritonitis 9 Postoperative intestinal obstruction 2
Rectovesical fistula	1	Uraemia
Stricture of ileum	1	Postoperative septicaemia
Proctocolitis and colorectal stricture	1	Postoperative bronchopneumonia

* Nine patients were free of tumour.

RADIOLOGY

Radiation strictures of the large bowel were generally smooth and concentric in outline (*Fig.* 4), but in 1 patient the stricture had the radiological features of malignancy (*Fig.* 5). A distinctive pattern was observed in the terminal ileum of 2 patients with small-bowel strictures (*Fig.* 6). The bowel lumen was narrowed with an irregular spiky outline, and folds of mucosa were drawn outside the contour of the bowel and angulated by adhesions. Nodular filling defects were also seen (*Fig.* 7). Striking mucosal changes were found in the small bowel. The normal feathery pattern was replaced by broad mucosal 'barring', and there was dilution of the barium in fluid-filled loops in 2 patients with steatorrhoea (*Fig.* 8). These changes are similar to those found in coeliac disease. Other patients were observed to have an extensive finer mucosal 'barring' throughout the majority of the small intestine (*Fig.* 9).

DISCUSSION

The latent period between the completion of radiotherapy and the development of symptoms of chronic intestinal damage varies from a few months to many years. More than one complication commonly occurs at the same time and further manifestations may develop later. Radiation damage should be regarded as a potentially progressive disease. The factors which may predispose to the development of intestinal complications have been suggested by several authors, including Bloedorn, Young, Cuccia, Mercado, and Wizenberg (1962), Graham and Villalba (1963), and DeCosse and others (1969). The dose of radiation is generally agreed to be an aetiological factor in some patients. In this series less than one-third of the patients had high doses of radiotherapy. Pelvic adhesions which may anchor a loop of bowel in the irradiated field have also been suggested as a factor. The equal incidence of pre-radiotherapy abdominal operations (or pelvic sepsis) in patients with small-bowel complications and in those sustaining damage to the already immobile rectum suggests that adhesions were not of aetiological importance in this series.

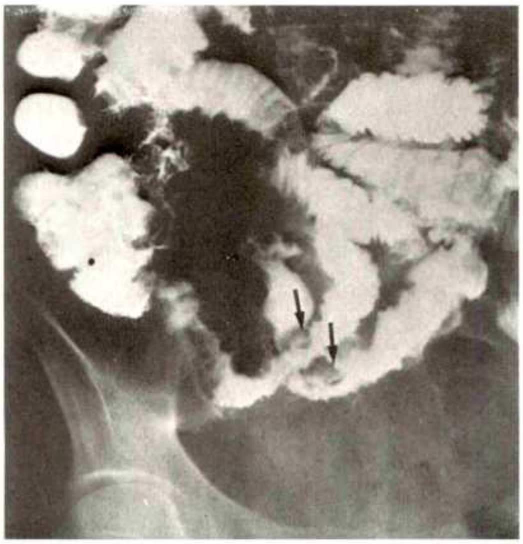

FIG. 7.—Small-bowel radiograph showing multiple nodular filling defects (arrowed) and narrowed lumen caused by radiotherapy.

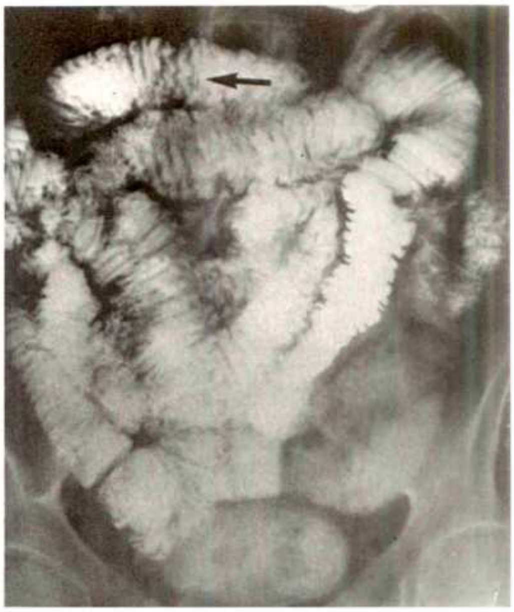

FIG. 8.—Small-bowel radiograph showing broad mucosal 'barring' (arrowed) and dilution of barium in fluid-filled loops.

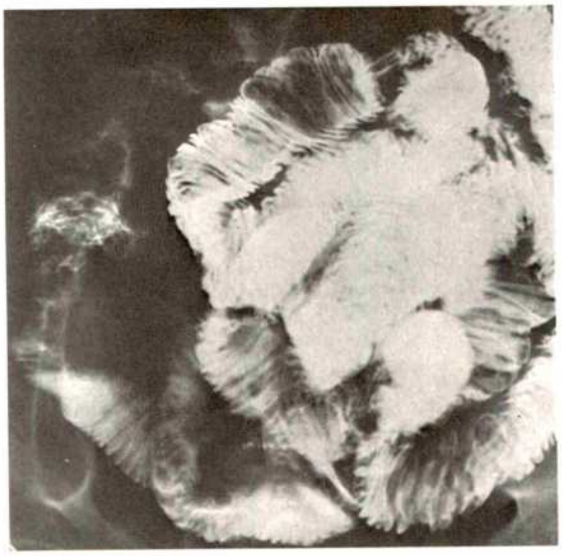

FIG. 9.—Small-bowel radiograph showing fine mucosal 'barring' in the small intestine. These changes were present throughout the majority of the small bowel.

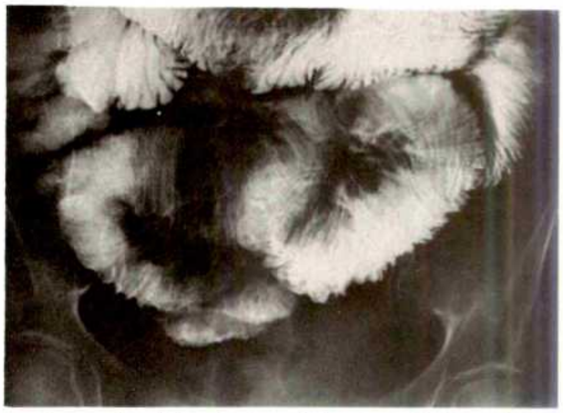

FIG. 10.—Small-bowel radiograph showing residual irregularity of outline and mucosal changes in a patient 2 months after the resection of an ileal stricture. At laparotomy the remaining intestine appeared macroscopically normal.

Calame and Wallach (1967) and DeCosse and others (1969) believed that the development of chronic intestinal complications is caused by vascular occlusion. Vascular sclerosis was prominent in the histology of specimens obtained in the present series and was associated with excessive deposition of dense fibrous tissue in the submucosa, producing an appearance similar to that seen in ischaemic colitis (*Fig.* 1). The late appearance of a rectovaginal fistula in 1 patient coinciding with the development of severe aorto-iliac atheroma also suggests that the precarious intestinal blood-supply caused by radiotherapy may become inadequate when in addition the general vascular state worsens.

Although there may be no clinical evidence of intestinal damage, sclerotic vessels in the intestinal wall may be unable to provide the increased blood-supply necessary for reparative processes, and post-radiotherapy intestinal anastomoses may fail to heal. All patients who have received pelvic or abdominal radiotherapy must be considered to be at risk if intestinal surgery is undertaken. The field irradiated in the treatment of pelvic cancer may extend as high as the lower border of the fourth lumbar vertebra, and long segments of bowel may therefore be inadvertently and unavoidably irradiated. The extent of the radiation damage may be much greater than is detectable macroscopically. This is illustrated by *Fig.* 10, which shows residual changes in the ileum after the apparently complete resection of a localized radiation stricture. Wide resection is therefore advisable and frozen-section examination of the bowel ends may be of value before anastomosis is performed (Higgins, Hamilton, and Hope-Stone, 1966). In the present series when primary healing of anastomosis did not occur further resection with restoration of intestinal continuity was uniformly unsuccessful and we feel that exteriorization of the bowel ends is a safer procedure in these circumstances. An unexpected finding was that severe malabsorption occurred in association with small-bowel lesions which were apparently localized. Possible aetiological factors include bile-salt malabsorption and the 'blind-loop' syndrome. Submucosal lymphatic ectasia was a prominent histological feature in this series and such lymphatic changes may be more extensive than is generally realized. It may be that the dilated submucosal intestinal lymphatics are secondary to radiation sclerosis obstructing the proximal lymph-vessels where they converge in the mesentery. This may explain the widespread alterations in mucosal pattern observed radiologically and the functional changes leading to malabsorption. The occurrence of a 'fat-losing enteropathy' following radiotherapy was reported by Tankel, Clark, and Lee (1965), and we confirm this in 1 patient in our series.

Radiological changes in the irradiated small bowel may mimic those seen in Crohn's disease, Whipple's disease, or coeliac disease and should not be confused with them. Multiple nodular filling defects resembling small-bowel metastases may also be seen (Mason, Dietrich, Friedland, and Hanks, 1970).

The diverse manifestations of the intestinal complications of radiotherapy may develop insidiously, are often progressive, and may be fatal. We advocate a combined surgical/radiotherapy clinic where close follow-up and investigation of patients at risk can be performed. Prompt radiological investigation of the large and small bowels should be performed if symptoms suggestive of radiation damage are elicited, and tests for malabsorption should be performed.

Acknowledgements.—We would like to thank Mr. H. E. Lockhart-Mummery and Dr. Thelma Bates for their helpful advice and the consultant staff of St. Thomas's Hospital, London, for permission to record the details of patients under their care.

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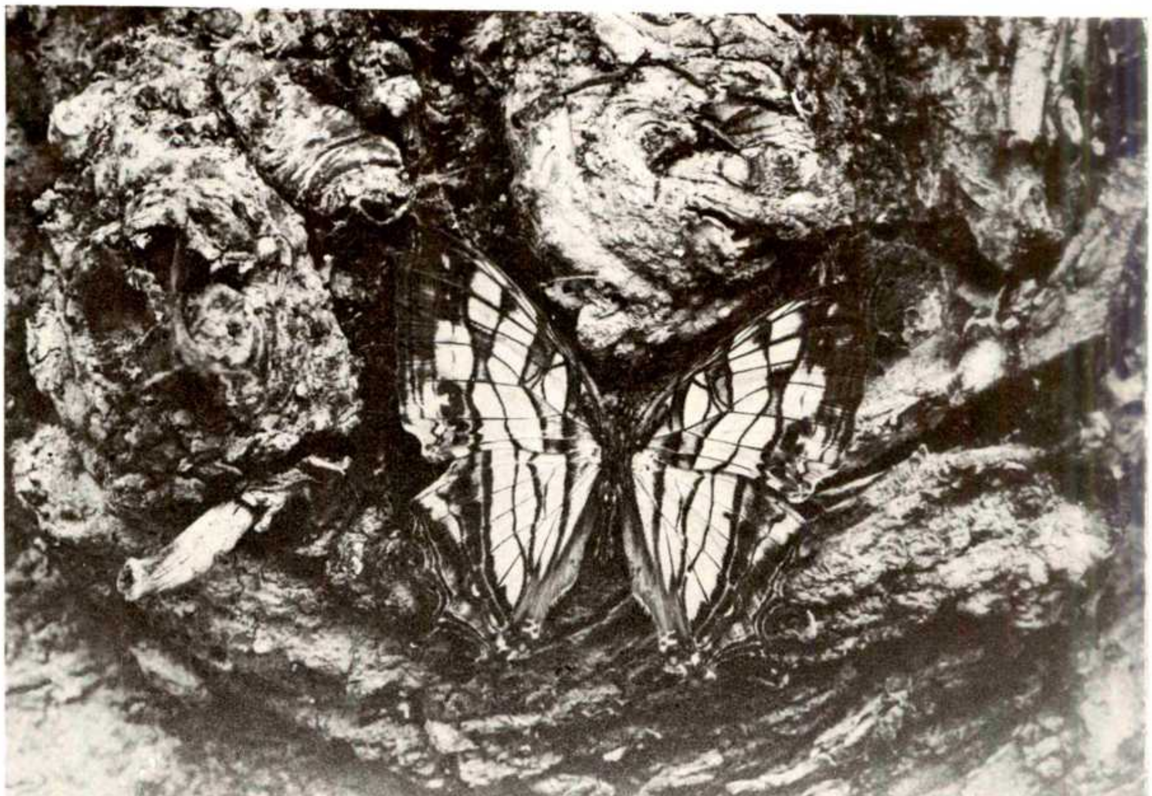

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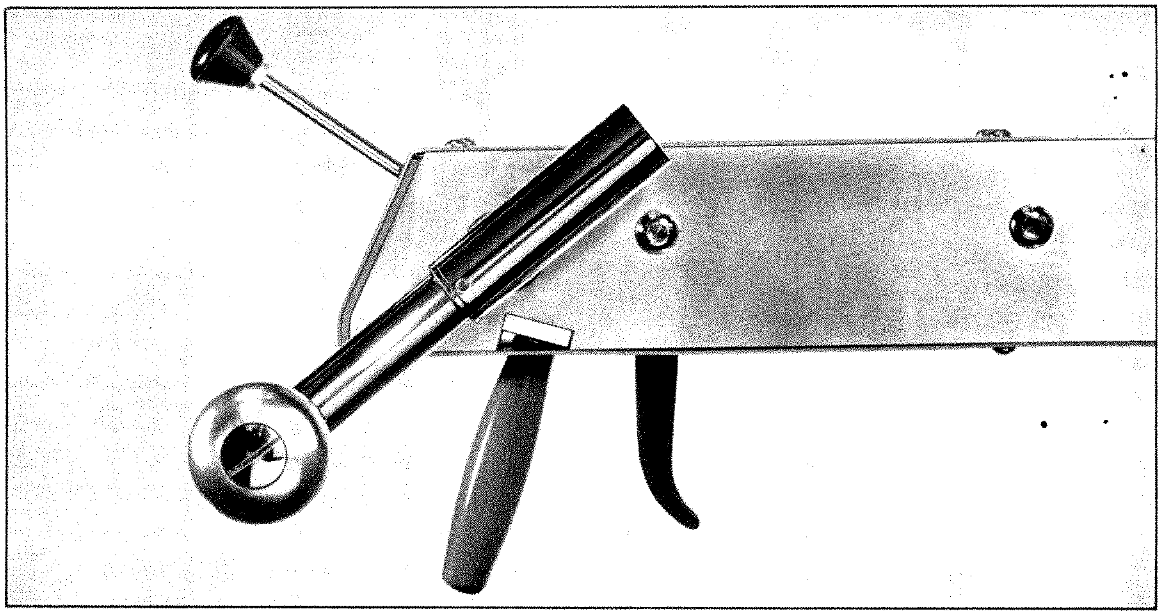

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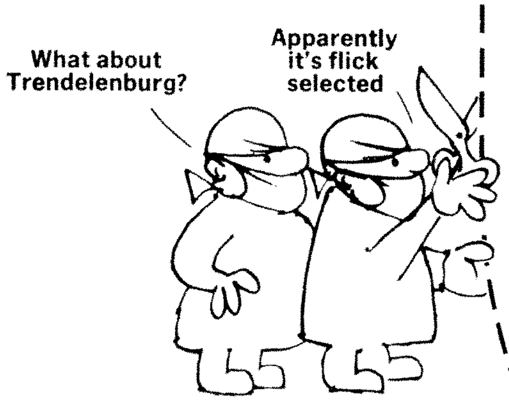

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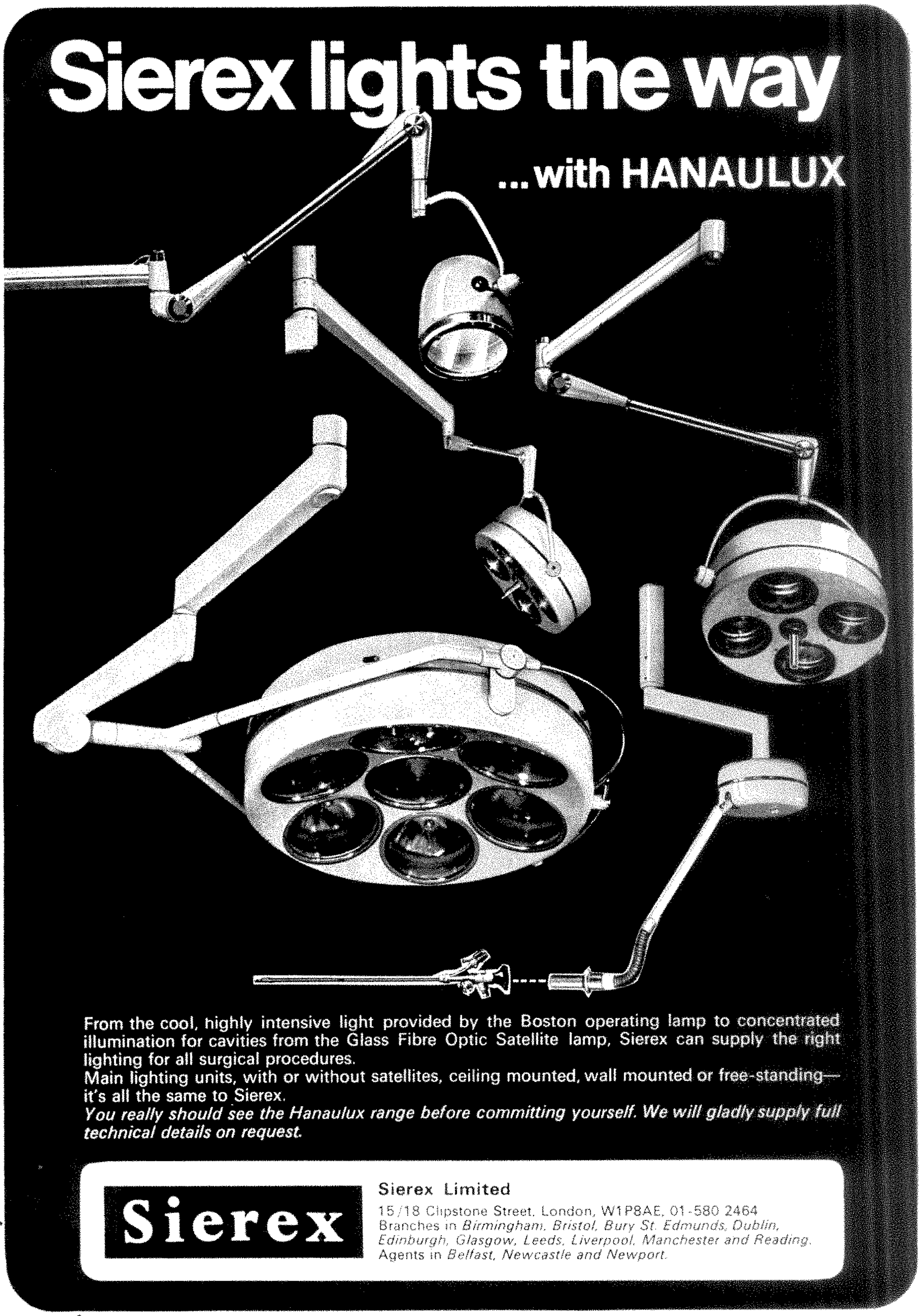

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THE AETIOLOGY OF HYPERTENSION AFTER RENAL TRANSPLANTATION IN MAN

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SUMMARY

The renin-angiotensin-aldosterone system was studied in renal allograft patients, 70 per cent of whom were hypertensive.

Plasma-renin levels were found to be normal, and a normal increase was observed when patients were changed from the supine to the erect posture ($P < 0.01$). However, aldosterone-secretion rates were found to be approximately four times normal, and a positive correlation between these values and diastolic blood-pressure was observed ($r = 0.5$, $P = 0.05$). In patients with intact kidneys a highly significant correlation between plasma-renin activity and aldosterone-secretion rate was observed ($r = 0.8$, $P < 0.05$), but this normal correlation was not apparent in the patients with transplanted kidneys ($r = 0.1$, $P > 0.5$). Thus the aldosterone-secretion rates in these patients was not under the control of the renin-angiotensin system.

Concurrent studies in adrenalectomized patients showed that they also had elevated aldosterone-secretion rates, and the injection of ^{14}C-labelled cortisone acetate showed that they were capable of converting this steroid into aldosterone or an aldosterone-like metabolite. It is suggested that the hypertension seen after renal transplantation is related to the conversion of prednisone to a mineralocorticoid.

Further support for this hypothesis was obtained from studies in patients who had their therapy changed from daily prednisone to alternate-day methylprednisolone. They were found to secrete less aldosterone and all the patients became normotensive following this régime ($P < 0.01$). In addition, patients treated with an aldosterone antagonist, spironolactone, showed a prompt decrease in blood-pressure.

It is concluded that the denervated transplanted kidney is able to maintain normal blood-pressure homeostasis in man, and that hypertension seen after renal allografting is largely due to the therapy with immunosuppressive steroids.

RENAL transplantation has gained widespread acceptance in the treatment of terminal renal failure and to date nearly 10,000 of these operations have been carried out. One of the less desirable sequelae of these procedures has been the development of hypertension in a high proportion of allograft recipients (Starzl, Porter, Andres, and others, 1970). This increase in blood-pressure has been variously ascribed to the presence of the recipient's own diseased kidneys (Papadimitriou, Chisholm, and Shackman, 1969), stenosis at the arterial anastomosis of the transplant (Smellie, Vinik, and Hume, 1969), acute rejection (Pasternack, Kuhlback, Koivunen, Lindstrom, and Tiilikainen, 1970; Flanigan, Caldwell, Williams, Brewer, Glenn, Headstream, and Campbell, 1971), and chronic rejection (Starzl and others, 1970). While these factors undoubtedly play a role in the development of hypertension they do not account for the blood-pressure changes observed in the majority of patients.

We have previously shown that renal allograft recipients tend to have higher aldosterone-secretion rates than normal (Sampson, Kirdani, Sandberg, and Murphy, 1972), and that this occurs in spite of normal plasma-renin activity. In addition, we have shown that changes in the steroid therapy of these patients can profoundly influence the course of hypertension after a renal allografting procedure (Sampson and Albert, 1973). The preliminary studies suggested the possibility that orally ingested steroids can be converted in man to aldosterone or an aldosterone-like metabolite and that this hitherto undescribed phenomenon may account for the subsequent development of hypertension in renal transplant recipients.

The present report describes further studies on the renin-angiotensin-aldosterone system of both renal allografted and adrenalectomized patients which support the hypothesis that post-transplant hypertension is steroid dependent.

MATERIAL AND METHODS

Two groups of patients were studied, comprising 20 renal allograft recipients and 7 adrenalectomized subjects. Normal volunteers were used as controls, and some patients with renal disease were also included in the study. The patients with transplants were studied between 6 months and 2½ years after transplantation. These patients were studied while taking prednisone 10 mg. twice daily, and also after conversion to a régime of methylprednisolone, 32 mg. on alternate days. The patients also received azathioprine, 2 mg. per kg. per day, as additional immunosuppression. Serial blood-pressure determinations were carried out over a 6-month observation period. The patients were seen mainly in the out-patient clinic but were admitted to hospital for determination of 24-hour aldosterone-secretion rates and plasma-renin activity. Plasma-renin activity was estimated in both the supine and erect positions. For estimation during the supine position blood was collected at 8.00 a.m. after the patient had been in bed all night.

The patients then walked around the hospital for 4 hours and blood was again collected for determination of renin activity. The corresponding 24-hour aldosterone-secretion rates were determined after the patients had received 10 μc. 1,2-^{3}H-aldosterone intravenously. The 24-hour urine specimen following the injection was collected and assayed for tetrahydroaldosterone by a modification of the method of Nicolis, Wotiz, and Gabrilove (1968) using the gas chromatograph which we have described previously (Sampson and others, 1972).

Plasma-renin activity was determined by two methods. At the commencement of the study the rat bioassay was used (Gunnells, Grim, Robinson, and Wildenmann, 1967). During the course of the study a commercially manufactured radio-immunoassay kit became available (Schwatz-Mann Inc., New York) and this was subsequently used instead of the slower bioassay.

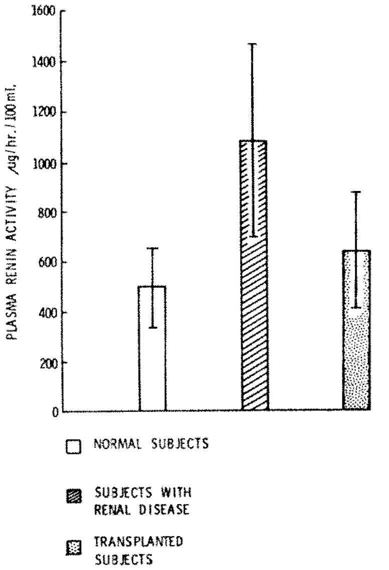

FIG. 1.—Plasma-resin activity in a group of renal allograft patients did not differ significantly from normal, while patients with renal disease had elevated levels. In this study a rat bioassay was used for the estimation of plasma-resin activity. (Values given as the mean ± S.E.M.)

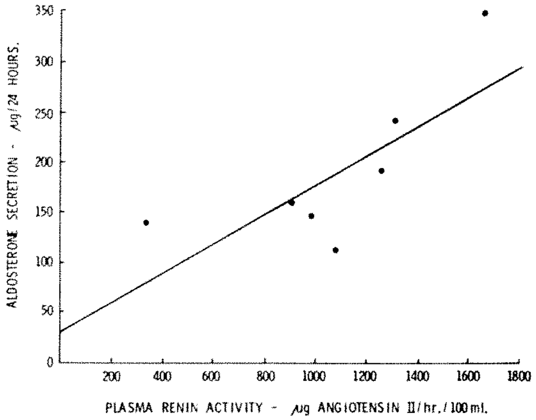

FIG. 3.—In a small sample of subjects with intact kidneys, some of whom had renal disease, a statistically significant positive correlation was observed between plasma-renin activity and aldosterone-secretion rate: $y = 0{\cdot}15x + 29$, $n = 7$, $r = 0{\cdot}8$, $P < 0{\cdot}05$. Patients with renal disease were included with normal subjects in order to obtain a wide range of values. The rat bioassay was used for the plasma-renin estimation.

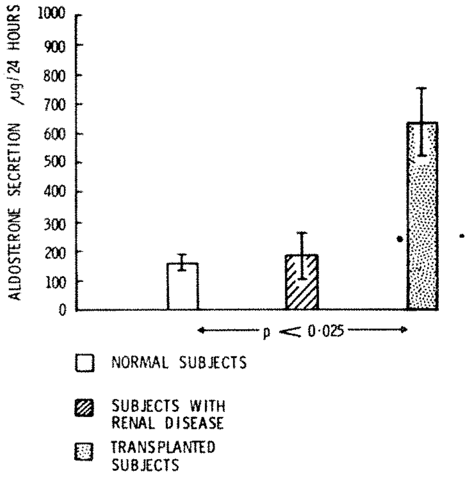

FIG. 2.—Aldosterone-secretion rates were significantly elevated in a group of renal allograft recipients. Patients with renal disease had normal aldosterone-secretion rates. (Values given as the mean ± S.E.M.)

The transplant patients were allowed a free diet with no sodium restriction, and diuretic and antihypertensive drugs were not given during the period of the renin or aldosterone assays. However, some hypertensive patients were treated with spironolactone, 25 mg. four times daily, once their baseline data had been established. All the transplant recipients had stable renal function and none had rejection episodes during the observation period.

The adrenalectomized patients were randomly selected from a population who had undergone this procedure for advanced prostatic carcinoma. These patients required maintenance therapy of cortisone acetate, 50 mg. by mouth daily. One of the patients studied in this group required additional medication with deoxycorticosterone acetate, 200 mg. per day, in order to prevent a life-threatening salt-losing state. The adrenalectomized subjects had their aldosterone-secretion rates determined in the same way as that for the transplant recipients, but in addition some of them were given 2 μc. ^{14}C-cortisone acetate intravenously, and the urine was then examined for tetrahydroaldosterone by comparing the peak activity obtained in the urine by chromatography with that produced by two known tetrahydroaldosterone standards. The urines of 6 of these patients were pooled for the specific identification of the aldosterone metabolite.

RESULTS

The plasma-renin activity for normal individuals, for patients with advanced renal disease, and for patients bearing renal allografts is illustrated in *Fig.* 1. Patients with renal disease had significantly higher renin activity than normal subjects ($P < 0{\cdot}05$), but the transplant recipients did not differ significantly from normal ($P > 0{\cdot}5$).

In contrast, *Fig.* 2 shows the aldosterone-secretion rates for the transplant patients to be significantly higher than normal ($P < 0{\cdot}05$) by a factor of about 4.

A comparison between plasma-renin activity and 24-hour aldosterone-secretion rates for normal individuals and those with diseased kidneys is shown in *Fig.* 3. The heterogeneous sample of patients was necessary in order to obtain a wide range of renin values with which to compare the corresponding aldosterone values. In the small number of patients examined a highly significant correlation between plasma-renin activity and aldosterone secretion was obtained ($r=0{\cdot}8$, $P<0{\cdot}05$).

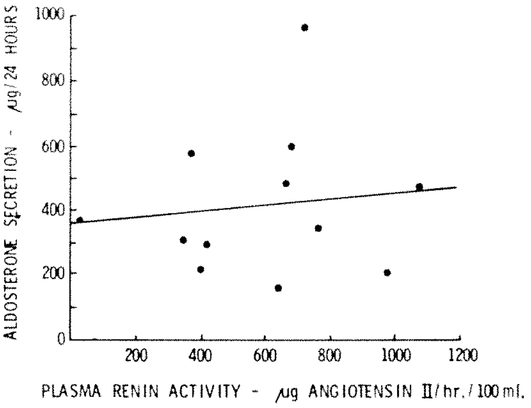

FIG. 4.—In a group of renal allograft patients maintained on an immunosuppressive steroid régime a slight but statistically insignificant positive correlation was observed between plasma-renin activity and aldosterone-secretion rate: $y=0{\cdot}1x+356, n=11, r=0{\cdot}1, P>0{\cdot}5$. This is in sharp contrast to the highly significant correlation shown in *Fig.* 3 for patients with intact kidneys.

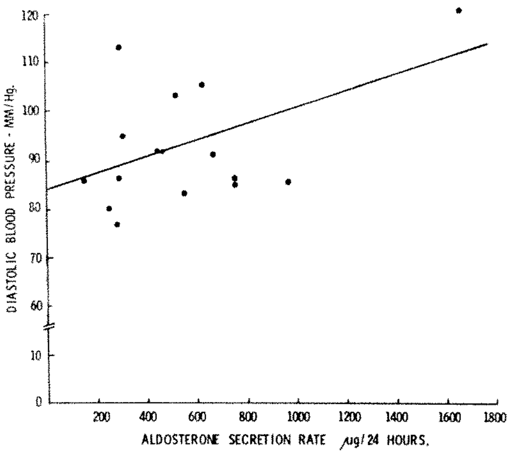

FIG. 6.—A significant correlation between diastolic blood-pressure and aldosterone-secretion rate was observed in a group of renal allograft patients: $y=0{\cdot}016x+84, n=15, r=0{\cdot}5, P<0{\cdot}05$.

A similar correlation carried out in the transplant patients, depicted in *Fig.* 4, shows there to be no significant relationship between the two variables ($r=0{\cdot}1$, $P>0{\cdot}5$). This reflects the fact that these patients secrete relatively large quantities of aldosterone in the presence of normal renin levels.

The response in terms of plasma-renin activity to changes of posture in the transplant patients is shown in *Fig.* 5. All the patients bearing a renal allograft were able to increase their plasma-renin levels following adoption of the erect posture. Using the paired *t*-test a highly significant difference between the supine and erect values was observed ($P<0{\cdot}01$). These results were obtained using the radio-immunoassay and, like the rat bioassay, indicate normal levels in the patients with transplants (normal value, $1{\cdot}25 \pm 0{\cdot}25$ ng. per hour per ml.).

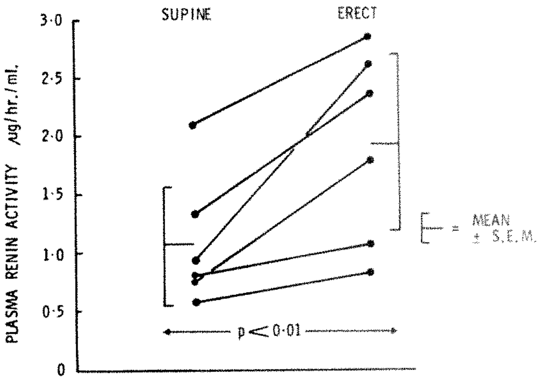

FIG. 5.—A highly significant rise in plasma-renin activity was observed when renal allograft patients adopted the erect position for 4 hours after having been supine for 8 hours. This is a normal response and the values are within the normal range. A radio-immunoassay was used for the plasma-resin estimations in this study.

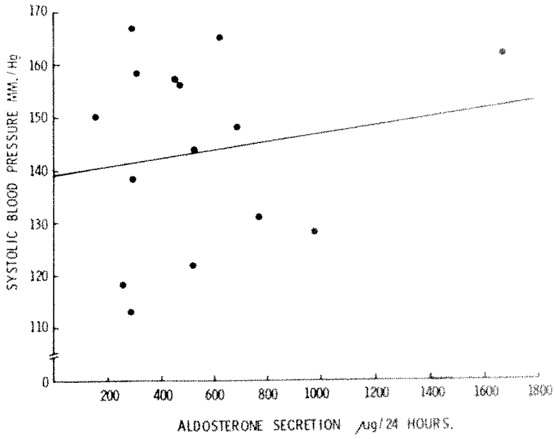

FIG. 7.—A slight positive correlation between systolic blood-pressure and aldosterone-secretion rate was seen in a group of renal allograft patients but this was not statistically significant: $y=0{\cdot}008x+139, n=15, r=0{\cdot}18, P>0{\cdot}5$.

The relationship between aldosterone-secretion rate and systolic and diastolic blood-pressure for patients bearing a renal allograft is shown in *Figs.* 6 and 7. While a slight positive correlation was seen for systolic blood-pressure and aldosterone-secretion rate this was not statistically significant ($r=0{\cdot}18$, $P>0{\cdot}5$). On the other hand, a more clearly defined positive correlation was seen for diastolic blood-pressure and aldosterone secretion which was statistically significant ($r = 0{\cdot}5$, $P = 0{\cdot}05$).

Figs. 8 and 9 illustrate the changes of systolic and diastolic blood-pressure which occurred when the transplant patients were switched from continuous therapy with prednisone to alternate day therapy with methylprednisolone. Each point shows the mean of serial observations taken over a 3-month period. Using the paired t-test a highly significant fall in systolic blood-pressure was seen following the change of therapy ($P < 0{\cdot}01$), and a fall in diastolic pressure was seen which was also statistically significant ($P < 0{\cdot}01$).

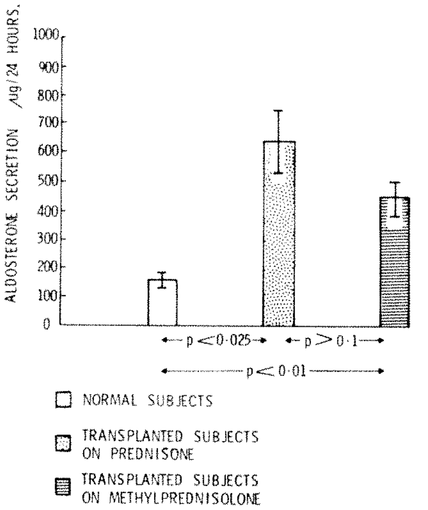

FIG. 8.—Effect of a change in steroid régime on aldosterone-secretion rate in transplant patients. The change from daily therapy with prednisone to alternate-day therapy with methylprednisolone resulted in a decreased aldosterone-secretion rate, but this was not statistically significant and the transplant patients continued to have significantly elevated secretion rates when compared with normal subjects. (Values given as the mean ± S.E.M.)

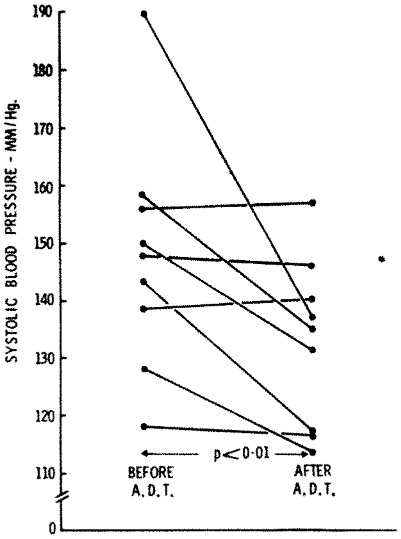

FIG. 9.—A highly significant fall in systolic blood-pressure occurred in transplant patients when the steroid maintenance therapy was changed from daily prednisone to alternate-day methylprednisolone. Each point represents the mean of serial observations taken over a 3-month observation period. P was derived from a paired t-test.

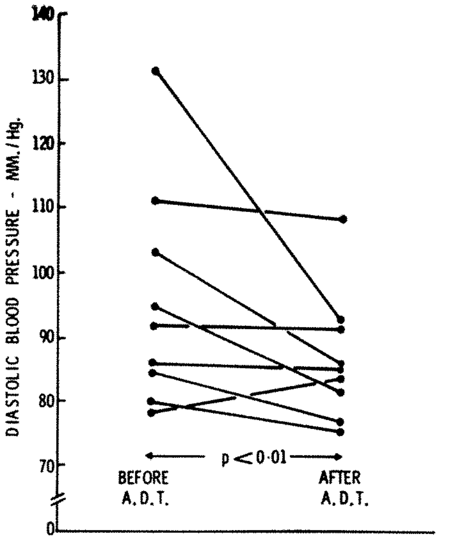

FIG. 10.—As for systolic blood-pressure, a highly significant drop in diastolic blood-pressure occurred when the steroid therapy in transplant patients was changed. The data were derived in the same way as for *Fig.* 9.

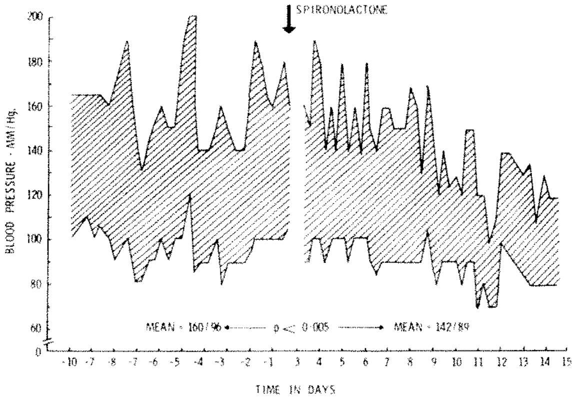

FIG. 11.—Serial blood-pressure determinations in a renal allograft patient before and after treatment with an aldosterone antagonist, spironolactone. A highly significant fall in both diastolic and systolic blood-pressure occurred following the treatment.

The effect of the change in steroid therapy on aldosterone-secretion rates in the transplant patients is shown in *Fig.* 10. While a drop in aldosterone secretion was seen after the change of therapy this was not statistically significant, and secretion remained significantly higher than normal.

An aldosterone-secretion rate determination carried out on an adrenalectomized patient as a check of the blank value surprisingly gave an excretion of 850 µg. per day (normal value, 160 ± 26 µg. per day). The urine of 6 further adrenalectomized patients, previously injected with 2 µc. of ^{14}C-cortisone acetate, showed a peak activity on paper chromatography which corresponded to a tetrahydroaldosterone standard. Further proof of aldosterone production by adrenalectomized patients was obtained by finding a peak corresponding to a tetrahydroaldosterone-γ-lactone standard, and following acetylation of both the standard and the patients' urine the two peaks continued to run together in a counter-current distribution system. Statistical analysis of the peaks of the standard and of the patients' urine showed them to be identical.

The adrenalectomized patient who required deoxycorticosterone acetate to prevent salt depletion was found to have no aldosterone secretion at all.

The renal transplant patients who were hypertensive postoperatively and were treated with spironolactone while on continuous prednisone therapy showed a fall in blood-pressure as a result of the use of the aldosterone antagonist. The blood-pressure record of such a patient is illustrated in *Fig.* 11. However, in a severely hypertensive 8-year-old transplant recipient no decrease in blood-pressure occurred following treatment with spironolactone. He was subsequently shown to have a stenosis of his transplant renal artery, and following surgical correction his blood-pressure returned to normal.

DISCUSSION

The finding of normal renin levels after renal transplantation is in agreement with the observations of others (Blaufox, Birbari, Hickler, and Merrill, 1966; Nielsen, Clausen, and Jensen, 1970). We found this to be the case both by the rat bioassay and the radio-immunoassay. Similarly, the normal increase in plasma-renin activity following the change of posture from the supine to the erect position which was observed after renal transplantation confirms the work of Greene, Vander, and Kowalczyk (1968), who also found that transplant recipients could increase their renin levels in response to sodium depletion. Thus, although it has been shown that an intact nerve-supply is necessary for normal renin responses in the dog (Mogil, Itsovitz, Russell, and Murphy, 1970), it seems that the completely denervated renal allograft in man maintains its normal renin responses. On this evidence, therefore, the renin-angiotensin system cannot be implicated in the development of hypertension after renal transplantation.

In contrast, aldosterone-secretion rates were greatly elevated in renal transplant recipients, and this was related to some extent to the degree of hypertension. Evidence has been obtained which suggests that a renal hormone exists which stimulates the adrenal gland to secrete aldosterone (Davis, Carpenter, Ayers, Holman, and Bahn, 1961; Ganong and Mulrow, 1961), and it has been subsequently demonstrated that this is almost certainly angiotensin II (Peart, 1970). Laragh, Sealey, and Sommers (1966) have shown a close correlation between plasma-renin activity and aldosterone-secretion rate in both normal and hypertensive subjects, and our studies in volunteers and patients with renal disease have shown the expected correlation. However, such a correlation could not be observed in the transplant patients, the implication again being that in these individuals the aldosterone-secretion rate had escaped from the normal renal control mechanisms.

Surprisingly a chromatographic peak corresponding to tetrahydroaldosterone was observed in adrenalectomized patients, and subsequent injection of labelled cortisone acetate resulted in the label being detected in the peak corresponding to tetrahydroaldosterone. To date there is no known pathway for the conversion of cortisone to aldosterone, and it could be that an aldosterone-like metabolite is being detected. However, the data strongly suggest that such a conversion is possible. The secretion rates that we have observed agree well with the normal values of others, and the close correlation with the plasma-renin activity in subjects with intact kidneys suggests that the assay is reliable.

The role of maintenance steroids in controlling the apparent aldosterone-secretion rate was further suggested by the finding of a decrease when continuous prednisone therapy was changed to alternate-day therapy with methylprednisolone. Although the subsequent decrease in aldosterone-secretion rate was not significant statistically, this may have been due to the small number of patients studied. Concurrent with the observed fall in aldosterone-secretion rate, a highly significant fall in both systolic and diastolic blood-pressure occurred following the change of steroid therapy. It was of interest in this respect that the patient who required deoxycorticosterone acetate supplements in addition to cortisone acetate following adrenalectomy had no detectable aldosterone in the urine. It is possible that such patients are unable to convert orally administered cortisone to a mineralocorticoid.

Of course, further proof of the role of steroid in the genesis of hypertension after transplantation could be obtained by withholding such drugs, but such a study is not possible at present. However, a transplant recipient who received no steroids has been reported (Rosenfeld, Levi, de Vries, and Levy, 1971), and this patient remained completely normotensive for a 5-year postoperative observation period.

One of the features of hypertension secondary to mineralocorticoid excess is a prompt response to the use of aldosterone antagonists such as spironolactone, (Spark and Melby, 1971). The hypertensive transplant recipient depicted in *Fig.* 11 showed just such a good response to treatment with spironolactone, which was further evidence that the hypertension in her case was related to excessive mineralocorticoid production. No such response was seen in the patient whose hypertension was the result of stenosis of the renal transplant artery.

It is common to treat renal allograft patients with high doses of steroids in the early postoperative period, and hypertension has been observed to be a very frequent postoperative complication, especially in children (Gonzalez, Martin, West, Spitzer, and McEnery, 1970; Fine, Edelbrock, Brennan, Grushkin, Korsch, Riddell, Stiles, and Lieberman, 1971; Najarian, Simmons, Tallent, Kjellstrand, Buselmeier, Vernier, and Michael, 1971). Thus, steroid therapy is strongly implicated in the aetiology of the hypertension, as all these authors agree that this complication becomes less of a problem as the steroid dosage is reduced.

In conclusion, it is suggested that the main cause of hypertension after renal transplantation in man is use of steroids for immunosuppressive therapy. This contention is based on the following observations:—

1. In the renal allograft patient bearing a denervated kidney the renin system is normal.

2. Aldosterone-secretion rates are elevated in renal transplant recipients.
3. In transplant patients there is a positive correlation between blood-pressure and aldosterone-secretion rate.
4. Adrenalectomized patients receiving maintenance steroid therapy have been shown to have aldosterone or an aldosterone-like substance in the urine, and labelling studies suggest that this is derived from administered cortisone.
5. A change of steroid therapy in transplant patients which tends to reduce the apparent aldosterone-secretion rate is accompanied by a significant fall in blood-pressure.
6. Treatment of hypertensive transplant patients with an aldosterone antagonist, spironolactone, can result in a significant fall in blood-pressure.

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THE ROLE OF CELLULAR IMMUNITY IN CONTROL OF NEOPLASIA

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SUMMARY

Using assessment of the delayed hypersensitivity response to a new antigen—in this study 2-4-dinitrochlorobenzene—as a measure of cellular immunity in patients with rectal cancer has shown highly significant correlation with pathological staging. No relationship between cellular immunity and rate of proliferation of rectal tumours could be established. The significance of these results is discussed.

Despite a more aggressive technical approach the results of surgery for carcinoma of the rectum have not improved over the past 30 years (Registrar General, 1969). Further increase in survival rates will depend on the exploitation of any factors which will assist in the eradication of malignant cells; therefore a fundamental question in cancer research is to determine the extent to which patients possess the ability to delay or to control the progress of malignant disease.

Immune mechanisms have often been implicated as possible factors in the restriction of neoplastic proliferation (Himmelweit and Ehrlich, 1957), and there is an impressive accumulation of evidence to support the concept of immunological surveillance in neoplasia (Burnet, 1970). For example, it has been found that in patients with reduced immunological competence, either congenital or iatrogenic, there is an increased incidence of neoplasia (Dent, Peterson, and Good, 1968; Penn, 1970), and assessment of cellular immunity in patients with malignant disease using their cutaneous delayed hypersensitivity responses to various antigens has shown a decreased ability to respond as the disease progresses (Hughes and Mackay, 1965; Solowey and Rapaport, 1965). Furthermore, inability to produce delayed hypersensitivity to new antigens after initial sensitization has been found to correlate with early recurrence of malignant growth after surgery (Eilber and Morton, 1970). Other evidence supporting immunological control of malignant proliferation is that cancer is more likely to be initiated at the extremes of life

(Registrar General, 1969) when the effectiveness of the immune system is low as assessed by *in vivo* and *in vitro* tests (Sample, Gertner, and Chretien, 1971). Further confirmation is that there is a significant correlation between the relative intensity of lymphocyte infiltration in a tumour and length of survival of the patient (Black, Opler, and Speer, 1954; Lauder and Aherne, 1972).

Thus, there is powerful support for cellular immune control of neoplastic spread but little is known about the actual mechanisms involved. We know that a cancer may increase in mass either by an increased rate of proliferation or by a decreased rate of cell loss as compared with the tissue from which it arises, so that either restriction of proliferation or encouragement of cell loss could play a role.

A study was planned to investigate cellular immunity in patients suffering from rectal carcinoma by assessing their cutaneous delayed hypersensitivity responses to 2-4-dinitrochlorobenzene (DNCB) after initial sensitization with this chemical. In addition, the rate of proliferation of the rectal carcinomas and the mucosa from which they arise was measured using a stathmokinetic technique (Refsum and Berdal, 1968). In this way any evidence of restriction of proliferation of malignant cells by cellular immune mechanisms could be discovered.

MATERIAL AND METHODS

Patients.—Forty patients (age range, 36–81 years, mean age, 62 years), 23 males and 17 females, suffering from adenocarcinoma of the rectum were selected from the general surgical wards of one hospital. All the patients had biopsies confirming their malignant disease and all were submitted to operation. Patients who had received radiotherapy, chemotherapeutic drugs, or corticosteroids were excluded from the study. From this group of patients 21 had an estimation of the proliferative rates of their tumours performed. The rate of proliferation of the normal mucosa from which the tumour arose was studied in 11 cases.

Control Patients.—Twenty patients from the same hospital population were used as controls (age range, 44–80 years, mean age, 64 years); there were 9 males and 11 females. All were admitted for large-bowel investigations; 7 patients had no obvious pathology and 13 were found to have diverticulosis.

Clinical and Pathological Staging.—The clinical assessment of the extent of the disease was noted for each patient at laparotomy; particular care was taken to record any evidence of liver metastases.

A pathological grading was obtained for patients whose neoplasms were resected.

The classification of Dukes was used and a further category, D, was added to denote signs of widespread metastases.

Classification.—

A, Rectal cancer limited to the wall of the rectum.
B, Extrarectal spread but no lymphatic metastases.
C, Lymphatic metastases.
D, Distant metastases.

DNCB Sensitization and Testing.—The technique employed was adapted from that of Ratner, Waldorf, and Scott, 1968). The patients were sensitized by the application of 4000 μg. of DNCB dissolved in acetone and applied to a 3-cm.^{2} area of skin on the volar aspect of a forearm. An occlusive polythene dressing was put over the site and left in position for 4 days.

Sensitivity tests were carried out by applying four A1 patch test squares (Imeco, A.B., Stockholm), each impregnated with a different strength of DNCB in acetone (200, 100, 40, and 2 μg.). These squares were applied to the opposite forearm *at least* 14 days after sensitization. The test was read at 48 hours. A positive response showed erythema and induration under the patch test square.

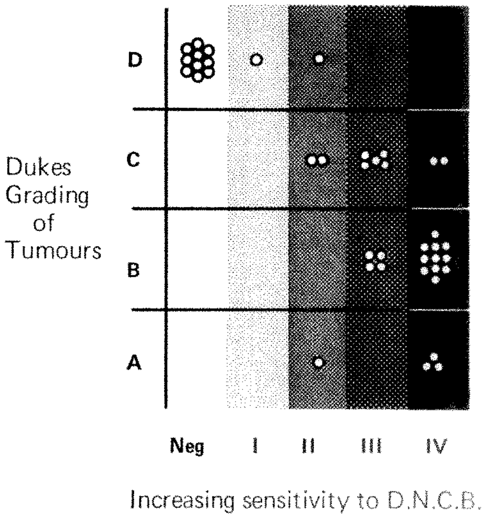

FIG. 1.—Relationship of tumour grading to DNCB sensitivity.

Table I.—CUTANEOUS DELAYED HYPERSENSITIVITY RESPONSES TO DNCB IN CANCER AND CONTROL PATIENTS

PATIENTS	RESPONSE TO DNCB					TOTAL
	Negative	Grade I	Grade II	Grade III	Grade IV	
Cancer	10	1	4	9	16	40
Control	1	0	4	11	4	20

Patients were then graded according to their sensitivity: negative; grade I (sensitive to 200 μg. only); grade II (sensitive to 100 μg.); grade III (sensitive to 40 μg.), and grade IV (sensitive to 2 μg.).

Findings.—*Table I* shows the gradings of the cancer and control groups. Twenty-five per cent of the cancer patients had a negative response, i.e., evidence of poor cellular immunity, compared with only 5 per cent of the control patients. Nevertheless 40 per cent of the cancer patients had a grade IV reaction, i.e., evidence of good cellular immunity.

Fig. 1 shows the relationship of the patients' cellular immunity as assessed by their response to DNCB to the pathological grading of their tumours. There is an obvious relationship between good cellular immunity and favourable grading. This also corresponds with prognosis, for within 6 months of operation all the anergic patients were dead whereas only 2 of the patients with good responses were dead, both dying from cardiac conditions.

Table II shows a comparison of the patients without metastases (tumour grades A and B) and those with metastases (tumour grades C and D) with their respective responses to DNCB. Sensitivity grades I and II have been grouped together for statistical analysis.

The results show that there is a homogeneity between the groups ($\chi^2 = 20{\cdot}86$, d.f. $= 3$, $P < 0{\cdot}001$) and that there is a linear trend ($\chi^2 = 20{\cdot}29$, d.f. $= 1$, $P < 0{\cdot}001$) with no significant deviation from this trend ($\chi^2 = 0{\cdot}57$, d.f. $= 2$, $P > 0{\cdot}3$). In other words there is a highly significant relationship between cellular immune competence and the degree of progression of the malignant disease.

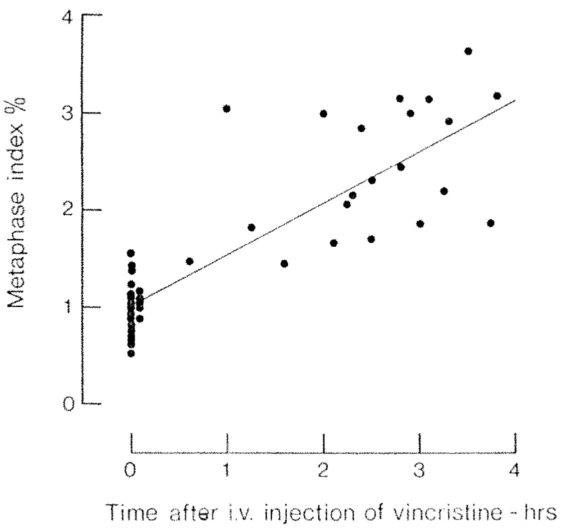

FIG. 2.—Metaphase index compared with time after the injection of vincristine. The regression line was obtained by the least-squares regression method.

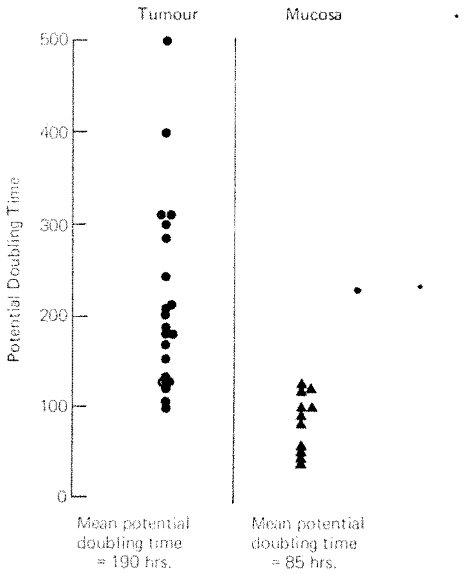

FIG. 3.—Proliferation rates of rectal tumour and mucosa.

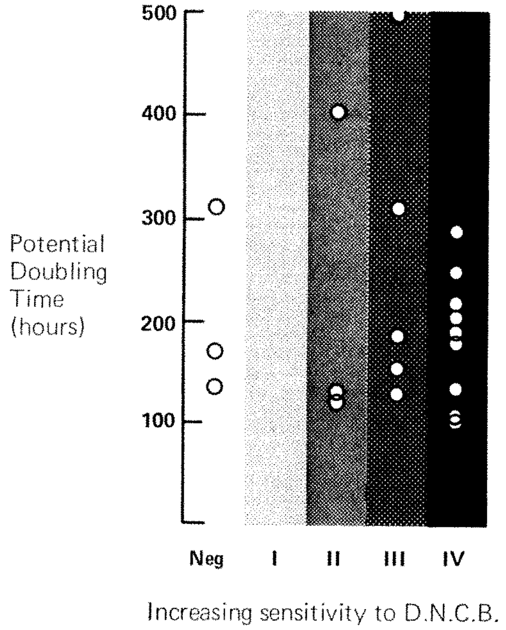

FIG. 4.—Relationship of tumour proliferation to DNCB sensitivity.

Table II.—CORRELATION OF TUMOUR GRADING WITH SENSITIVITY TO DNCB

GRADING OF TUMOURS	SENSITIVITY TO DNCB				TOTAL
	Negative	Grades I + II	Grade III	Grade IV	
A + B	0	1	4	14	19
C + D	10	4	5	2	21

Estimation of Cell Birth-rate.—This was estimated by using a stathmokinetic agent (vincristine sulphate) which blocks proliferating cells in mitosis.

First, a biopsy was taken from the tissue (either tumour or mucosa) to be studied. Further biopsies were taken at known time intervals after the intravenous injection of a single dose of vincristine sulphate (Lilly), 0·045 mg. per kg. Histological slides were prepared in the usual manner from the biopsy specimens and stained with haematoxylin and eosin. Using an eyepiece graticule 6000 tumour cells were counted and the number of metaphases and other stages of mitosis were noted. For the mucosal specimens whole crypt counting was employed and the total number of cells (usually 6000–8000) and mitoses in 100 crypts per biopsy were counted. The metaphase index, which is the number of metaphases per 100 cells, was calculated for each specimen. The increase in the index following vincristine was plotted against time and the rate of entry into mitosis per hour was obtained.

Although all stages of mitosis (i.e., prophase, metaphase, anaphase, or telophase) were scored when present, metaphase counts rather than mitotic counts were used for the purpose of calculation. Metaphase counts were considered to be more reliable because prophases in particular proved difficult to recognize and may have been underestimated. This is not the case with metaphases, which were easily recognized.

Fig. 2 shows the results of metaphase counts made on the tumour biopsy specimens. The results from the 21 tumour cases were pooled and the metaphase index was plotted against time after the injection of vincristine. The line best fitting the points was obtained by the least-squares regression method. This line gives the mean rate of entry into mitosis for these tumours, and the reciprocal of the slope of the line gives a parameter called either the potential doubling time TP(D) or the apparent cell cycle time TC(a). The value obtained was 190 hours. This is the time that the tumour would take to double in size if no other factors were acting. Using the same technique for the rectal mucosal specimens the mean potential doubling time was found to be 85 hours. *Fig.* 3 shows the proliferation rates of individual cases of both tumour and mucosa. These results show that the mean proliferation rate of the rectal mucosa is more than twice that of the rectal carcinomas.

Fig. 4 shows the potential doubling times of each rectal carcinoma studied plotted against the response to DNCB in the patient in whom it arose. There is no significant correlation, indicating that cellular immunity as assessed by DNCB sensitivity tests has no obvious effect on the proliferation rates of the rectal tumours.

DISCUSSION

This study was initiated to investigate the proliferation rate of rectal carcinomas and to establish whether cellular immune mechanisms have the ability to repress proliferation. We have shown that in rectal carcinomas the rate of proliferation does not exceed that of the rectal mucosa from which they arise. The increase in volume of these tumours must therefore be due to a reduced cell loss as compared with rectal mucosa, the rate of cell loss in the mucosa being 100 per cent, i.e., for every cell produced one is lost.

Steel (1968) has shown that cell loss (ϕ) can be calculated from the formula:—

$$\phi = 1 - \frac{\text{Potential doubling time}}{\text{Actual doubling time}}\,.$$

We have calculated that the potential doubling time for rectal carcinomas is 190 hours. Welin, Youker, Spratt, Linnell, Spjut, Johnson, and Ackerman (1963) have measured the actual doubling time in a group of 20 rectal carcinomas using a double-contrast barium-enema technique and found the mean doubling time to be 620 days. If we substitute these figures in the formula we obtain

$$\phi = 1 - \frac{190 \text{ hours}}{14{,}880 \text{ hours (620 days)}}$$
$$= 0{\cdot}987 \text{ (or } 98{\cdot}7 \text{ per cent).}$$

In other words, for every 100 cells produced in rectal carcinomas 99 are lost. This difference between the cell loss of 100 per cent in the mucosa and 98·7 per cent in tumours is enough to account for the growth of tumours. These findings are in accord with those of Spratt and Ackerman (1961), who calculated a net increase of only 1 cell per 1000 cells per day in a patient whose rectal carcinoma was studied with serial barium enemas over a period of 7·5 years.

We have also shown that there is no correlation between the rate of proliferation of the rectal carcinomas and the cellular immune competence of the individual patients as assessed by their cutaneous delayed hypersensitivity response to DNCB. However, there is a good correlation between a strong response to DNCB and a favourable pathological and operative staging of the growths. This would indicate that although cellular immunity as assessed by delayed hypersensitivity reactions is concerned with control of neoplastic spread the effect is not mediated by a restriction of the proliferation rate of the tumours.

It is more probable that cellular immunity acts by altering the percentage of cells lost either in the tumour or its metastases. Thus in cases with good immune competence cell loss should approach 100 per cent and the reverse would occur with decreased competence. These findings have important implications as to the management of rectal carcinomas, especially when planning adjuvant therapy together with surgery.

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INHIBITION OF HUMAN GASTRIC SECRETION BY PROSTAGLANDIN

BY D. C. CARTER, S. M. M. KARIM, D. BHANA, AND P. A. GANESAN

UNIVERSITIES OF EDINBURGH AND MAKERERE, UGANDA

SUMMARY

The synthetic analogue prostaglandin 15(R)15 methyl-E_2 methyl ester is a potent inhibitor of basal and pentagastrin-induced acid secretion when given orally to male volunteers. Intravenous injection of the same dose of the analogue did not result in significant inhibition. The analogue is thought to reduce acid secretion by a direct effect on the parietal cell and differs from its parent prostaglandin E_2 by its resistance to rapid enzymic degradation.

The possible physiological significance of prostaglandin E_2 in human gastric secretion is considered and the potential therapeutic role of its 15(R)15 methyl analogue is discussed.

PROSTAGLANDIN E_2 (*Fig.* 1) is now known to occur naturally in human gastric mucosa (Bennett, Murray, and Wyllie, 1968), but a physiological role for this compound has not yet been defined. In a recent preliminary communication we reported that prostaglandin E_2 did not inhibit basal acid secretion in man when given orally but that marked inhibition followed oral administration of its synthetic analogue 15(R)15 methyl-E_2 methyl ester (*Fig.* 1) (Karim, Carter, Bhana, and Ganesan, 1973). The study of this analogue has now been extended to an assessment of its effect on basal secretion when given orally or intravenously and on pentagastrin-induced secretion when administered orally. The results of this extended study will be discussed in terms of the therapeutic potential of the compound and the possible physiological significance of prostaglandin E_2 in human gastric secretion.

MATERIALS AND METHODS

All tests were performed on healthy male volunteers without previous dyspeptic history.

In 11 tests 200 μg. of prostaglandin 15(R)15 methyl-E_2 methyl ester were given orally to assess its effect on basal acid secretion, while in 9 tests the same dose was administered by bolus intravenous injection. For 17 of these tests data are available from control studies of basal secretion in the same individuals.

In 12 subjects 200 μg. of the analogue were given orally to challenge the acid secretion induced by pentagastrin (6 μg. per kg. i.m.). In all 12 cases control tests were performed using pentagastrin alone. Four of the 12 subjects underwent an additional two tests in which 50 and 100 μg. of prostaglandin were given orally to challenge pentagastrin-induced secretion.

After a 12-hour overnight fast a nasogastric tube (FG 14–16) was passed into the stomach and the fasting residue was discarded. The tube position was adjusted to allow the ready recovery of a trial 20-ml. instillate of water and continuous suction (2–4 mm. Hg) was then applied. Tube patency was ensured by periodic air insufflation. Specimens of gastric juice were collected every 15 minutes and assessed in terms of volume (ml.), *p*H, acid concentration (mEq./l.), and acid output (mEq.). Titrations were performed to end-point *p*H 7 using a glass electrode and 0·05 *N* NaOH solution.

After a basal period of two 15-minute collections the prostaglandin analogue was administered. For oral administration the dose was diluted to 10 ml. with water and instilled through the nasogastric tube. Suction was discontinued for 30 minutes to allow contact with the gastric mucosa. Collection was then restarted and continued for a further 3 hours. Where oral administration was used to challenge pentagastrin-induced secretion the pentagastrin (6 μg. per kg. i.m.) was injected at the moment of recommencing aspiration. When prostaglandin was given intravenously the dose was diluted to 2 ml. with *N* saline and given at the end of the basal period. Collection of gastric juice was then continued for 3 hours.

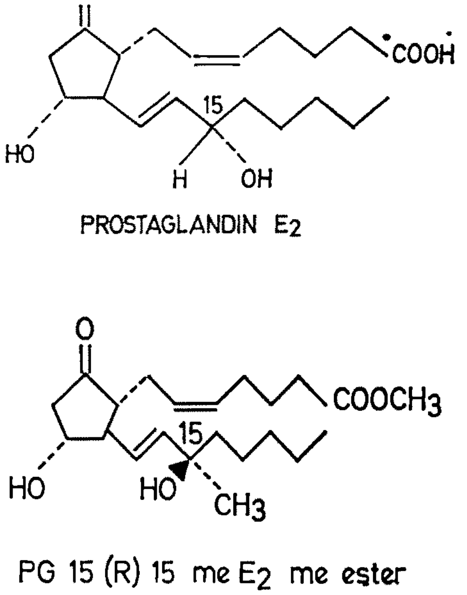

FIG. 1.—Chemical structure of prostaglandin E_2 and 15(R)15 methyl-E_2 methyl ester.

Control tests differed only in the exclusion of prostaglandin from the vehicle of administration. The order of the control test and the test using prostaglandin was randomized.

Subjects were questioned specifically during the tests for untoward gastro-intestinal and other side-effects and asked to report any alteration in bowel habit in the succeeding 24 hours.

RESULTS

No adverse side-effects or alteration in gastro-intestinal function were reported in any tests using the prostaglandin analogue.

Effect of Prostaglandin 15(R)15 Methyl-E_2 Methyl Ester on Basal Acid Secretion.—

Oral Administration (11 tests).—As shown in *Fig.* 2 a marked and sustained reduction in acid secretion was noted in all the cases after the oral administration of 200 μg. of the analogue. In 8 cases the aspirate became alkaline after instillation of the dose. Control tests were performed in 9 individuals and, as shown in *Table I*, the mean 3-hour acid output in control studies was reduced by 76 per cent by prostaglandin administration, a reduction which is statistically highly significant ($t = 5{\cdot}80$, $P < 0{\cdot}001$).

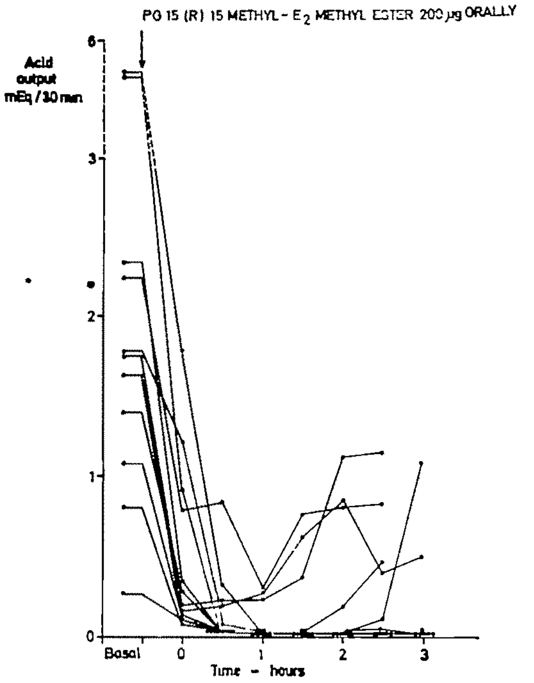

FIG. 2.—Effect of oral administration of 200 μg of prostaglandin 15(R)15 methyl-E_2 methyl ester on basal acid output.

Table I.—EFFECT OF PROSTAGLANDIN 15(R)15 METHYL-E_2 METHYL ESTER ON BASAL ACID SECRETION

ROUTE OF ADMINISTRATION	NO OF TESTS	MEAN 3-HOUR ACID OUTPUT AFTER PROSTAGLANDIN (mEq.)	MEAN CONTROL 3-HOUR ACID OUTPUT (mEq.)	MEAN PERCENTAGE REDUCTION IN 3-HOUR ACID OUTPUT
I.v. bolus	8	7·50 ± 1·08	9 69 ± 1·49	24·5
Oral	9	1·94 ± 0·58	8·09 ± 1·01	76

In all the cases the fall in acid output after prostaglandin administration resulted primarily from a reduction in acid concentration rather than an effect on the volume of secretion (*Fig.* 3).

Intravenous Administration (9 tests).—In only 1 subject was a marked and sustained rise in the *p*H of the aspirate observed following prostaglandin injection. In one other subject the *p*H rose transiently to 5·3 after prostaglandin injection, but in the remaining 7 tests no definite inhibition of acid secretion was noted (*Fig.* 4). This is reflected in a comparison with the 3-hour acid output in the corresponding control tests. As shown in *Table I* the mean 3-hour output in control studies was only reduced by 24·5 per cent following prostaglandin injection, a reduction which is not statistically significant ($t = 1{\cdot}51$, $p > 0{\cdot}10$).

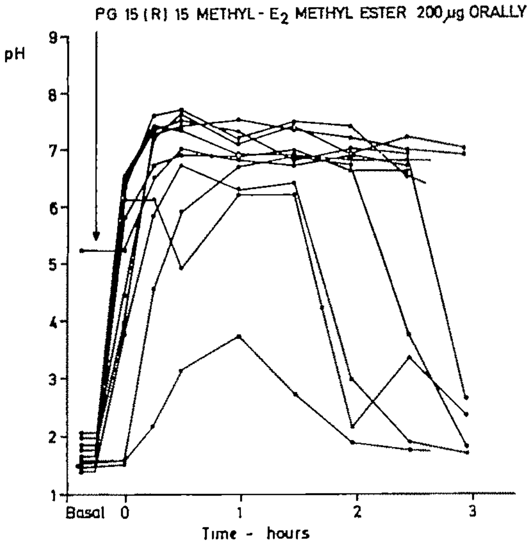

FIG. 3.—Effect of oral administration of 200 μg of prostaglandin 15(R)15 methyl-E_2 methyl ester on the *p*H of the gastric aspirate

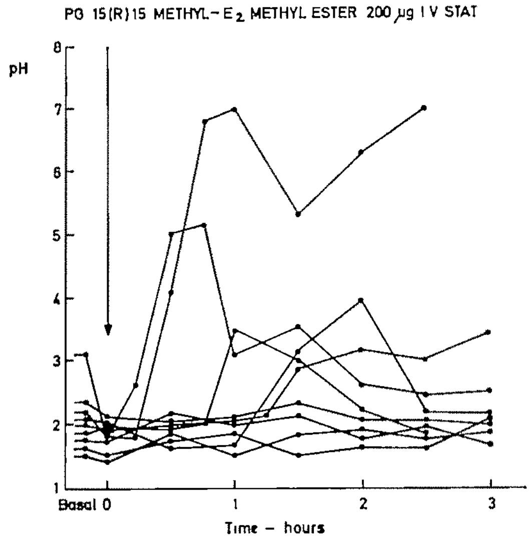

FIG. 4.—Effect of bolus intravenous administration of 200 μg. of prostaglandin 15(R)15 methyl-E_2 methyl ester on the *p*H of the gastric aspirate.

Effect of Prostaglandin 15(R)15 Methyl-E_2 Methyl Ester on Pentagastrin-induced Secretion.—

In all but one of the 12 individuals tested the maximal acid output (M.A.O. = sum of the four highest consecutive 15-minute samples after pentagastrin injection, expressed as mEq. per hour) was lowered by prior instillation of the prostaglandin analogue. A comparison between the M.A.O. after pentagastrin alone and the M.A.O. when pentagastrin was preceded by prostaglandin is shown in *Fig*. 5. A mean reduction in M.A.O. of 64·8 per cent was achieved by prostaglandin and this is statistically significant ($t = 4{\cdot}37$, $P < 0{\cdot}01$).

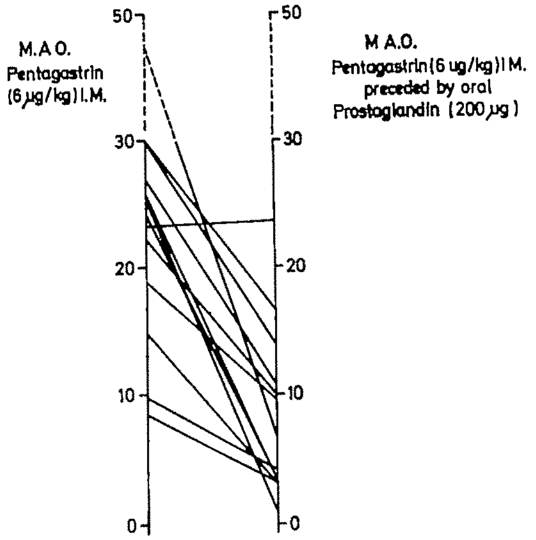

FIG. 5.—Effect of oral administration of 200 µg. of prostaglandin 15(R)15 methyl-E_2 methyl ester on the maximal acid output induced by pentagastrin (6 µg. per kg. i.m).

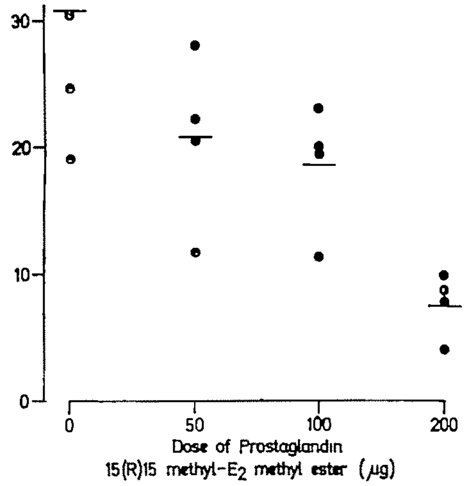

FIG. 7.—Effect of graded doses of prostaglandin 15(R)15 methyl-E_2 methyl ester on the maximal acid output induced by pentagastrin (6 µg. per kg. i.m.) in 4 subjects.

The effect of graded doses of oral prostaglandin on the pattern of pentagastrin-induced secretion is seen in *Fig*. 6, which shows the results of four separate tests carried out in 1 individual. *Fig*. 7 displays the effect of graded doses of prostaglandin on pentagastrin-induced secretion in terms of M.A.O. in 4 individuals each undergoing four separate tests.

DISCUSSION

The synthetic analogue prostaglandin 15(R)15 methyl-E_2 methyl ester is a potent inhibitor of both basal and pentagastrin-induced secretion when given orally to male volunteers. In the case of pentagastrin-induced secretion the inhibitory effect of the analogue is dose-related. On the other hand, bolus intravenous injection of the same 200-µg. dose did not inhibit basal acid secretion to a significant degree. It is therefore probable that the inhibition produced by oral administration results from a direct primary action on the gastric secretory cell rather than from a secondary effect due to peripheral vasodilatation with a consequent reduction in gastric mucosal blood-flow. This is supported by observations in our laboratory that in the dose range employed in the present study the analogue does not affect systemic arterial blood-pressure in male volunteers (Karim, Somers, and Ganesan, 1973). Furthermore, as Jacobson (1970) has demonstrated in the dog, any decrease in gastric mucosal blood-flow observed during intravenous infusion of prostaglandin E_1 is the result rather than the cause of gastric secretory inhibition.

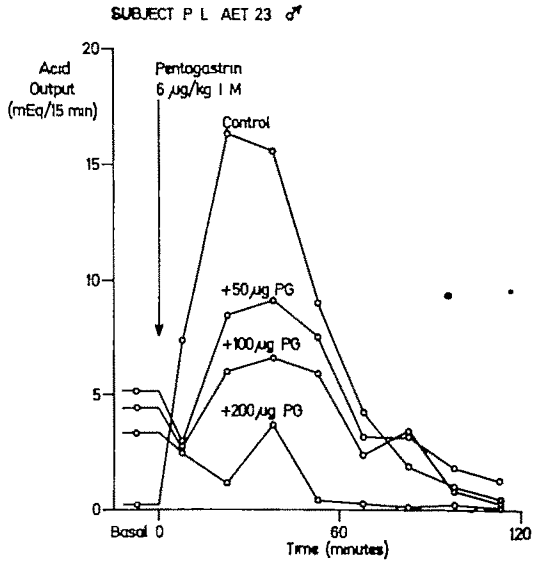

FIG. 6.—Effect of graded doses of prostaglandin 15(R)15 methyl-E_2 methyl ester on the acid output induced by the injection of pentagastrin (6 µg. per kg i m.) in 1 individual.

The inhibition of gastric acid secretion in man by intravenous administration of the naturally occurring prostaglandins E_1, E_2, and A_1 has been previously reported (Classen, Koch, Deyhle, Weidenhiller, and Demling, 1970; Wada and Ishizawa, 1970; Wilson, Phillips, and Levine, 1971). However, the degree of inhibition has been far from impressive and a constant intravenous infusion technique has been necessary for any reduction in secretion to occur. Similarly, attempts to influence human secretion by oral administration of the naturally occurring compounds prostaglandin E_1 and E_2 have not been successful (Horton, Main, Thompson, and Wright, 1968; Karim and others, 1973). The probable explanation for the failure of naturally occurring prostaglandins in this context is their susceptibility to rapid inactivation and metabolism. This process is initiated by the enzyme prostaglandin 15-OH dehydrogenase which is widely distributed in the body. The synthetic analogue prostaglandin 15(R)15 methyl-E_2 methyl ester differs from its parent prostaglandin E_2 in that it is not a substrate for the enzyme and consequently enzymic degradation at carbon 15 is prevented. In view of the fact that prostaglandin E_2 occurs naturally in the human gastric mucosa it is conceivable that the synthetic analogue mimics the physiological role of its parent E_2 compound, differing only in its immunity from enzymic attack. The failure of intravenous bolus injection of the analogue may simply reflect a dilution effect, with a lower ineffective concentration arriving at the parietal cell. If prostaglandin E_2 does enjoy a physiological role in the control of gastric secretion, then interaction with the enzyme adenyl cyclase and inhibition of cyclic AMP formation are potential mechanisms of action suggested by the effect of prostaglandins on other biological systems (Steinberg, 1967; Shaw and Ramwell, 1968).

Whatever the physiological significance of prostaglandin E_2 the synthetic analogue prostaglandin 15(R)15 methyl-E_2 methyl ester must be considered as a compound of therapeutic potential. The sustained inhibition of acid secretion which follows oral administration is now known to extend to pepsin secretion as well (Salmon, 1973), and the alterations are achieved without detectable side-effects on blood-pressure or gastro-intestinal motility. Further indication of the analogue's potential has come from the demonstration of a marked ulcer-sparing effect when administered locally in the Shay rat preparation (Carter, Ganesan, Bhana, and Karim, 1973). If the absence of side-effects is confirmed prostaglandin 15(R)15 methyl-E_2 methyl ester may prove a valuable aid in the management of the peptic ulcer diathesis.

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PROPHYLAXIS IN ILIOFEMORAL VENOUS THROMBOSIS

THE MAJOR AMPUTEE AS A CLINICAL RESEARCH MODEL

By D. R. HARPER, D. P. DHALL, and P. W. H. WOODRUFF

ABERDEEN ROYAL INFIRMARY

The clinical evaluation of the effectiveness of various 'anti-thrombotic' agents has never been adequately undertaken owing to the low incidence of clinically significant deep venous thrombosis and, in many instances, the difficulties of its clinical diagnosis. The criteria of high incidence and clinical significance are found in the major amputee, where pulmonary embolism contributes to a high mortality (Eastcott, 1969). That the most important source for such an embolus is from the iliofemoral segment is known (Mavor and Galloway, 1967), and the common problem of stump oedema reinforces this view.

The control series comprised 15 patients who had mid-thigh amputations for obliterative arterial disease. At amputation a cannula was placed in the long saphenous vein and 540 ml. of 0·9 per cent saline were infused over a period of 5–10 days, during which time serial phlebography of the iliofemoral segment was undertaken at intervals via the cannula. Ten patients subsequently developed thrombus in their iliofemoral segments, progressing to complete occlusion in 5 patients. Four of the 15 patients developed pulmonary embolism, 1 of whom died.

The cannula-phlebographic technique not only provides objective confirmation of the incidence and extent of iliofemoral venous thrombosis but also presents the opportunity to study the effect of various 'anti-thrombotic' agents.

A clinical trial with dextran 70 was undertaken using the cannula-phlebographic technique. Six patients received 500 ml. of 6 per cent dextran 70 in isotonic saline immediately after amputation and the same dose on the first, third, and fifth postoperative days. Daily cannula phlebograms revealed only 1 iliofemoral venous thrombosis (in the only patient to have a swollen stump), while in 5 cases there was no evidence whatsoever of iliofemoral venous thrombosis on the amputated side. A further 6 patients were studied in whom the dextran dose was related to body-weight and the fifth-day aliquot was omitted. No patients developed iliofemoral venous thrombosis as shown by cannula phlebography.

It is concluded that dextran 70 used in this way has a highly significant anti-thrombotic action. This confirms in an objective way the previous work *in vitro* and in animal experiments. The question of dosage schedule as well as the effectiveness of the many other 'anti-thrombotic' agents available may now be relatively easily resolved using the cannula-phlebographic technique in the major amputee as described in this investigation.

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A REPORT OF THE SYMPOSIUM ON GENERAL SURGICAL TRAINING

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THE final afternoon at the meeting of the Association of Surgeons of Great Britain and Ireland was devoted to a Symposium on General Surgical Training chaired by Mr. Norman Barrett, Director of Postgraduate Studies of the Royal College of Surgeons of England.

The stage was set by four short papers designed to describe the problems. Following this a panel of eight, including the original speakers, discussed questions from the floor.

Although the principles and problems discussed were relevant to the whole of Great Britain it transpired that most of the examples and all the figures given related exclusively to England, Wales, and Scotland.

Professor Ivan Johnston, Chairman of the Specialist Advisory Committee in General Surgery, explained the constitution of the Joint Committee of the Royal Colleges of Surgeons, which has charged itself with the duty of arranging satisfactory training programmes in all branches of surgery. The Joint Committee will ensure that trainees are ripe for consultant responsibilities 8 years after registration and will recognize their status as successful trainees after completion of their programmes by granting a certificate without examination. Because of the multiple disciplines in surgery, the Joint Committee has set up several Specialist Advisory Committees. In General Surgery, which is relevant to the symposium, the Specialist Advisory Committee consists of six members of the Association (until recently this figure was four), together with six representatives of the Royal Colleges and three representatives of the Association of Professors of Surgery.

The Specialist Advisory Committee in General Surgery has been charged by the Joint Committee with the duty of advising on the principles underlying a sound training in general surgery, and of identifying individual posts which by combination with others are suitable for training programmes. Trainees on completion of the programme should be accredited as being ready for consultant responsibilities.

The Advisory Committee has agreed that the 4 final years of higher surgical training must for logistic reasons be identified with the achievement of senior registrar status, either as National Health Service senior registrars or as lecturers with honorary senior registrar contracts. These programmes, which normally last 4 years, though designed with great flexibility to meet individual problems and opportunities, should expose the trainee to contrasting periods of surgical experience, each being excellent of its kind. In general, programmes should normally involve periods of service in university and district general hospitals during the 4 years, including 1 optional year attached either to an academic department doing research or to a centre providing specialized experience in this country or abroad.

When looking at posts for suitability for inclusion in a recognized programme particular emphasis is laid on their capacity to provide for the trainee adequate clinical responsibility, operative experience, and intimate contact with the trainers, as well as the availability of good investigational facilities.

The approval of programmes is a continuing process and is as yet by no means complete, but so far 182 programmes have been approved in England, Wales, and Scotland; 140 for senior registrars and 42 for lecturers, involving 49 university and 47 district general hospitals. These are the *Category I* posts, the location of which will be published in due course.

While visiting hospitals members of the Committee have become aware that there are several posts which provide training in every way equivalent to senior registrar posts but which for logistic reasons can only be graded as registrar status. Eighty-seven of these posts have so far been identified and placed in a separate category (*Category II*).

It has been agreed by the Joint Committee that a trainee who has held one of these posts can after obtaining senior registrar status apply for retrospective recognition of 1 year of his service in such a post towards his 4 years of higher surgical training, and also that should it be more expedient for a trainee's experience to do so a senior registrar can spend 1 year in such a post during his 4 years' rotation.

To make the most of this flexibility it is essential that each region sets up a General Surgical Training Committee, containing representatives of the university and district general hospitals, the postgraduate dean, and medical administrators, to supervise and to advise individual trainees in their programmes and prospects. Professor Johnston made a special plea that regions which had not already done so should set up such a committee.

Finally, there are numerous posts which provide excellent training either aimed at giving the trainee the experience to obtain his Fellowship or providing increased experience immediately after obtaining it but before he is likely to be able to obtain a post of senior registrar status. These posts providing basic training in surgery in general are of great importance and are complementary to those designated for higher surgical training. They are placed in *Category III*.

Mr. John then made a plea for increased use of the training facilities at district hospitals where 85 per cent of all patients are treated. While 61 senior registrar posts are in district general hospitals compared with 80 in the university hospitals the discrepancy is much greater at registrar level, where the ratio is 513 : 111. Rotation would ensure that the excellent training facilities at registrar level in the district hospitals are fully utilized.

Dr. Elizabeth Shore of the Department of Health and Social Services then discussed the implications of logistics. The position is that while the number of senior registrar posts in general surgery is more or less in step with the anticipated number of consultant vacancies, a considerable imbalance has occurred over the years in two ways. First, the number of consultants per head of population is much higher in some regions, particularly in the south, than in others. In order to correct this the Central Manpower Committee, in whose province this problem now lies, is encouraging differential expansion within the 4 per cent per annum of consultant posts to help the deficient areas, so that eventually the number of consultants in general surgery per head of population should be evened up.

Secondly, the number of registrar posts in general surgery is considerably out of balance with the number of vacancies at senior registrar level; the latter cannot be increased without upsetting the present fairly satisfactory balance with consultant vacancies until the consultant establishment itself has been increased. This applied to many surgical specialities such as gynaecology and orthopaedic surgery. The Central Manpower Committee therefore proposes not to increase the number of registrar posts in these specialities until the consultant establishment has expanded by the planned 4 per cent per annum for several years and there is convincing evidence that the present imbalance between registrar and senior registrar posts has been rectified.

Mr. Birt, Chairman of the Educational Advisory Committee of the Association, discussed the implications. He felt that the interests of the trainees must come first. Rotation through a variety of posts in one good hospital or hospital group met the needs of the trainee before obtaining his Fellowship.

After obtaining his Fellowship and while waiting and competing for a senior registrar appointment the trainee was in great need of adequate guidance and counselling to make the best of his abilities, so that, for example, those who were unlikely to be successful in their ambitions should be diverted to less competitive fields without undue waste of time. This was the function of the Regional Surgical Training Committees and of the trainee's consultants.

It should be recognized that as far as case load and teaching responsibility are concerned the distinction between university hospitals and the larger district hospitals is becoming blurred. Nevertheless, while serving in post-Fellowship (Category III) and higher surgical training (Categories II and I) posts rotation of the trainee between different institutions so as to be influenced by different consultants is desirable. This implies an active surgical training committee to manipulate available rotations in the trainees' interests, and to arrange the provision of good accommodation at each post so as to cause the minimum disturbance of the trainee's family life.

Finally, there is at the moment a discrepancy between the number of posts required to train replacements for consultants retiring and the number required to deal with the service load. This gap can be filled only by increasing the consultant establishment and possibly establishing some non-consultant grade to deal with some of the simpler but time-consuming forms of surgery, such as repair of hernias and excision of haemorrhoids.

In the discussion which followed, various points were raised.

A fear was expressed that training programmes might become too rigid, that individual posts would vary over the years in their training capacity, and that some men who had had unconventional careers, particularly those who had served for a part of their time overseas or in the Services, might have difficulty in breaking into the system.

The Panel in answer emphasized that the work of the Specialist Advisory Committee is a continuing process, with constant modifications. The Advisory Committee would rely heavily on the Regional Surgical Training Committees who could advise them about any posts where training capacity had altered and which should be re-examined. They could also make arrangements to fit in the 'odd man out' as seemed most suited to his needs and abilities.

A similar fear was voiced that it might prove difficult for a surgical trainee to obtain adequate experience in genito-urinary surgery if he wished to offer this as a special interest in his consultant post. The Panel felt there should be no difficulty in seconding such a trainee for a year, or if necessary longer, to a Category II post in a specialist unit during his higher surgical training.

Several speakers felt that trainees at the moment were deficient in training in operative surgery; it was hoped that with the emphasis on rotation to district hospitals where there is a large load of clinical material and good training is available this difficulty would be overcome.

It was suggested from the floor that the logistic gap between the trainee posts and service load could be met by lengthening the senior registrar period to 6 or 8 years, but this did not gain the support of the platform. Professor McColl, emphasizing that security is of great importance to the trainee, described the 7-year programme established in Guy's Hospital and the South-east Metropolitan Region where, subject to satisfactory progress, a trainee is rotated through district and university hospitals and the professorial unit at yearly intervals, progressing automatically from registrar to senior registrar grade.

Finally, the needs of overseas graduates in search of higher surgical training were touched upon. Dr. Shore explained that it was possible to establish supernumerary honorary posts, provided that the holder was financed by his own government and undertook to return overseas and not to apply for established posts in this country.

The Panel felt that certain Category II posts might well be used for this purpose.

Mr. Barrett, summing up, said that clearly the discussion had only skated on the surface of the problems involved in higher surgical training but that he hoped the debate now started would continue.

SHORT NOTES OF RARE OR OBSCURE CASES

ABDOMINOSCROTAL HYDROCELE

BY M. R. TANGA, P. R. AVARADI, AND G. MOHANDAS GANDHI

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SUMMARY

1. Four cases of abdominoscrotal hydrocele presenting within a short span of 5 months are reported.

2. In one of our patients there was associated an incompletely descended testis and this testis had a seminoma. Such an association has not been reported previously. Abdominoscrotal hydrocele may be more common than is generally believed.

SINCE Dupuytren's (1834) first description of abdominoscrotal hydrocele, cases have been frequently reported in the literature. Burkitt and Williams (1964) collected 59 cases from the world literature. From India, Ramakrishnan and Swami (1959), Kaur, Sekhon, and Manchanda (1965), Razdan (1968), and Gupta, Mital, and Razdan (1971) have reported a total of 11 cases of abdominoscrotal hydrocele. We have encountered 4 such cases in a short span of 5 months at the Government General Hospital, Gulbarga. The present report is based on these 4 patients.

CASE REPORTS

Case 1.—A 40-year-old male was admitted to the Government General Hospital, Gulbarga, on 29 Dec., 1971, with a 1-month history of a swelling over the right groin. The swelling was reduced by pressure over the scrotum or on lying down and it increased on walking and on coughing. There was also pain on coughing. The scrotal swelling had gradually increased in size. The patient gave a history of a cough with expectoration of 5 months' duration. There was no history of trauma. He had suffered from guinea-worm infestation 15 years earlier.

There was a right-sided swelling measuring about 12·5 × 10 cm. extending from the scrotum to the right inguinal region. There was no tenderness. His local temperature was normal. There was impulse on coughing. A hard mass was felt in the upper part of scrotal skin, and it measured about 2·5 × 1 × 1 cm. The testis was palpable and normal. A diagnosis of abdominoscrotal hydrocele with calcified guinea-worm was made.

The haemoglobin was 11·5 g. per cent and the E.S.R. was 30 mm. per hour (Westergren). Urinalysis was normal. He was first treated for his cough for 10 days. Operation was performed on 9 Jan., 1972. The approach was via a longitudinal incision over the scrotum. At operation the sac was found to be extending well beyond the deep inguinal ring. The entire sac was excised. The postoperative course was uneventful.

Case 2.—Mr. B., aged 40 years, was admitted on 26 Jan., 1972, with a history of left groin and scrotal swelling of 3 months' duration with pain in the swelling for 1 month. Examination revealed a left inguinoscrotal swelling. The inguinal extension reached the left anterior superior iliac spine. There was visible and palpable impulse on coughing and this was not reducible. The swelling was soft and fluctuation could be elicited between the inguinal and scrotal parts of the swelling. The testis on the left side could be felt vaguely, just below the left superficial inguinal ring. The lower part of the scrotum on the left side was empty.

The patient was found to be anaemic with a haemoglobin of 65 per cent. His E.S.R. was 35 mm. per hour (Westergren). Urinalysis was normal. A diagnosis of left inguinoscrotal hydrocele with an incompletely descended testis was made. At operation about 750 ml. of clear fluid were drained. The testis looked much larger than normal and there was suspicion of malignancy. A left radical orchidectomy was therefore carried out. The complete hydrocele sac was excised and a drain was left in position. The postoperative course was uneventful. Histopathological examination of testis showed seminoma (*Fig.* 1).

Case 3.—Mr. B., aged 25 years, was admitted on 13 Feb., 1972, with a history of right scrotal swelling of 3 years' duration and abdominal swelling of 10 days' duration. The right-sided scrotal swelling had been insidious in onset and slow in progression. The abdominal swelling had also been insidious in onset. There was no pain in the scrotum and lower abdomen, no fever or rigor, and no history of a cough.

Examination revealed a right-sided inguinoscrotal swelling. This swelling was continuous with a suprapubic intra-abdominal swelling, measuring 10 × 12·5 cm. (*Figs.* 2, 3). The skin over the swelling was stretched and shiny. There was visible and palpable impulse on coughing. There was cross-fluctuation between the scrotal and abdominal swellings. A diagnosis of right abdominoscrotal hydrocele was made. The haemoglobin was 70 per cent. Other haematological and urinary examinations were within normal limits. Screening of the chest was also within normal limits.

On 18 Feb. the patient was operated on under spinal anaesthesia. A 7·5-cm. incision over the anterolateral aspect of the right scrotum was made. The sac was exposed and tapped; 2 litres of clear hydrocele fluid were drained. The sac was explored. Superiorly the sac extended up to the umbilicus, laterally it extended to the anterior superior iliac spine, and posteriorly up to the upper border of the sacrum. Partial excision and eversion of the sac were done. A drain was placed. After obtaining perfect haemostasis the wound was closed in layers. The postoperative course was uneventful. At the time of discharge the suprapubic mass which had been felt earlier was absent.

Case 4.—Mr. S, aged 20 years, was admitted on 19 April, 1972, with a history of left-sided scrotal swelling of 18 months' duration and left-sided lower abdominal swelling of 15 months' duration. The onset of the swelling had been insidious. The scrotal swelling tended to disappear in the recumbent position. Six months previously the patient had had high fever with rigors and pain in the abdomen which had subsided after 2 days without treatment.

Examination revealed a left-sided hydrocele which reduced in the recumbent position with the appearance of lower abdominal fullness on the left side. There was visible and palpable impulse on coughing. There was cross-fluctuation between the scrotal and abdominal swellings. An internal inguinal ring occlusion test was negative. Invagination of the finger into the external ring revealed a passage behind the anterior abdominal wall to a big cavity whose periphery could not be reached with the finger. A diagnosis of left abdominoscrotal hydrocele was made. The haemoglobin was 80 per cent and urine examination was normal.

On 22 April under spinal anaesthesia the patient was operated on via an 8-cm. inguinoscrotal incision. The sac was explored and it was found to extend into the abdomen deep to the anterior abdominal wall. The upper limit was at the level of umbilicus, laterally it was limited by the iliac bones, and below by the inguinal ligament. Posteriorly it could be easily separated from the peritoneum, medially it extended up to the midline, and inferiorly the communication with the scrotum was 5 cm. wide. The whole of the abdominal part was excised with eversion of the scrotal part of the sac (*Fig.* 4). The posterior wall of the inguinal canal was repaired as it was found to be weak. The patient had an uneventful post-operative course.

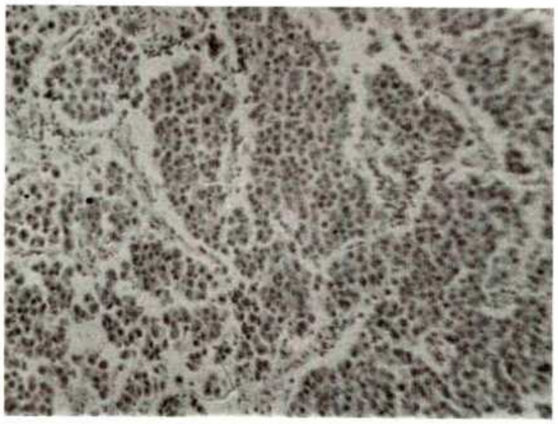
FIG. 1.—*Case* 2. Photomicrograph of seminoma of testis. H. and E. (× 135.)

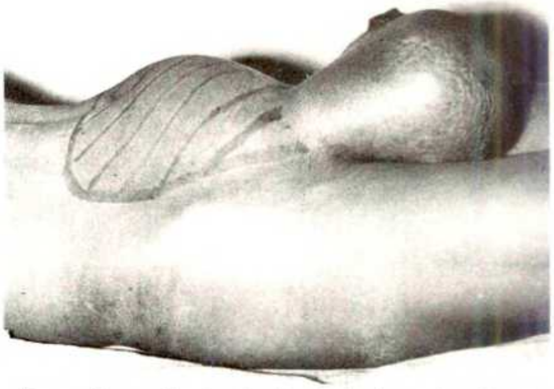
FIG. 2.—*Case* 3. Showing the abdominal and scrotal swellings in continuity.

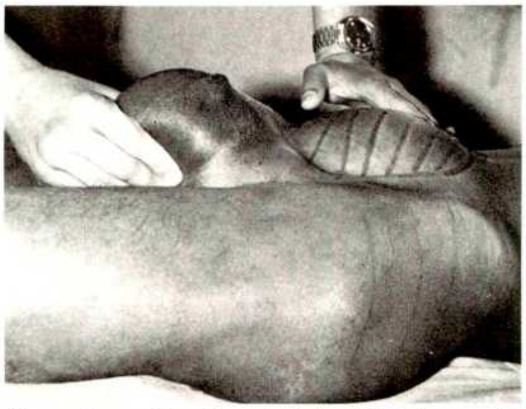
FIG. 3.—*Case* 3. Cross-fluctuation being elicited between the abdominal and scrotal parts of the hydrocele.

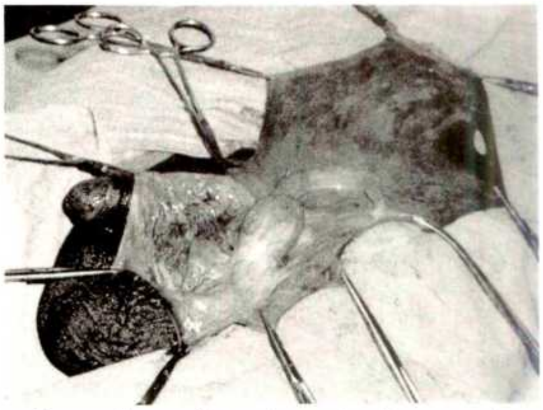
FIG. 4.—*Case* 4. The entire sac has been opened up vertically. The upper part of the sac is the abdominal portion and this has been dissected.

DISCUSSION

It would appear from a review of the world English literature that abdominoscrotal hydrocele is quite rare. In 1964 Burkitt and Williams (1964) could collect only 59 cases from such a review. In India Ramakrishnan and Swami (1959) collected 6 cases from the records of the Madras General Hospital between 1953 and 1958, to which they added 1 case of their own, while during the same period there were 4256 cases of all varieties of hydrocele. Other reports from India are by Kaur and others (1965; 1 case) and Gupta and others (1971; 3 cases out of 1787 cases of all types of hydrocele). However, in a short span of 5 months at the Government General Hospital, Gulbarga, we have encountered 4 cases of abdominoscrotal hydrocele. We are not certain whether this disease is more common in this part of the country or whether it is a mere coincidence that we have encountered several cases in such a short period. The latter reason is the more likely one because in the same unit there was not a single case during the previous period of 2 years.

There are many possible explanations for the occurrence of such a hydrocele. Jacobson (1893) put forward the theory that an infantile hydrocele extends up between the peritoneum and anterior abdominal wall. This is the usually accepted theory, but it is difficult to explain the retroperitoneal extension of this hydrocele. According to Dupuytren (1834) an ordinary tense hydrocele may extend into the abdomen. Dupuytren's theory is supported by Currie (1953) and Burkitt and Williams (1964). If Dupuytren's theory is to be accepted this type of hydrocele should occur more frequently in India since a large percentage of Indians have tense hydroceles for many years, and yet the reported incidence of abdominoscrotal hydrocele in India is very low. A third possible theory was outlined by Cabot (1936), who believed that abdominoscrotal hydrocele occurs as a result of a bottle-neck connexion between the hydrocele of the cord and tunica vaginalis, but this view is not generally accepted.

Abdominoscrotal hydrocele has been given various names by different people. Dupuytren (1834) called it 'hydrocele-en-bissac' and the name 'abdominoscrotal hydrocele' was proposed by Bickle in 1919. Other names which are sometimes used are 'bilocular hydrocele' and 'abdominal hydrocele'. The term 'abdominoscrotal hydrocele' seems to be the most appropriate because it is simple and self-explanatory. Various subvarieties of abdominoscrotal hydrocele are described and these are properitoneal, interstitial, and retroperitoneal, the first type being the commonest. Three of the present cases were of the properitoneal type and 1 case had a retroperitoneal extension. Prather (1942) and Ramakrishnan and Swami (1959) felt that the properitoneal variety is the most usual type, while Gupta and others (1971) stated that the retroperitoneal variety is the commonest. Ramakrishnan and Swami (1959) and Gupta and others (1971) believed that right-sided abdominoscrotal hydrocele is more common than the left-sided type. In the present series there was an equal distribution between the two sides. Prather (1942) also encountered an equal distribution between the right and left sides.

The majority of these patients are asymptomatic except for the presence of the swelling. A few of them have dull pain in the abdomen and scrotum. Very few patients have pressure symptoms or acute abdominal manifestations. Richards (1908) reported frequent micturition due to pressure on the bladder. Litvak's (1958) patient presented with acute abdominal symptoms due to torsion of the upper lobe of the sac on the inguinal neck. Our patients complained of a mass in the groin and abdomen and dull pain in this region. Pain in the region of the swelling could be due to haemorrhage in the sac or an increase in the tension in the sac. Razdan (1968) has described a new physical sign, which he claims is present only in abdominoscrotal hydrocele. This sign constitutes the presence of a prominent skin fold overlying the neck of the scrotal portion and the external inguinal ring. He claims that a similar fold is seen in the photograph of Lord's (1959) patient. This sign was later propagated by Gupta and others (1971) from the same institution but does not seem to be very convincing, at least in our patients.

The majority of abdominoscrotal hydroceles are idiopathic. In some cases they may be secondary to such conditions as epididymitis or epididymo-orchitis. Steele (1875) reported 1 case of abdominoscrotal hydrocele in a patient with an undescended testis.
The present *Case* 2 had an incomp
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At surgery the testis seemed to h
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wide partial excision and eversion o
were performed and the entire abdo
sac collapsed because of the drain
It was felt that any fluid secreted
part of the sac will find its way
through the wide opening and will b
scrotum. This impression has been
subsequent course of this patient.
fluid have been found in this type o
of our patients 2 litres of fluid wer
the sac.

Acknowledgements.—Our sinc
to the Principal of H.K.E.S. Med
B. B. Dhaded, and the District Surg
General Hospital, Gulbarga, for th
report these cases. We take great pl
the Professor of Pathology, Dr. K. R.
for providing the photomicrograph.

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REVIEWS AND NOTICES OF BOOKS

Allgemeine und spezielle chirurgische Operationslehre. Volume 10, Part 3, **Die Operationen an der Hand.** By W. WACHSMUTH, Würzburg, and W. WILHELM, Aschaffenburg. Pp. 641 + xxiv. Illustrated. 1972. Berlin: Springer-Verlag. DM.590.

THIS volume is one of a series of publications on general and special surgery. The editors, Dr. Wachsmuth and Dr. Wilhelm, are supported by a distinguished group of co-authors, mostly from the Federal Republic but including others with established international reputations. There is a formidable list of contents beginning with general principles, techniques, and armamentarium of hand surgery. Specific subjects discussed in detail include the surgical management of injuries requiring amputation; wounds of the skin including burns, both thermal and chemical; fractures in all regions of the hand and wrist; surgery of the rheumatoid hand; surgery of the peripheral nerves as they affect hand function, including the surgery of pain; injuries to and operations upon muscles, tendons, and vessels; infections; the pathological conditions of contractures of all types, with a large chapter on Dupuytren's contracture. Tumours are discussed and a very full appraisal is given of reconstructive tendon surgery with detailed analysis of techniques and indications. The reconstructive aspects of sensory loss and its restoration are given adequate coverage. A considerable section of the book is devoted to the congenital deformities of the hand and their reconstruction. The subject material covered, therefore, is of an extremely comprehensive nature.

The book throughout is beautifully produced. The illustrations without exception are first class, being lucid and totally understandable. A textbook of this nature must have a place in the libraries of all departments with a special interest in hand surgery and will have particular value for surgeons who are less experienced in the problems of hand surgery but who for geographical reasons may be required to undertake this work.

It is inevitable with a textbook of this nature that comparisons are drawn between it and comparable textbooks in English. This multi-authorship volume containing a great deal of personal experience with a comprehensive bibliography has a definite place in the literature of hand surgery but as a supplement to classic textbooks in this field rather than as a replacement.

The German authors are to be congratulated on the way that they have combined first-class illustrations of surgical procedures with a brief and concise text. It is perhaps inevitable, in view of the tragic German experience in recent years, that a considerable section of this book should be devoted specifically to the problems of the less common congenital abnormalities.

Inevitably there are some criticisms, albeit of a minor nature; thus, the normal techniques of nerve repair are dealt with very briefly while a considerable amount of text and illustration is devoted to the interesting but none the less unproven technique of microscopically assisted nerve-grafting. A similar criticism can be applied to the section on fractures where uncommon techniques are illustrated profusely but there is a lack of emphasis of the simpler and more common management of day-to-day problems. Although the text when looked at carefully goes some way towards detailing indications for the limitless procedures listed, one is still left with the uneasy feeling that the inexperienced hand surgeon might assume that the solution to many problems can only be by complex operative techniques. One would have wished for firmer emphasis on the need for careful case selection. In certain areas the text is not definite enough in emphasizing the fundamental point of the essential simplicity of hand surgery.

These minor criticisms apart, this is a magnificent publication on which the editors and all the authors are to be congratulated most warmly. Unfortunately the combination of the German language and, more importantly, the price may diminish the wide circulation which this book certainly deserves.

Surgery Annual 1972. Edited by PHILIP COOPER, M.D., University of Florida, and LLOYD M. NYHUS, M.D., Chicago. 9¼ × 6½ in. Pp. 445 + xii. Illustrated. 1972. New York: Appleton-Century-Crofts. $17.50.

THIS is a varied and variable volume. There is an excellent review on shock but the treatment of venous thrombo-embolism contains no references to the excellent contributions from the United Kingdom in the past few years. The chapter on peptic ulcer illustrates closure of the duodenum in several illustrations, as well as complementary photography which seems unnecessary in this kind of book. Curiously the references on follow-up after vagotomy omit the papers by Goligher and his colleagues. Chapters on the short-gut syndrome and the significance of ileal resection are complementary and well written, but elsewhere the book is less thorough and the references are sometimes limited and inadequate.

This book is for the library, and most British surgeons will consult it there.

Thoracic Surgical Management. Fourth edition. By J. R. BELCHER, M.S., F.R.C.S., London Chest Hospital, and M. F. STURRIDGE, M.S., F.R.C.S., London Chest Hospital. 8¼ × 5½ in. Pp. 192, with 60 illustrations. 1972. London: Baillière Tindall. £2·20.

THE production of a fourth edition of this book is sufficient recommendation of its value. It is an excellent manual containing practical information of use not only in thoracic surgery but also in the postoperative chest complications of general surgery. In this edition the section on cardiac surgery has been brought up to date.

The illustrations are clear line drawings which are easily understood. Trivial criticisms might include the omission of the use of an Argyll tube for intercostal drainage and scant reference to needle lung biopsy in the investigation of pulmonary lesions. This book is thoroughly recommended as essential for all surgical residents in general as well as in thoracic units and its price is extremely modest.

Problems in Paediatric Urology. Edited by J. H. JOHNSTON, M.B., F.R.C.S., F.R.C.S.I., Liverpool, and R. J. SCHOLTMEIJER, M.D., Ph.D., Amsterdam. 9½ × 6½ in. Pp. 301. Illustrated. 1972. Amsterdam: Excerpta Medica. $27·50.

THE pace of advance and the speed with which opinions change are perhaps most noticeable in the specialized but important field of paediatric urology. Here fashions in treatment change with a rapidity which bewilders those not closely involved in the subject. Only a short time ago it seemed correct to revise the bladder neck for stenosis; now we are told that it is the distal urethra which is so often stenosed. Sometimes conservative treatment of reflux is advocated, and on other occasions reimplantation is favoured. For those who want to keep abreast of this rapidly advancing field, Johnston and Scholtmeijer offer an excellent series of essays by acknowledged authorities in their own subjects. They have selected some of the more important and controversial topics. Hardy Hendren details his method of the surgical reconstruction of megaureter, without perhaps emphasizing how difficult this operation is. The diverse problems posed by ureterocele and ectopic ureters are described equally clearly by Johnston, and Innes Williams reviews his great experience with the surgery of vesical exstrophy, giving due emphasis to its associated and very important pathological conditions. In a characteristically sparkling attack, O'Donnell demolishes the current muddle-headed thinking which governs so much of what is done and written about childhood urinary infection—this review is a pleasure to read, no less outstanding for its prose than for its common sense. Memorable also is John Scott's account of bladder-outflow obstruction, and the chilling description of the urological aftermath of meningomyelocele from Zachary and Lister would make any reader ponder yet again the ethical dilemma posed by this difficult problem. Scholtmeijer reviews the current preoccupation with the distal urethra of little girls and seems to agree with the present fad for curing enuresis by splitting the urethra to an acceptable norm of capaciousness. This chapter certainly requires one to exercise some willing suspension of disbelief, but at least the reader is given the evidence and can draw his own conclusions.

Surgeons, paediatricians, and urologists in training will find this a clear and useful book which throws a lot of light on this important scene.

Clinical Anesthesia. Volume 9, Part 1, **Management of Patient for Radical Cancer Surgery.** Edited by WILLIAM S. HOWLAND, M.D., and OLGA SCHWEIZER, M.D., New York. 10 × 7 in. Pp. 162 + xi. Illustrated. 1972. Oxford: Blackwell Scientific Publications. £5.

THIS volume is the first section of the ninth part of the 'Clinical Anesthesia' series. It deals on a very broad front with the major problems that face the modern anaesthetist in radical cancer surgery. As the editors rightly point out in the introduction, the type of anaesthetic agent itself is of least importance in such cases, and the book therefore concentrates chiefly on subjects relative to disturbances in surgical physiology. Chapters on fluid balance, blood replacement, venous pressure monitoring, and shock are well presented with commendable correlation between basic physiological principles and clinical application. This volume will be of especial value to the postgraduate student of anaesthesia.

Die medizinische Rehabilitation der Querschnittsgelahmten. By I. KOCH, Berlin. 8½ × 5½ in. Pp. 141. 1972. Berlin: Veb. Verlag Volk und Gesundheit. 17.50M.

THIS paper-back monograph reports on some 300 patients with paraplegia who have been treated in a special rehabilitation unit in Berlin since the Second World War. The methods of treatment and the results achieved are compared with the various series reported in the world literature and it becomes clear that the facilities available in Berlin are inadequate to deal with the increasing number of patients with traumatic paraplegia.

This report should be of interest to all those involved in the care of paraplegic patients, but English-speaking readers are warned that because of the excessive use of abbreviations throughout this monograph it is a difficult book to read.

Klinisch Gastroenterologie, Volumes 1 and 2. Edited by L. DEMLING, Erlangen. 10½ × 7½ in. Vol. 1, pp. 546 + xix; Vol. 2, pp. 635 + xxviii. Illustrated. 1973. Stuttgart: Georg Thieme Verlag. DM.298.

THESE two closely packed volumes deal with current thoughts on a variety of topics in the diagnosis and treatment of gastro-intestinal disease.

The text is in German, but the authors are from many different parts of the world, although the majority are European. It is an excellent book of its type, drawing together the present concepts of disease in the alimentary tract. Depending on the author, some chapters have an emphasis on topics of surgical interest, but it is more a book for the specialist in gastro-enterology.

As a textbook for the specialist or a reference book it provides a concise and readable text which should make it a standard work available in the library.

Textbook of Surgery. The Biological Basis of Modern Surgical Practice. Tenth edition. Edited by DAVID C. SABISTON, jun. M.D., Durham, North Carolina. 10 × 7 in. Pp. 2135 + xxvii. Illustrated. 1972. London: W. B. Saunders Co. Ltd. £11·70.

SURGERY is now divided into so many sub-specialities that no individual can possibly keep up to date with more than a fraction of the current knowledge. This book, the tenth edition of the Davis-Christopher *Textbook of Surgery*, is one of the few which provides a truly encyclopaedic coverage of the whole field of modern surgery. It would therefore be a useful acquisition for anyone involved in surgical work, be he undergraduate, trainee, consultant, or teacher.

The theme of this book, made explicit in its subtitle, is the biological basis of surgery. The first 400 pages comprise 19 chapters on fundamental principles and problems applicable to all surgical practice, such as wound healing, the metabolic response to trauma, renal failure, etc. There follow 100 pages on transplantation and then 1600 pages on systematic surgery. Each chapter gives a satisfactorily complete account of the scientific and clinical aspects of its subject, but the prospective reader should not expect to find great emphasis on such problems as surgical judgement, differential diagnosis, and minutiae of operative technique. Most chapters are embellished with an historical introduction, and another special and helpful feature is a brief synopsis of key references. There are 142 contributors but the style and format are reasonably uniform. It is a pleasure to see Mr. Alan Parks as one of only two contributors from outside the North American continent.

This book is moderately expensive in absolute terms but is none the less excellent value as a basic and comprehensive reference work. With over 2000 pages it is a little cumbersome, but it can be purchased in two volumes which would be easier to handle.

Progress in Pediatric Surgery, Volume 5. Edited by P. P. RICKHAM, M.D., M.S., F.R.C.S., D.C.H., Liverpool, Professor W. CH. HECKER, München, and Professor J. PRÉVOT, Nancy. 9 × 6 in. Pp. 161. Illustrated. 1973. Berlin: Urban & Schwarzenberg. No price given.

THIS is the fifth in a series of reviews of progress in paediatric surgery and it follows the principles and maintains the standards of the previous numbers. The purpose of the series is to provide the opportunity for a rather fuller presentation, analysis, and discussion of current problems than is possible in the restrictive pages of surgical journals. Many editors look with more favour on contributions which occupy 3 or 4 pages than on those which need 10 or 12, and there must be few editors who could face with equanimity the prospect of publishing a volume in which the contributions ranged between 22 and 52 pages.

This volume has a very varied selection of articles and includes an extensive survey of hydatid disease from the paediatric surgical team in Marseilles, a topic which in these days of rapid travel must be of wider concern than previously. There is an excellent account of the experimental work on intestinal anastomosis by Herzog of Basel, demonstrating a technique which, although somewhat intricate, is likely to produce an anastomosis which is more secure in the early and late phases and less constrictive than any of the standard methods.

The contribution by Kathel from the Paediatric Surgical Department in Liverpool presents two aspects of isotope renography. The first part is concerned with the use of the analogue computer to quantify the isotope renograms in a series of older children and this is followed by a short account of the prognostic value of a qualitative renography which is applicable to neonates and has been used with success in the assessment of the neurogenic bladder.

Mollard and Paillot present what might be regarded as a typically French lucid and logical analysis of primary mega-ureter in children, describing in particular the presentation and management of the obstructive and non-obstructive types as well as the refluxing and non-refluxing primary mega-ureters; this is a very useful analysis. Pompino and his colleagues from the Department of Paediatric Surgery in Munich have attempted to confirm the reports of some Russian investigators that re-innervation of the neurogenic bladder is possible by the application of an isolated but innervated and vascularized loop of ileum to the surface of the bladder after the mucosa of the ileum has been removed. This careful experimental study showed no evidence whatever of innervation crossing from the intestine to the bladder.

This series has proved the value of a vehicle for the publication of the unusually long, the unusually complex, or even the unusual paper which might contribute to progress in paediatric surgery.

Urologische Operationen; Atlas zur Indikation, Technik, Nachbehandlung. Edited by GEORGES MAYOR and ERNST J. ZINGG, Zürich. 11½ × 8½ in. Pp. 659 + xii. Illustrated. 1973. Stuttgart: Georg Thieme Verlag. DM.298.

THIS is a new atlas of urological surgery. Both of the editors and most of the authors are Swiss. The book specifically excludes the problems of urological surgery in relation to gynaecology, paediatric urology, and transurethral procedures. The emphasis of this well-produced volume is on operative techniques, which is illustrated by many excellent half-tone diagrams, but peroperative and postoperative complications are stressed and discussed in the text. The book contains many excellent chapters, but the one dealing with surgery of urethral strictures is somewhat outdated and the management of hydronephrosis has received relatively little attention. For a book of this size the number of references given is rather small, and to the British reader this volume is unlikely to be worth £42.

Alexander's Care of the Patient in Surgery. Fifth edition. By WALTER F. BALLINGER, M.D., St. Louis, JACQUELYN C. TREYBAL, R.N., St. Louis, and ANN B. VOSE, R.N., B.S.N., M.S., St. Louis. 10 × 7 in. Pp. 905 + xvi. Illustrated. 1972. London: Henry Kimpton. £8·65.

THIS book is for all personnel employed in an operating-theatre suite, and as such provides a basic reference for patient care from a technological aspect. The book is well planned and provides informed comment on theatre administration, preoperative preparation of the patient, and details of most surgical procedures. The diagrams are very good and show the principal anatomical structures encountered at different stages of an operation. In addition it illustrates and names the majority of surgical instruments that are in current clinical use.

Although there are inevitably some differences in surgical practice across the Atlantic, this in no way detracts from the main objectives of this book. Its contributors are experienced theatre personnel who describe systematically basic surgical techniques. Each operation is defined, the indications for surgery are listed, the position of the patient is discussed, and both the instruments and sutures likely to be used are itemized.

This book fills an important gap for the theatre nurse who is not only interested to provide more than the correct instrument at the right time but also keen to understand operative technique and to anticipate the requirements of the surgeon.

Zentrale Storungen der Temperaturregulation. By Professor Dr. GERHARD LAUSBERG, Giesen. 9 × 6 in. Pp. 168, with 68 illustrations. 1972. New York: Springer Verlag. DM.80.

THIS is a monograph on disturbance of the temperature-regulating mechanism. Following a review of the literature the writer reports in detail his investigations on 238 patients with neurosurgical conditions or head injury, together with suitable control subjects on whom he performed experiments of raising or lowering the environmental temperature and recording essential parameters.

The book has an extensive bibliography and each chapter has a long English summary. This volume will undoubtedly be of great interest to physiologists and research workers but is rather outside the scope of the average neurosurgeon.

Thyroid Tumours, Lymphomas, Granulocytic Leukemia. Edited by M. FIORENTINO, R. VANGELISTA, and E. GRIGOLETTO. 9½ × 7 in. Pp. 210 + xii. Illustrated. 1972. Padova: Piccin Medical Books. L.8000.

SCIENTIFIC communication where a multidisciplinary subject such as oncology is concerned is obviously an important problem to solve. One good solution is holding workshops and seminars devoted to specific aspects of oncology where interested laboratory and clinical workers meet together for full discussions, and the proceedings are published later for the benefit of those not present. This particular seminar in Padua was concerned with the three important, but different, subjects of thyroid tumours, lymphomas, and granulocytic leukaemia. Fifty contributors from seven countries took part in the seminar.

The subject-matter of the section on thyroid tumours follows the usual pattern of pathology, epidemiology, and treatment with the presentation of results. Here we still have much to learn, for carcinoma of the thyroid is not one disease but many; this is highlighted on the first page, where the point is also made that the majority of tumours arise from the follicular cell and the minority from the parafollicular (C) cell, the tumours of the two groups behaving quite differently. The risk of women being affected is almost double that of men, but the tumours in women seem to be of lesser malignancy. The aetiological factors provide much food for thought, and include the importance of ionizing radiation, where the high incidecne of tumours in children in the United States is contrasted with that in Western Europe. When planning treatment the importance of studying the character and behaviour, including histology, of each tumour is rightly stressed. Consideration is given to radiotherapy as a prophylactic following surgery where excision has been incomplete, and for inoperable disease. In the latter group survival rates of 17 and 8·5 per cent at 5 and 10 years respectively are cited, and external radiotherapy is stated to be especially effective in medullary carcinoma. The tumour dose should be 5000–6500 rad to an adequate target volume. Preliminary data also showed the value of radio-isotope therapy for inoperable disease.

The discussions about chronic granulocytic leukaemia reveal its seriousness and the inadequacy of present therapy. The position regarding Hodgkin's disease is much better, however, for important advances have occurred in our understanding of this disease, including more precise histological diagnosis and staging, better clinical evaluation, and combined therapy with adequate supportive treatment. This is reflected in a marked improvement in prognosis. In the pathological staging of untreated patients with lymphoma, laparotomy and splenectomy are essential so that accurate therapy can be planned. There are also reports indicating that after splenectomy patients can tolerate larger amounts of radiotherapy and chemotherapy. An important point is made that diagnostic laparotomy provides an opportunity to transpose the ovaries from the radiation field, which is so important for pre-menstruating and menstruating females. The value of combined drug therapy is now accepted in achieving both complete and long remissions.

This volume contains many references for further reading, and whilst the text is in English there are additional sections of summaries and conclusions in Italian. There are many oncologists who will study this book with both interest and profit.

Blutgerinnung und Operation. By Professor Dr. ERWIN DEUTSCH, Wien. 9¾ × 7 in. Pp. 66 + vi. Illustrated. 1973. Berlin: Urban & Schwarzenberg. DM.19.80.

THIS monograph on blood coagulation and surgery was previously published in volume 5 of Breitner's *Surgical Textbook*. The physiology of the clotting mechanism is described in detail and the various tests available to diagnose the different diseases and conditions which interfere with normal blood-clotting are all described. The second half of the volume is devoted to the actual problems of practical surgery in patients with various clotting defects and the management is described in detail. There is a useful index and an extensive bibliography, and the book should be of particular interest to haematologists who are involved with surgical units.

Chirurgischer Ratgeber. By R. SCHROTH, Wittenberg. 7½ × 4¾ in. Pp. 315. Illustrated. 1972. Berlin: Veb Verlag Volk und Gesundheit. 19.80M.

THIS is a pocket book outlining most aspects of general surgery especially in relation to diagnosis and emergency treatment. The little book is full of sound advice and is illustrated by simple line diagrams.

The book contains 400 key sentences which are clearly marked and which summarize the important diagnostic or technical points, especially in relation to life-saving measures. Weekly or monthly medical journals might be well advised to copy and translate some of these key sentences and publish them as 'thoughts for the week'.

Oxygen Supply. Edited by M. KESSLER, D. F. BRULEY, L. C. CLARK, jun., D. W. LÜBBERS, I. A. SILVER, and J. STRAUSS, Dortmund, Germany. 9½ × 6½ in. Pp. 312 + xii. Illustrated. 1973. Berlin: Urban & Schwarzenberg. DM.78.

THIS is a report of a workshop on oxygen supply to the tissues and on oxygen, hydrogen, and enzyme polarography. The meeting was held in Dortmund in July, 1971, and was organized by D. W. Lübbers and M. Kessler. The 54 papers included in this volume were grouped into four sessions. The first session dealt with the theoretical

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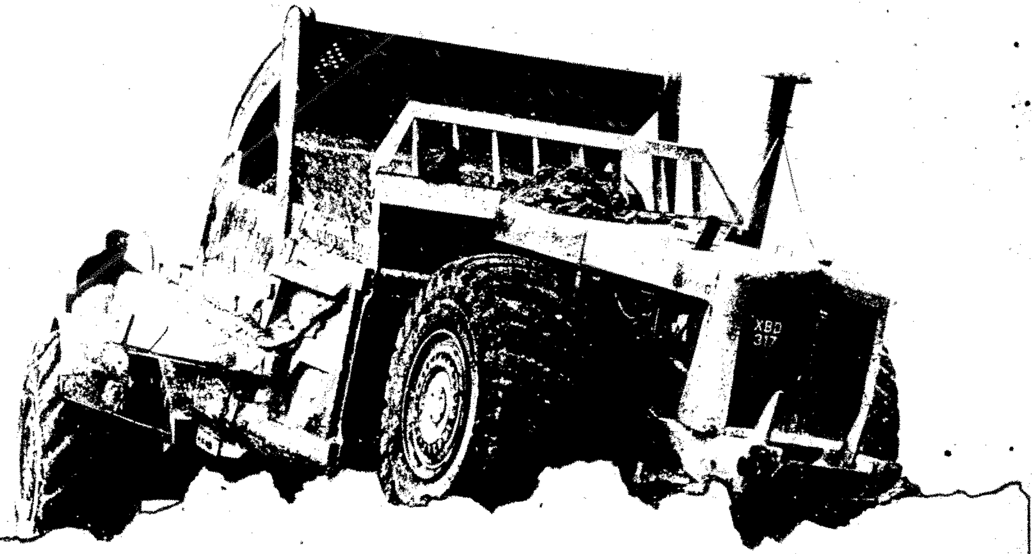

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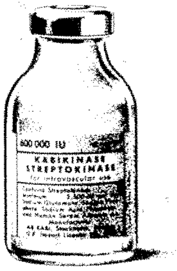

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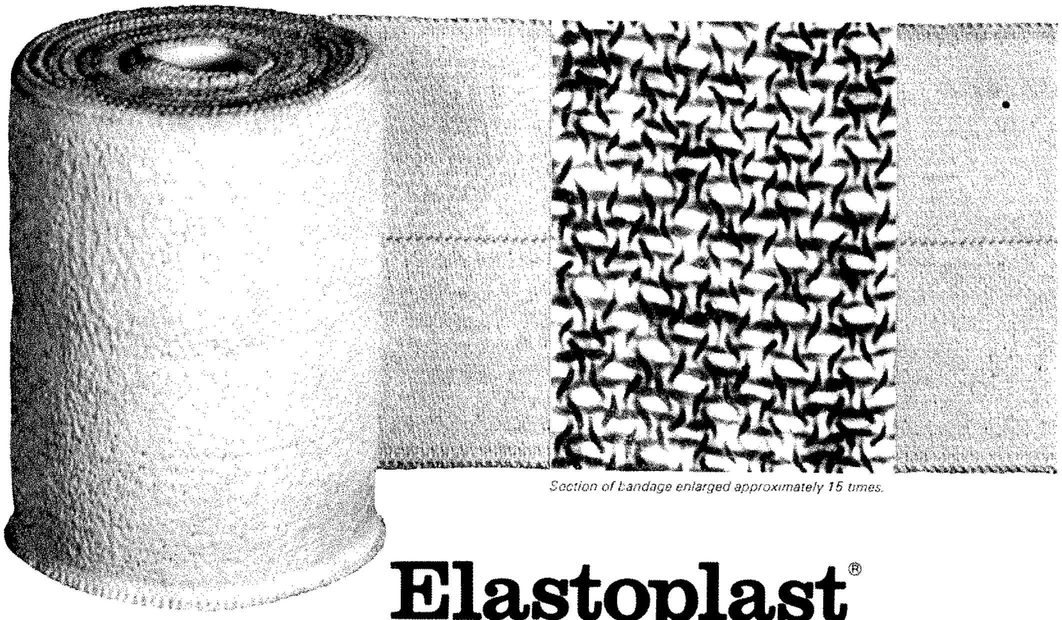

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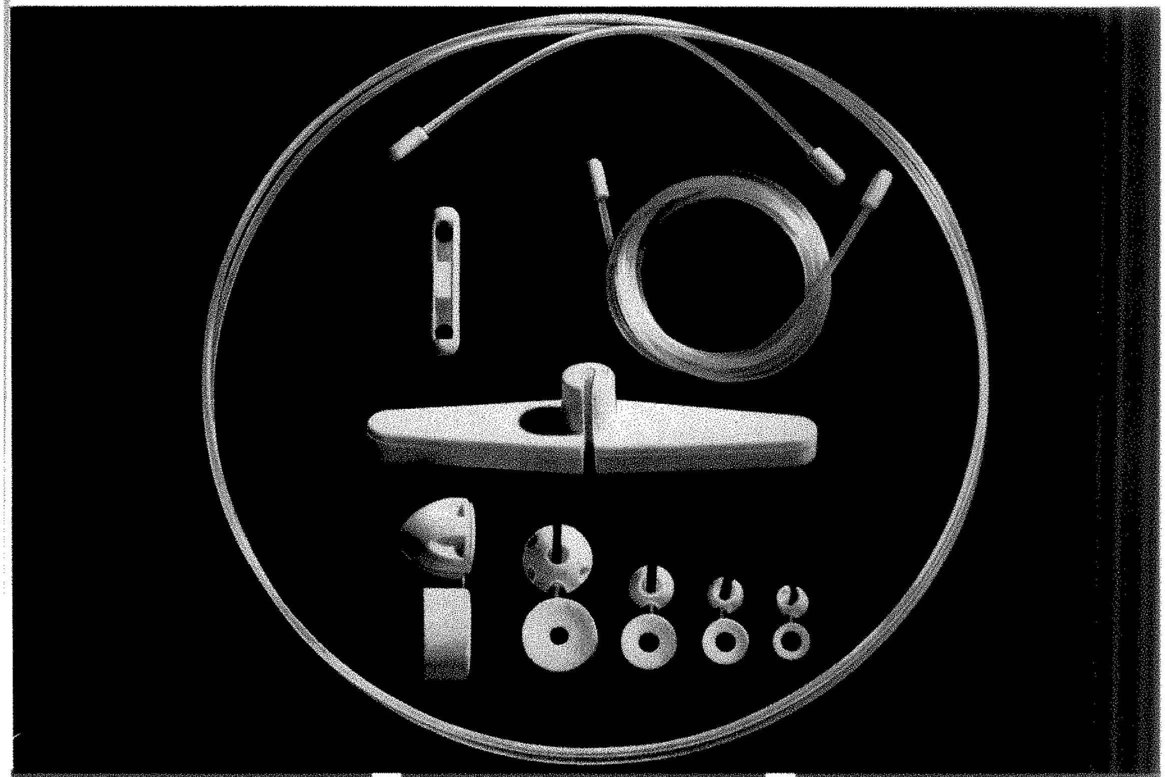

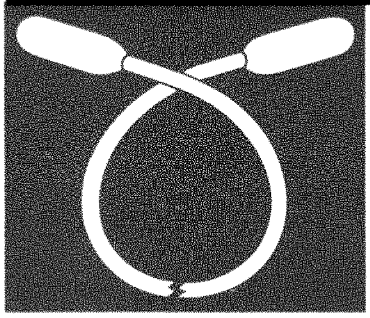

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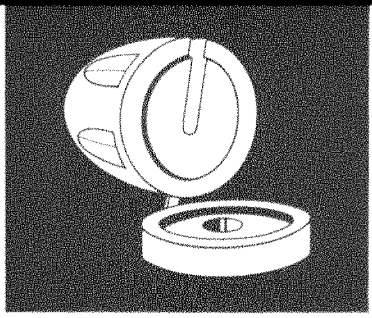

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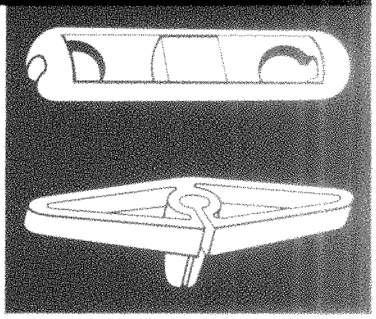

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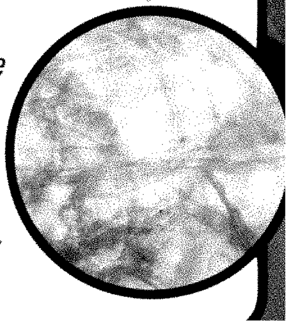

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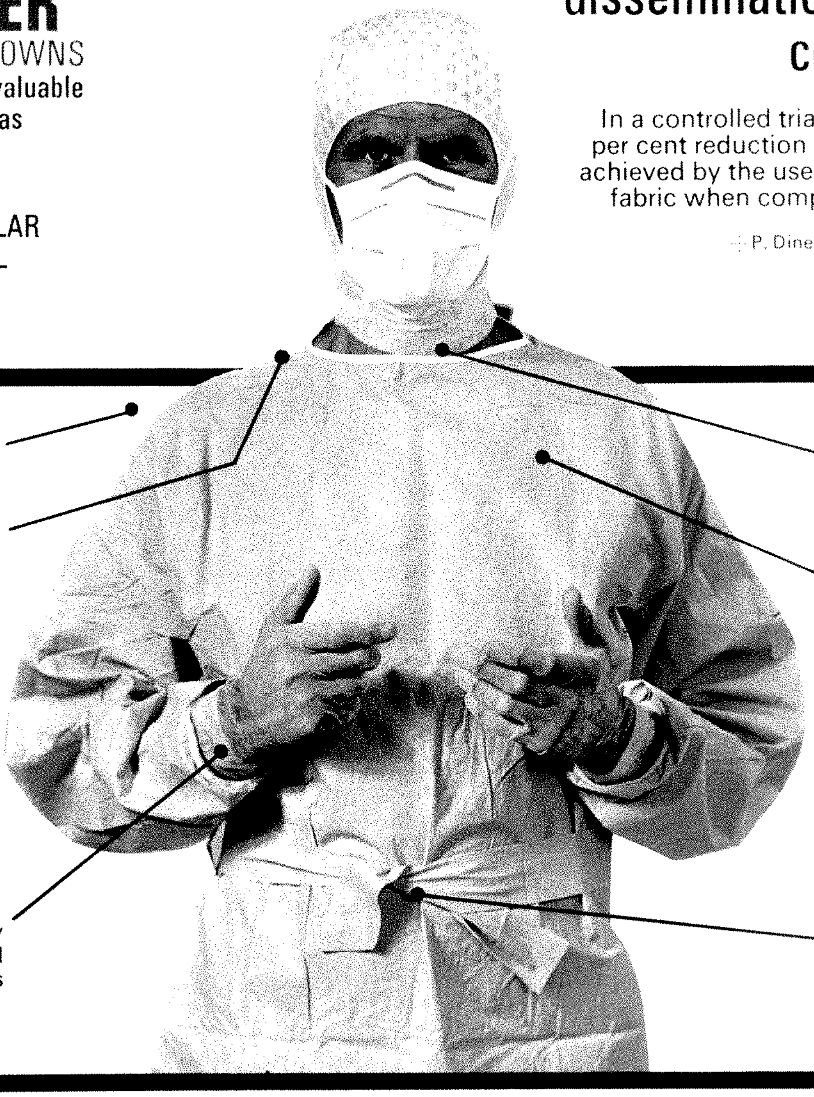

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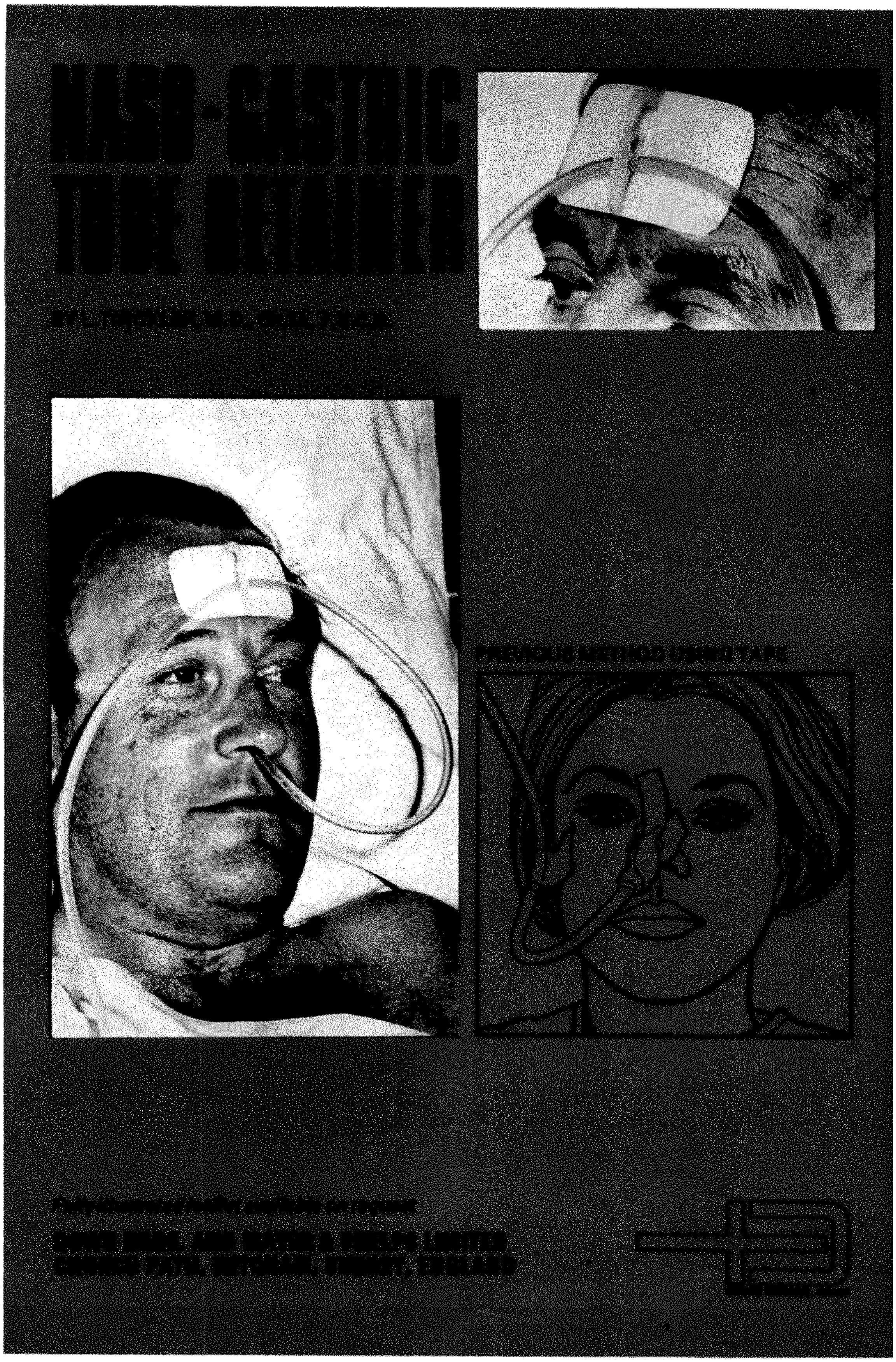

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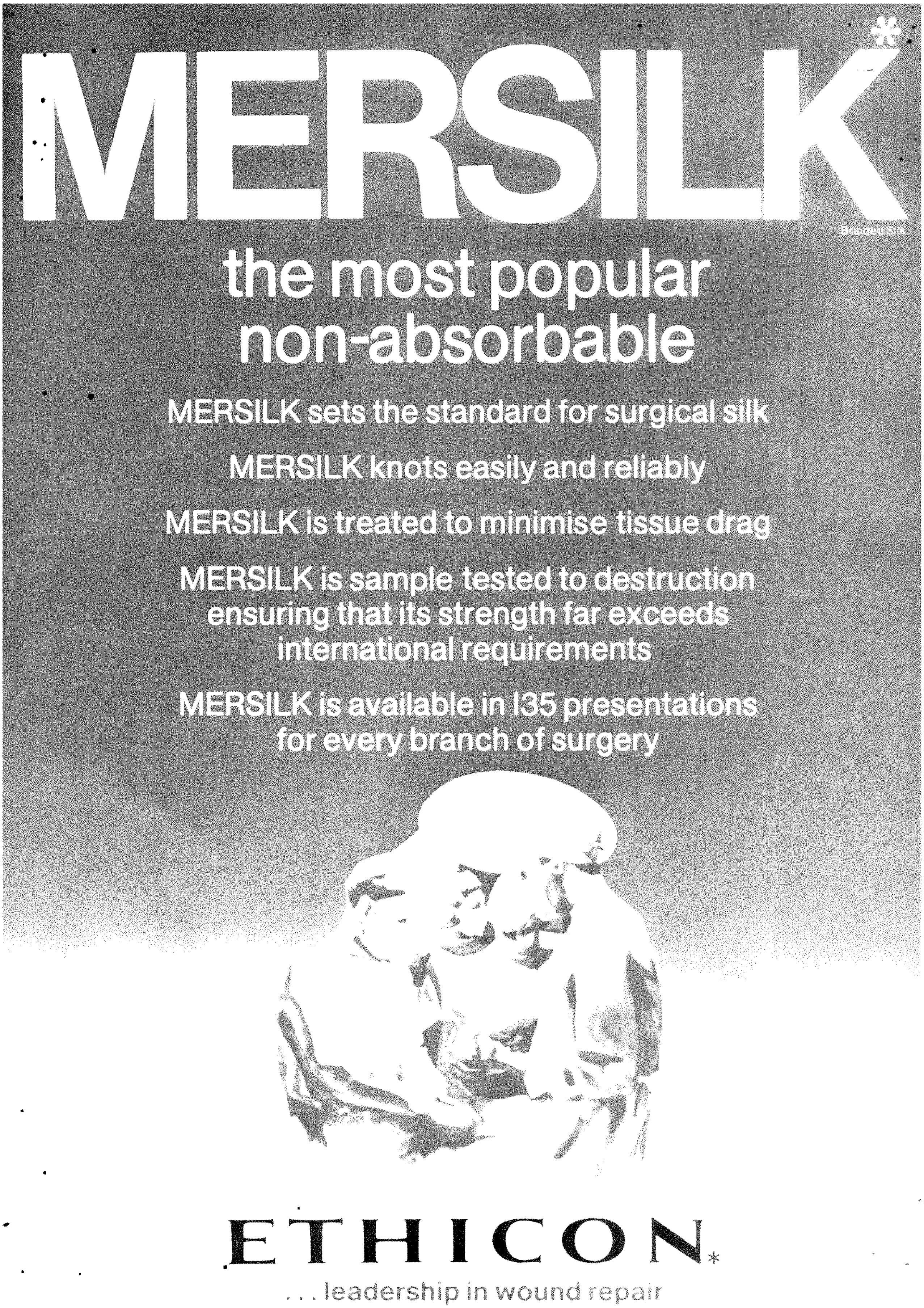

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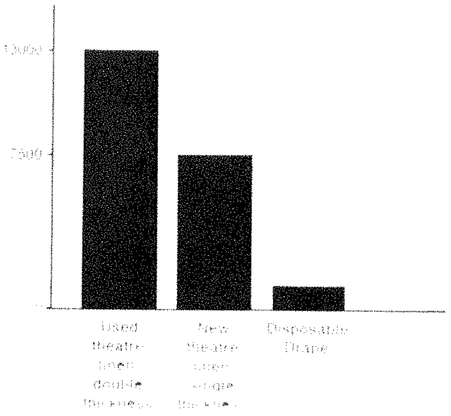
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1. Editorial *The American Journal of Surgery*, February 1952, Wm. C. Beck, M.D., Thomas S. Collette, B.A.
2. Penetration of Surgical Draping by Bacteria, Peter Dineen, M.D., Hospitals, *Journal of the American Hospital Association*, Vol. 43, Oct. 1st, 1969.

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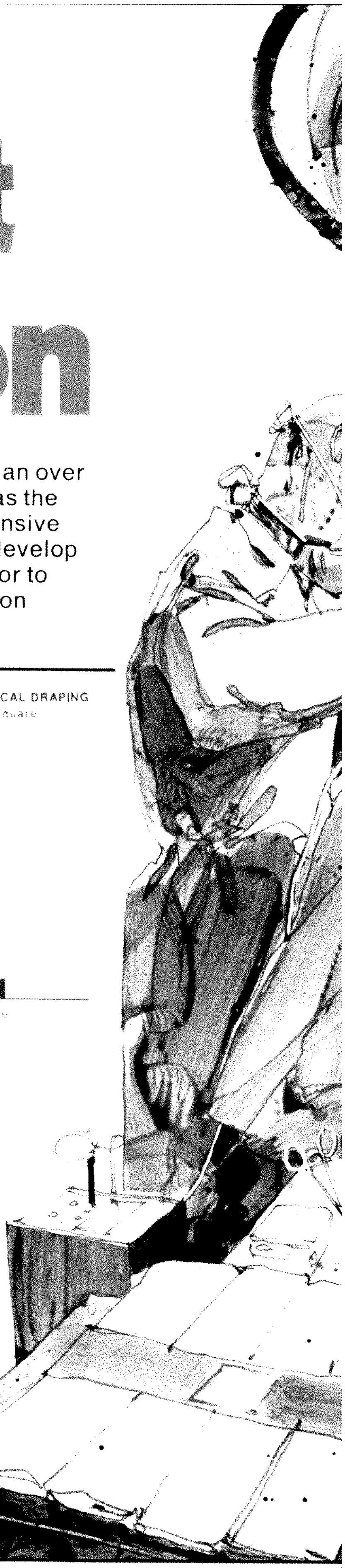

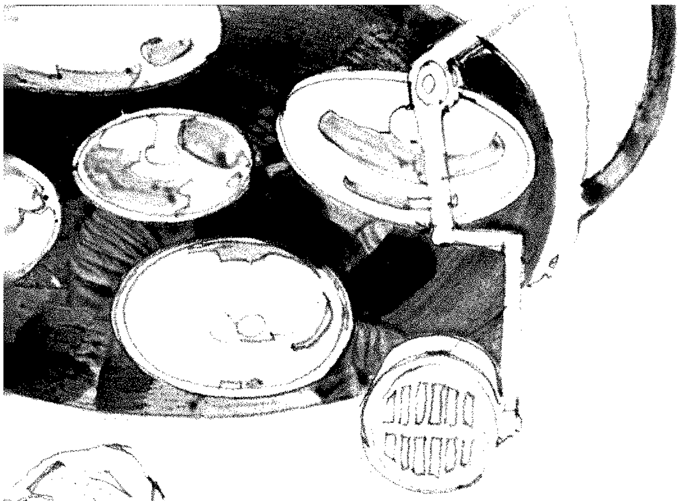

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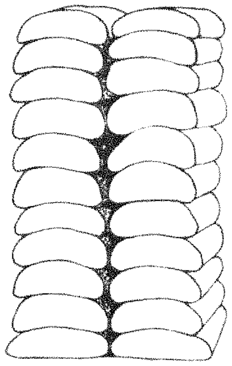

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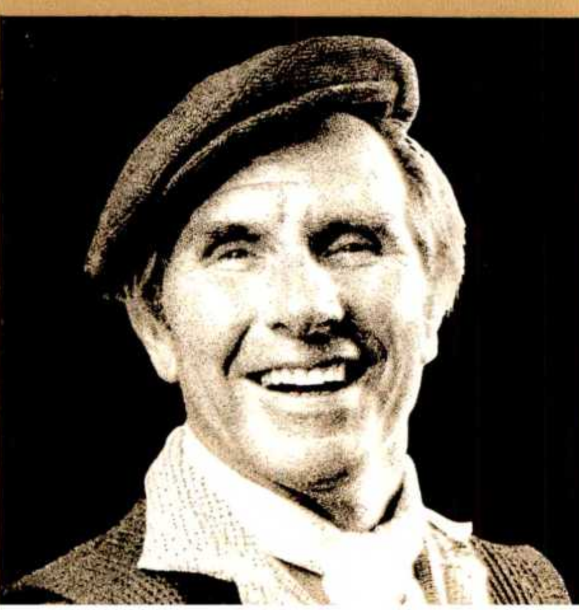

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References
1 *Brit med J*, (1969), **4**, 470
2 *Postgrad med J*, (1969), **45**, Supplement (November), 91
3 *S Afr med J*, (1970), **44**, Supplement (August), 12
4 *Med J Austr*, (1971), **1**, 526

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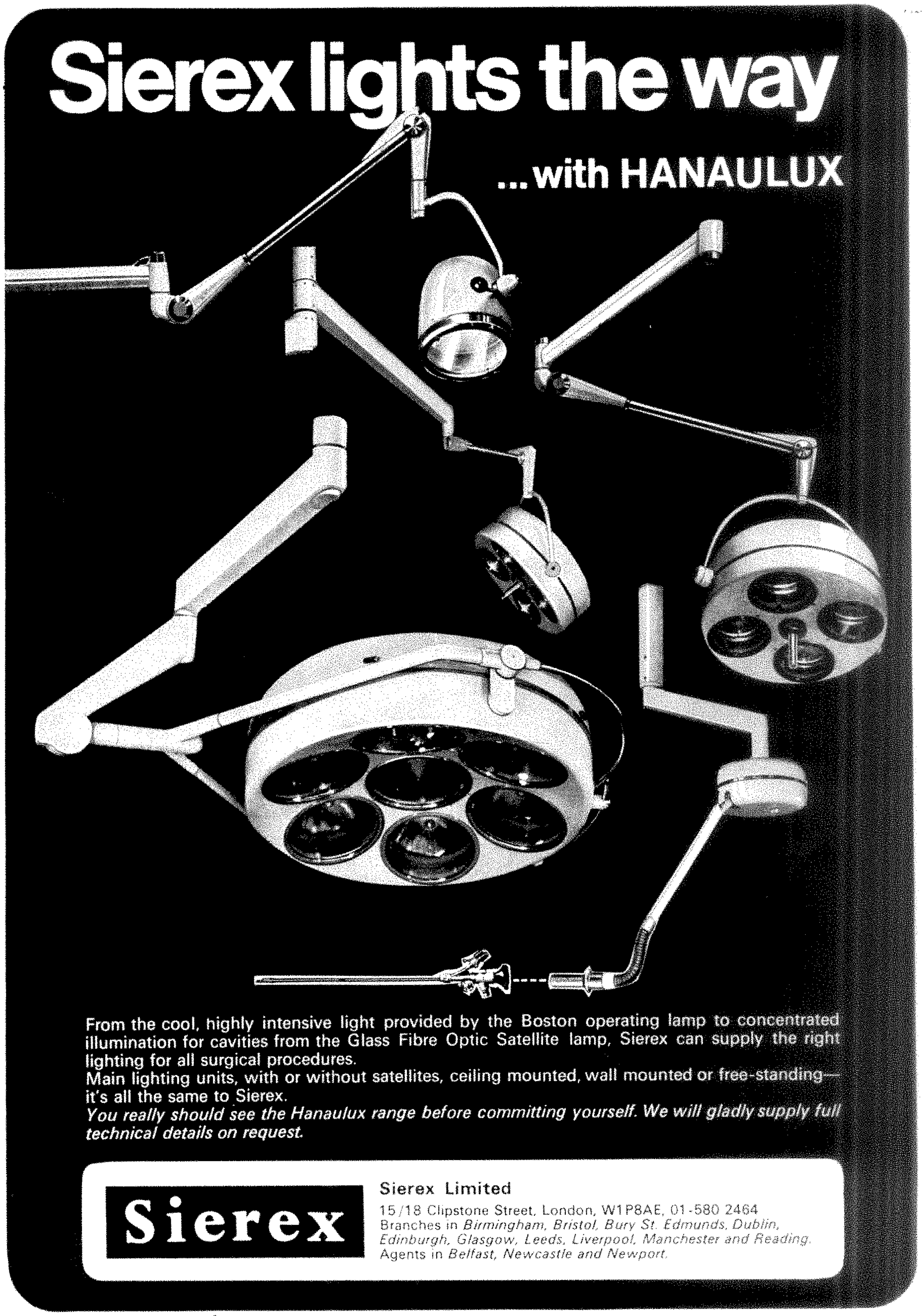

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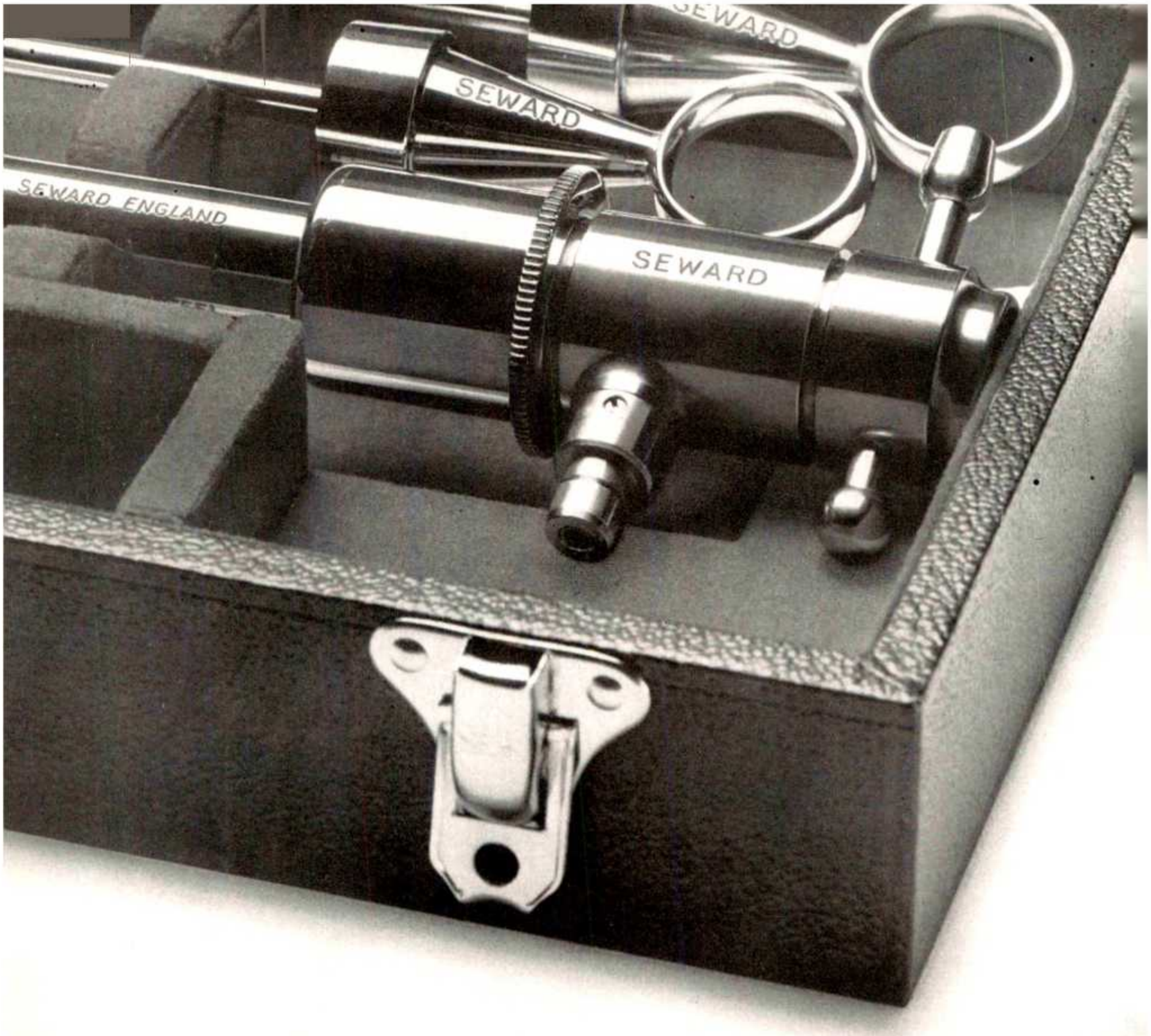

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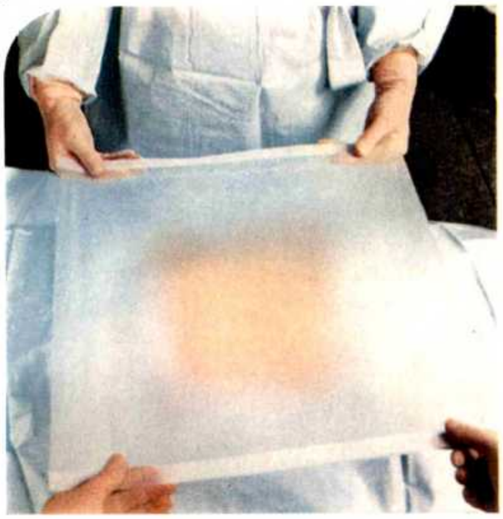

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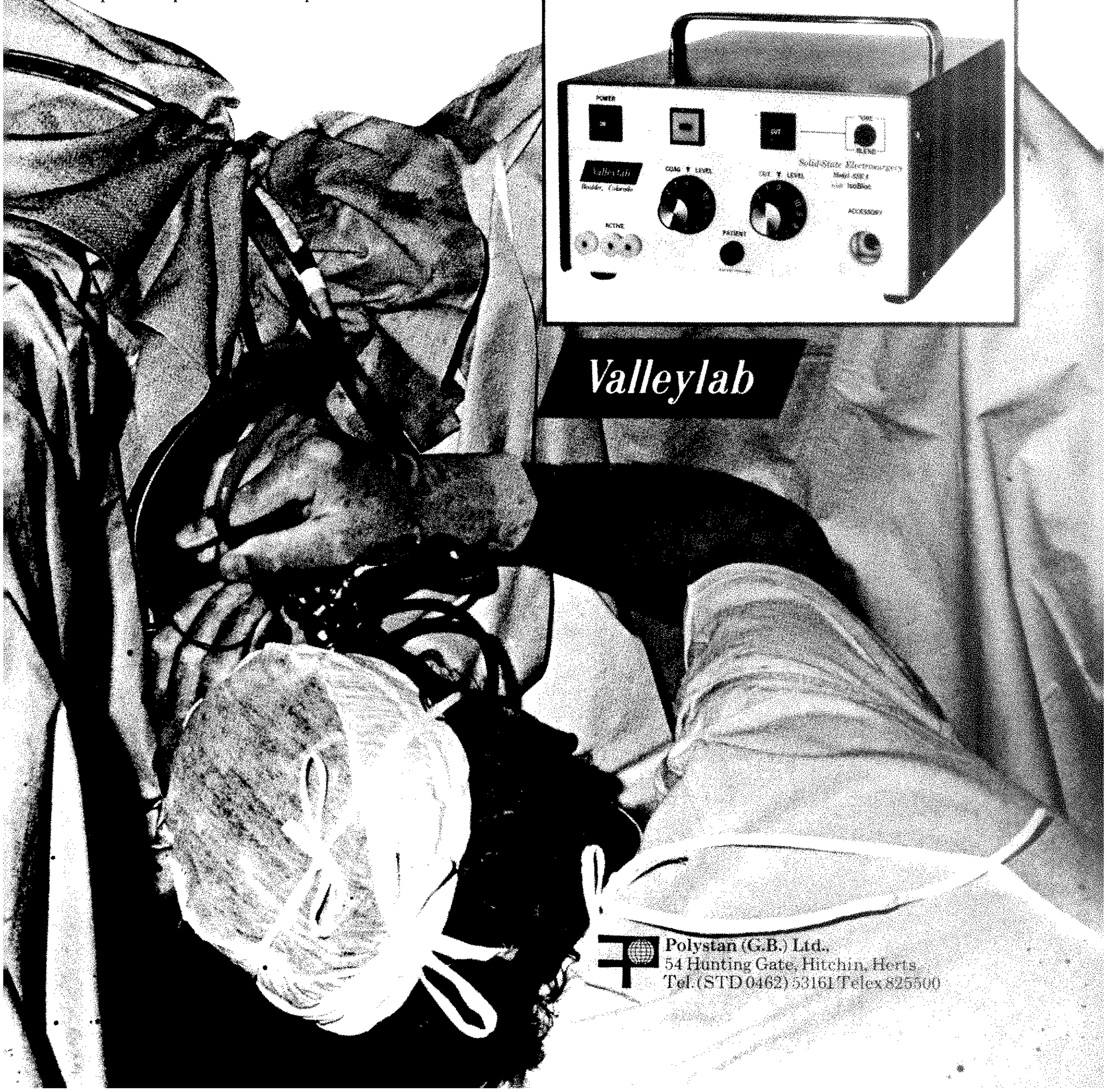

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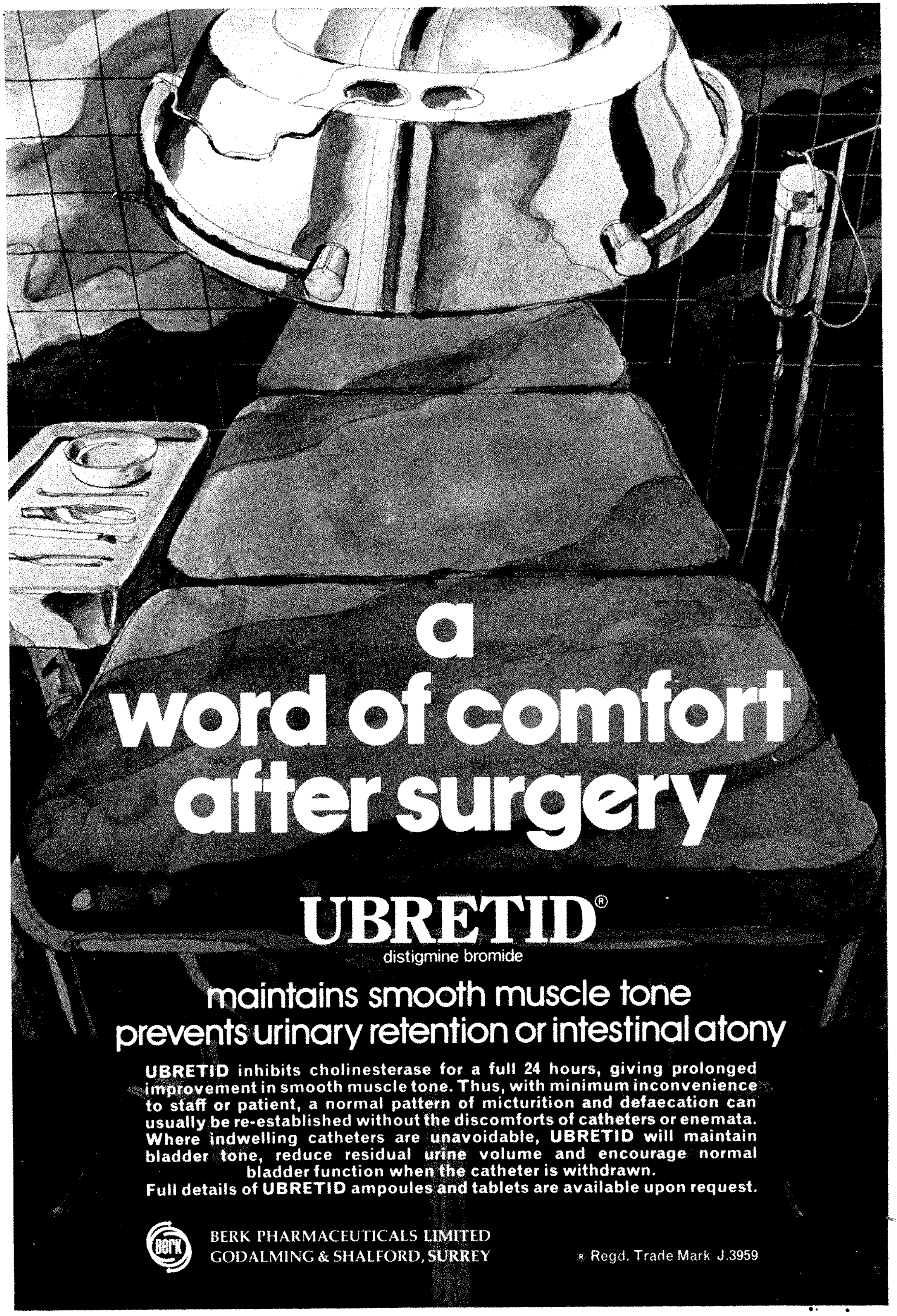

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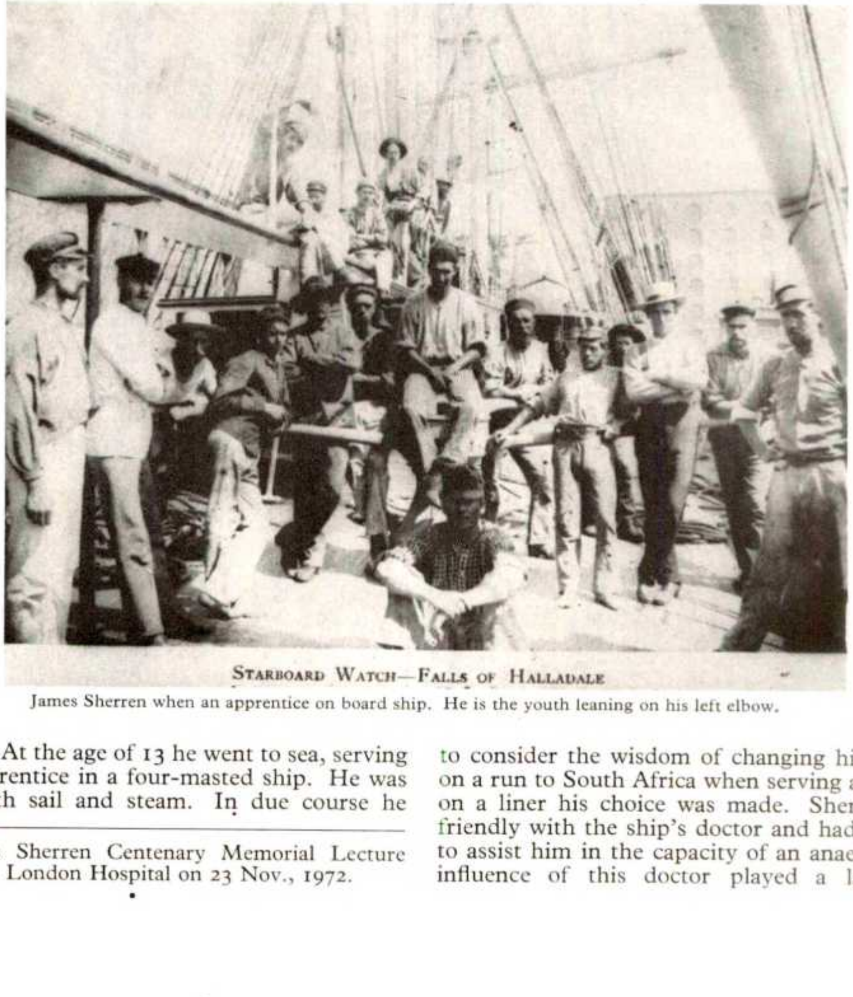
JAMES SHERREN—SURGEON AND SAILOR*

By A. M. A. MOORE
CONSULTING SURGEON TO THE LONDON HOSPITAL

JAMES SHERREN was born at Weymouth in 1872, just one hundred years ago. He was the son of John A. Sherren, a Justice of the Peace, who was a printer and publisher and a pillar of the Methodist Church. He was educated at Weymouth College. Early in his life he showed a great love of the idea of becoming a sailor and was very conscious that the sea has ruled our destinies. At the age of 13 he went to sea, serving first as an apprentice in a four-masted ship. He was trained in both sail and steam. In due course he obtained his master mariner's certificate (as Frederick Treves had done before him). He was 21 years of age at the time.



James Sherren when an apprentice on board ship. He is the youth leaning on his left elbow.

One can imagine that even in those early days he possessed an unusual determination and strength of character. Repeated attacks of malaria contracted at Delagoa Bay in Portuguese East Africa caused him to consider the wisdom of changing his calling, and on a run to South Africa when serving as chief officer on a liner his choice was made. Sherren was very friendly with the ship's doctor and had on occasions to assist him in the capacity of an anaesthetist. The influence of this doctor played a large part in persuading him to take up medicine. So began a career which was to enrich surgery.

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* The James Sherren Centenary Memorial Lecture delivered at the London Hospital on 23 Nov., 1972.

In May, 1894, Sherren entered the London Hospital as a student. It must have been difficult for one who had spent so many years at sea to take up studies in this new field, but he stuck to it and had a brilliant student career. He was awarded the prize in anatomy and physiology and in his final year gained scholarships in medicine and obstetrics.

James Sherren at the height of his career.

He was greatly influenced by the consultants under whom he worked. He served as clinical clerk to Sir Stephen Mackenzie and Dr. Gustav Schorstein, and as a dresser to Mr. Mansell Moullin and Mr. H. P. Dean, and to Sir Frederick Treves and Mr. Jonathan Hutchinson, junior. All these are famous names in the London Hospital's history. Sherren passed the Primary Fellowship of the Royal College of Surgeons in 1897 while still a student, and qualified in 1899.

After qualification he served as house physician to Dr. Sanson and Dr. F. J. Smith, whose portrait hangs in the Club's Union, house surgeon to Mr. Hurry Fenwick and Mr. Roxborough, receiving room officer, and finally junior and then senior resident accoucheur. When holding this last appointment he was President of the Residents' Mess. When he was junior resident accoucheur his senior was Dr. Cecil Wall, who later was to be the distinguished physician on the consultant staff of the London Hospital.

In 1900 he passed the Final Fellowship of the Royal College of Surgeons of England. His parents presented him with a suitably inscribed gold watch to celebrate his success. Early in 1901 he was appointed surgical registrar at the same time as Henry Newland, who was later to be the first President of the Royal Australasian College of Surgeons. Sir Henry Newland, as he became, used to visit the London Hospital frequently in later years. I first met him at the centenary meeting of the British Medical Association in 1932 when I was Sir Henry Souttar's registrar. In December, 1902, at the age of 30 James Sherren was appointed to the surgical staff of the London Hospital as assistant surgeon on the retirement of Mr. Waren Tay, the famous general surgeon and ophthalmologist whose name is remembered as one of the describers of Tay–Sachs disease. This was 8½ years after he had started as a medical student, a most remarkable record. At the same time in 1902 he was appointed surgeon to Poplar Hospital, which at that time was closely associated with the London Hospital, and surgeon to the Stanmore Cottage Hospital.

He quickly showed his soundness of judgement and technical skill and the fact that he could tackle almost any surgical problem.

For some years he served as a demonstrator of anatomy and of surgical pathology, and from 1903 to 1911 he lectured on elementary clinical surgery.

In 1908 he was joint editor with Sir Robert Hutchinson of the *Index of Treatment* published in Bristol.

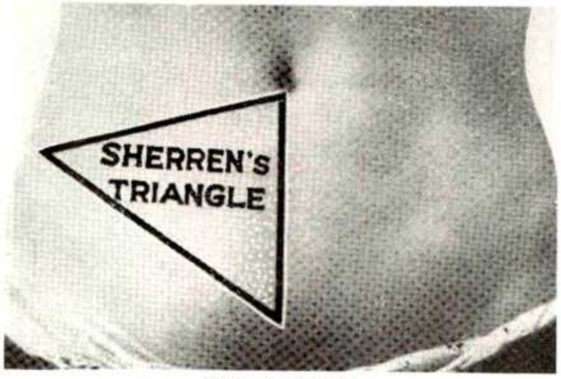
James Sherren did pioneer research work with Sir Henry Head, the brilliant neurologist, on the peripheral nervous system, and in 1908 published a *Monograph of Injuries of Nerves and Their Treatment*. In the First World War injuries of nerves were studied with great care. Much of this work was based on Sherren's monograph. The observations of Head, Rivers, and Sherren upon the nature of cutaneous sensation and its division into various types of sensitivity was derived from a study made upon the division of a cutaneous nerve in Head's forearm. This was done by Sherren. They described two sorts of sensitivity, namely, one of a delicate discriminatory sort (epicritic) and another of a vague coarse type of sensation (protopathic). Head and Sherren investigated the sensory qualities of the gastro-intestinal mucous membrane. They showed that ice-cold water and water at 50° C. introduced directly through gastrostomy and colostomy openings would give rise to sensations of cold and warmth usually in the region of the umbilicus. They finally concluded that the oesophagus and anal canal are always sensitive to heat and cold, the stomach rarely so, and the colon to a very limited extent.

They believed that most pain in visceral disease is referred and not direct. Head and Sherren showed that the afferent fibres running with motor nerves when stimulated by pressure cause pain and painful contractions of muscles. In peritonitis the nerves themselves are directly affected by the inflammation of the parietal peritoneum. This is the cause of the widespread rigidity of the abdominal wall in diffuse peritonitis. Sherren made a special study of the prognosis and treatment of brachial plexus, birth injuries, and the so-called Erb–Duchenne paralysis. He considered that the prognosis is on the whole favourable, but that unless improvement is evident within 3 months of delivery complete recovery is rare.

Albert John Ochsner, who had been born in Wisconsin and claimed to be directly descended from Vesalius, was Professor of Clinical Surgery in the

University of Illinois. In 1902 he published a *Handbook of Appendicitis*, in which he advocated the delayed treatment of this disease. At the same time Sherren championed the cause of the delayed treatment of appendicitis in this country and trained his assistants in its principles. In the *Practitioner* of June, 1905, he wrote: 'If we are able to see a case within the first 24 to 36 hours when the disease is probably limited to the appendix, operation should be performed and the appendix removed. After this most favourable time has passed I am strongly of the opinion that if possible we should wait until the attack is over and remove the appendix in a quiescent period in three months' time.' He emphasized that this method of treatment, which has come to be known as the Ochsner–Sherren régime, must only be undertaken in a hospital with a fully staffed theatre available at all times in case the patient's condition showed signs of deteriorating and an operation had to be undertaken without delay.

Sherren's description of the appendix triangle, which is outlined by lines joining the summit of the iliac crest, the pubic tubercle, and the umbilicus, refers to an area of skin hyperaesthesia met with in obstructive appendicitis and indicates that the appendix is distended and may burst at any moment. This is a certain indication for immediate surgery. This observation was one of the outcomes of the research he had carried out with Sir Henry Head on the problem of cutaneous hypersensitivity in visceral disease.



Sherren's triangle.

With the passage of time Sherren became more and more interested in abdominal surgery. At first he was a follower of Sir Frederick Treves who had performed the first properly recorded appendicectomy in the London Hospital in 1887, but on the early death in 1908 of Harold Barnard, a surgeon of the highest promise who had written the classic description of subdiaphragmatic abscess, Sherren decided to confine himself largely to abdominal surgery, which was then a rapidly growing speciality, and he quickly made an outstanding reputation.

His predominant surgical interest became the treatment of duodenal ulcer. This condition had first been treated by Codivilla in 1893 by the operation of gastrojejunostomy. During the early years of this century this procedure was developed in great measure by Moynihan, W. J. Mayo, and Sherren.

It is interesting to record Sherren's own description of the operation written in 1911:—

> 'The abdomen should be opened by displacing the right rectus muscle. The ulcer is usually found on the anterior surface of the first part of the duodenum. The peritoneum over it presents a speckled reddish appearance and a definite induration can be felt between the examining finger and the thumb. There may be adhesions binding the duodenum to the gall bladder and liver. In every case the appendix and gall bladder should be examined and treated if necessary. After examining the stomach for signs of ulcer, a posterior vertical no loop gastrojejunostomy should be carried out. That this is sufficient in most cases is shown not only by the long series recorded in which absolute relief of symptoms occurred, but by demonstration at a second operation performed later for some other condition.'

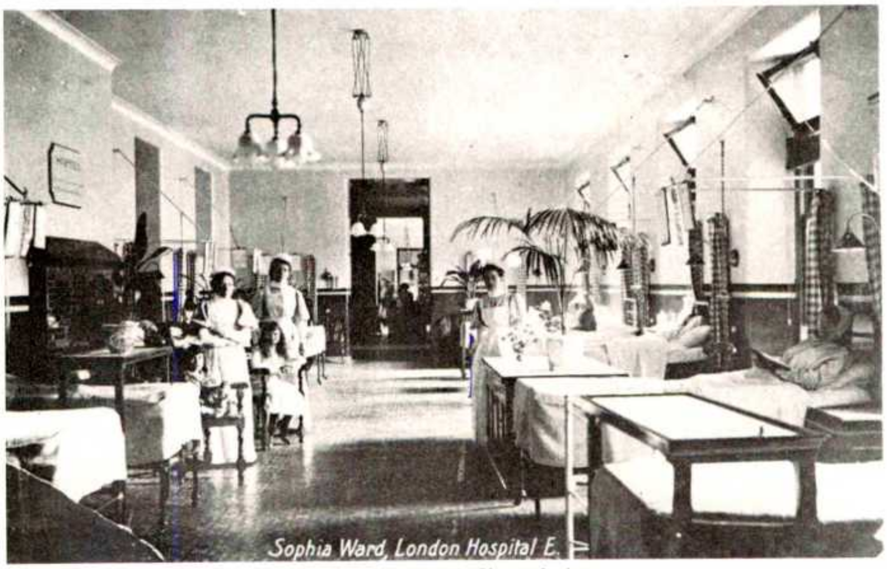
Sir Frederick Treves in his earlier years.

This operation was generally regarded at the time as giving extremely good results. Shortly before his retirement Sherren reported 537 cases of duodenal ulcer that he had operated on with 10 deaths. At about the same time Moynihan reported 563 cases with a mortality-rate of 0·53 per cent, and at the Mayo Clinic in the period 1914–19, 2734 cases were recorded with a mortality-rate of just 1 per cent.

In 1921 Sherren published a series of lectures on the stomach and duodenum, and was responsible for the chapters on the stomach and duodenum in Choyce's *System of Surgery*.

In addition to numerous operative procedures, Sherren devised a retrocolic anterior gastrojejunostomy of special use in relieving the symptoms in cases of inoperable carcinoma of the stomach. Donald Balfour of the Mayo Clinic made much use of this procedure.

Sherren's success as an abdominal surgeon created a great impression on the medical profession all over the world. His very distinguished colleague Sir Robert Hutchison, later to be President of the Royal College of Physicians, on whom he had successfuly operated for a duodenal ulcer, spoke of him in these words: 'He was, perhaps with the exception of Moynihan, the best abdominal surgeon of his day, and not a few of his colleagues owed much to his care and professional skill.' I am grateful to Sir Peter Hutchison, Sir Robert's son, for this helpful information. He confirms his father's high regard for the professional ability of Sherren and mentions that in 1907 his mother and Mrs. Sherren used to go for carriage drives together when they were expecting their first babies.



Sophia Ward as it was in Sherren's time.

Amongst his junior colleagues who had developed the greatest regard for him was Russell Howard, who in time was to become one of the most distinguished surgical teachers this country has produced. Sherren was an excellent diagnostician and a meticulously careful surgeon. His punctuality was proverbial and if he was due at the London Hospital at 2 p.m. the hall porter clocked him in at 1.59 p.m. with the greatest regularity. As a student I can remember waiting in the front hall for his arrival. He would step out of his car, walk into the front hall, shake hands with his registrar and house surgeon, and then, followed by the firm, walk to the staff room where he put on a white coat and emerge to commence his ward round in Sophia Ward just after 2 p.m. He expected his dressers to be exactly on time for all his ward rounds. I must quote from a letter from Dr. William Evans who was on his firm. He says: 'My old chief was a brilliant operator and never once late for an appointment whether to meet his equals or his betters or his humble dressers.'

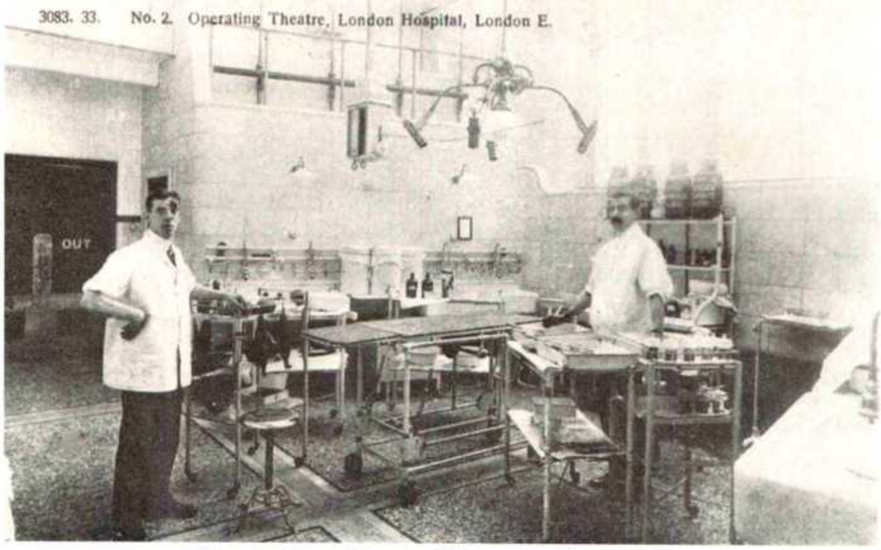
James Sherren was frequently consulted by Miss Eva Luekes, a remarkable woman who was Matron of the London Hospital for 39 years, on the problems of the training and education of the student nurses, matters in which he was intensely interested. For many years he was Surgeon to the Nursing Staff and performed numerous operations on our nurses. At this time sick nurses were admitted to Upper Wards, and the Sister in charge had the intriguing idea of getting every nurse that Mr. Sherren had operated on to embroider a special scarf with her initials. This scarf was presented to Mr. Sherren on his retirement. After his death it was given to the London Hospital where I was able to trace it in the Archives.

At the Royal College of Surgeons Sherren played a very active part. In 1906 he was Erasmus Wilson Lecturer in Surgical Pathology and in 1909 he became an examiner in anatomy for the Primary Fellowship examination. In 1917 he was elected to the Council of the College. In 1920 as a Hunterian Professor he delivered a lecture on: 'Late results of the surgical treatment of chronic ulcers of the stomach and duodenum'. This lecture was published in the *Lancet* on 27 March, 1920. He served as a member of the Court of Examiners from 1921 to 1923 and in 1925 was Bradshaw Lecturer. His subject for this lecture was 'Gastro-jejunostomy'. This lecture was also published in the *Lancet* on 14 Nov., 1925. Mr. Sherren was elected Vice-President of the College in 1925 and 1926. In the University of London he served as an examiner in surgery for the final medical degrees and for the Mastership in Surgery. He was also a member of the Senate of the University.

During the First World War he served with the rank of Colonel in the Army Medical Service as a consultant surgeon attached to the War Office, as surgeon to the King George Military Hospital and to the King Edward VII Hospital for Officers, and as consulting surgeon to the Yarrow Military Hospital at Broadstairs. In 1919 he was honoured by being made a Commander of the Most Excellent Order of the British Empire.

At the summit of his career when he had become a full surgeon to the London Hospital his private practice was enormous. He practised at 6 Devonshire Place and most of his private operating work was done at Fitzroy House which was almost his own nursing home. His numerous famous private patients included Sir Pelham Warner, the eminent cricketer, who referred to him with great gratitude in his biography.

Sherren was a man who owed his advancement to sheer ability and strength of character. For many years whenever he operated his theatre would be crowded with visiting surgeons from abroad, particularly from the United States of America, who had come to witness his great technical skill. It was at this time, before green operating kit had become popular, that Sherren gave instructions that the dressers on his firm should wear green caps in the theatre so that he could easily recognize them when he was operating and direct questions to them. These caps were changed to blue after some years.


3083. 33. No. 2. Operating Theatre, London Hospital, London E.
OUT

Operating theatre No. 2 that Sherren worked in at one time.

Sherren had greatly impressed Lord Knutsford, that greatest of all hospital chairmen and affectionately known as the 'Prince of Beggars', who presided over the hospital's destiny from 1896 to 1933. I well remember when I was a junior student seeing Lord Knutsford and Mr. Sherren walking along a corridor arm in arm in deep and earnest conversation.

Amongst his many gifts Sherren was an accomplished violinist. Sir James Walton, who had been his registrar and on whom the mantle of Sherren descended, spoke of him in the following terms: 'As a chief Jimmy Sherren, as he was affectionately known, was a little frightening but very invigorating. Slackness and slipshod work were intolerable to him and he did not mind saying so. But he liked to be stood up to and respected the sharp retort. In the conventional sense he was ambitious, but his ambition was not of the selfish kind. He wanted the work he was responsible for to be done supremely well. There was a burning zeal about the way he worked and there was something inspiring about that restless, incredibly efficient small man with the sailor's rolling gait.'

He was unceasing in his search for truth. One of his distinguished colleagues has said that it was when he became to know him socially that he realized that there was a great humility about him, coupled with a streak of kindliness which he was very reluctant to show.

It must always be remembered that this great surgeon was working in the days before the discovery of penicillin and the other antibiotics, and he did not have the benefits of modern anaesthesia, pathological and radiological investigations, and the advances in blood transfusion.

In 1926 at the height of his career when he had gained a reputation not only in Britain but throughout the civilized world which he shared only with Lord Moynihan of Leeds, Finisterer of Vienna, and Balfour of the Mayo Clinic he suddenly decided to retire.

Sir Henry Souttar has described the dramatic fashion in which he took his leave of the London Hospital: 'One afternoon when he had finished his operating list, he took off his gloves and said to his senior theatre technician, Macgowan: "Well, goodbye, that was my last operation." He shook hands with everyone in the theatre and then, having changed in the surgeon's room, he went down in the lift alone.

'In the front hall waiting for him was Sir Ernest Morris, the House Governor, the only man who knew that he had resigned, holding his hat and coat. The hall porter came forward to turn off his light on the board, but Sherren waved him away, stood for a moment looking at his name, and then himself turned off the switch. He shook hands with Ernest Morris, and then left the scene of his surgical triumphs for ever.'

Within a few days of resigning from the staff of the London Hospital he left the Council of the Royal College of Surgeons. Sir Hugh Lett, later to be President of the Royal College of Surgeons, was elected to his vacancy on the Council.

Just as he had entered the London Hospital he left it dramatically. What the overwhelming urge was no one knows. Probably he felt again the call of the sea and was determined to answer it while still of an age to enjoy it.

I personally have no doubt that Mr. Sherren had had in mind the idea of returning to the sea as a ship's surgeon for a long time; a possible factor that may have influenced him was the 20-year rule that was in force at the London Hospital at that time. As far as I can determine he became a senior on a firm in 1911. This meant that he would have to retire from the staff in 1931, after 20 years as a senior, at the age of 59 years of age. He may have felt that it would be difficult to start a new life as a ship's surgeon at this age and this may have led him to decide to retire 5 years earlier at 54.

He could leave surgery with the satisfaction of knowing that seldom, if ever, had any man accomplished so much and advanced so far in the short 30 years or so that he had devoted to it.

Returning to his country home overlooking Poole Harbour he found that even here he was unable to rest on land, and so within a few months of retiring from the London Hospital staff, he went back to the sea as a ship's doctor, where he was able to do much to better the conditions of the marine medical service. He served as a ship's surgeon for the P. & O., the Orient, and the Cunard lines until shortly before the outbreak of the Second World War.

Soon after my own appointment to the consultant staff of the London Hospital in 1934 the staff gave a dinner at the old Langham Hotel in honour of Mr. Sherren, who had just returned from a trip to Australia as a ship's surgeon. My memory of him at this time was that he was a very impressive-looking man with a fine head of white hair and a fresh complexion.

In his speech replying to the toast of his health he told an amusing story. Shortly before the liner entered port he was called to see an elderly wealthy lady in her cabin. He gave her some advice about her abdominal trouble. She was loath to accept this. 'Doctor,' she said, 'thank you for seeing me, but I think I will wait until we land when I will consult a proper specialist.' It happened that the local medical association had heard that the ship's doctor of the incoming liner was the world-famous surgeon, James Sherren. They sent a deputation on board to welcome him and he was seen receiving them on the deck by the lady patient who was being taken on shore by stretcher. On inquiring she was told who the ship's doctor really was. As soon as she was settled in a nursing home she sent him a message of apology for her unwitting discourtesy, and begged him to call on her. He did so the next day, taking her a bunch of flowers.

He told of another amusing incident when he was summoned to see a lady patient in her cabin. It turned out that she was an old private patient who had paid him a large fee for an abdominal operation in London. She was indignant to find that after all he was only a ship's surgeon. His closing years were lived at White Barn, Broadstone, in Dorset, where he was able to indulge in his hobby of sailing and his favourite relaxations of golf and playing the violin.

During the Second World War he served on the staff of the local hospital and he died on 29 Oct., 1945, 2 days before his birthday, after a long illness, at the age of 73.

And so passed a figure memorable in the long story of the London Hospital. His life had been full, active, and varied, during the course of which he had earned the respect and admiration of all with whom he had worked and the real affection of his friends.

While Britain breeds such men her position in surgery remains assured.

PHYTOBEZOAR AFTER VAGOTOMY WITH DRAINAGE OR RESECTION

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SUMMARY

Two cases of bezoar formation after vagotomy and drainage are reported. A review of the literature reveals the stomach to be the most common site of bezoar formation after operations involving vagotomy, whereas most bezoars occurring after gastrectomy are found in the small intestine. The reasons for this difference are discussed, as well as the clinical features and treatment of bezoar.

THE word bezoar comes originally from 'pad-zahr', a Persian word meaning anti-poison. The reason for this terminology is that in primitive communities the solid masses found occasionally in the stomach of goats or other animals were accredited with magical healing, invigorating, and even youth-restoring properties. In man these masses are generally composed of densely entangled vegetable fibres (phytobezoar) or hair (trichobezoar).

Quain (1854) was the first to report an example of phytobezoar formation in an apparently healthy stomach, and there have been many subsequent reports of similar cases. In recent years several descriptions of bezoar formation after gastrectomy have suggested that this is a relatively specific complication of gastric resection (Ward-McQuaid, 1950; Norberg, 1961; Hollander, 1965; Olivier, Prévost, and Rettori, 1966; Cain, Moore, and Patterson, 1968; Pollard and Block, 1968; Vernon, 1969). In most of these patients the bezoar was found in the small intestine; for example, Olivier and others (1966) referred to 50 phytobezoars after gastric resection, 48 of which were in the small intestine.

The preponderance of bezoars in the small intestine after gastrectomy may be explained as a consequence of rapid emptying of gastric contents. Bezoars consist of a thick and concentrated chyme which is inadequately mixed and contains indigestible fibres of vegetable origin. In some patients the bezoar is in the gastric remnant, when a faulty anastomosis may be the aetiological factor.

Vagotomy with drainage or resection has been practised with increasing frequency for more than 20 years for the treatment of duodenal ulcer. Reports concerning the formation of phytobezoar after these operations are relatively recent. Olivier and others (1966) reported the first case of phytobezoar in a patient who had undergone vagotomy for recurrent ulcer after a previous gastric resection. Moseley (1967) published the first case of phytobezoar after vagotomy and pyloroplasty. The bezoar was discovered 2½ months after the operation.

Between 1963 and 1971 at the Pahlavi Medical Centre, Tehran University, we have performed 300 vagotomy and drainage procedures for the treatment of duodenal ulcer. Two cases of phytobezoar occurred after such a procedure.

CASE REPORTS

Case 1.—A 41-year-old man who had been submitted to vagotomy and gastro-jejunostomy for duodenal ulcer in February, 1967, remained well for 2 years, but in March, 1969, he was readmitted for cramp-like pains in the epigastrium of 1 month's duration. Barium-meal examination showed a perfectly patent anastomosis without any marginal ulcer. The stomach contained no residual fluid and the patient was discharged after being given some dietary advice. Four months later, i.e., 2½ years after vagotomy and gastro-jejunostomy, the patient was admitted again as an emergency with acute intestinal obstruction. The patient had suffered from subacute intestinal obstruction for 2 months, terminating in the acute episode. In spite of distension a sausage-shaped lump could be felt in the right iliac fossa. At laparotomy the small intestine was distended, and at about 60 cm. from the ileocaecal valve a hard sausage-shaped mass, 14 cm. long and 6 cm. in diameter, was felt in the lumen of the ileum. It was extracted by an enterotomy and was found to be a hard bezoar composed of unrecognizable fibres tightly entangled together. The gastrojejunal anastomosis was patent without any anastomotic ulcer. The duodenal ulcer had healed. The patient's postoperative course was uneventful. There was no history of any regular or frequent consumption of special fruits or vegetables. The patient left the hospital in a healthy condition. Since then he has been followed up as an out-patient; he remains well and there are no signs pointing to the formation of a new bezoar. He has been advised to avoid uncooked vegetables.

Case 2.—A 45-year-old man underwent vagotomy and gastrojejunostomy for duodenal ulcer in October, 1966. The postoperative course was satisfactory and the patient was in good health for 6 months. After that period he started complaining of vague abdominal pains accompanied by food and biliary vomiting. These symptoms persisted intermittently with varying intensity for nearly 2 years. Medical treatment gave only temporary relief. In November, 1969, i.e., 3 years after vagotomy and gastrojejunostomy, the patient was readmitted as an emergency with acute intestinal obstruction of 12 hours' duration. At laparotomy the duodenum and the first loops of the jejunum were distended. Some 20 cm. below the duodenojejunal junction a hard sausage-shaped lump, 12 cm. long and 4 cm. in diameter, was felt in the lumen of the jejunum. It was found to be a bezoar which was extracted by an enterotomy. It was formed of vegetable fibres stuck tightly together. The gastrojejunal anastomosis was patent without any anastomotic ulcer. The duodenal ulcer had healed. The patient's postoperative course was uneventful and the patient was discharged in a satisfactory condition. He has been followed up for 6 months as an out-patient. There has been no symptom pointing to the formation of a new bezoar.

REVIEW OF LITERATURE

We have reviewed the literature on bezoar formation after vagotomy with drainage or resection (*Table I*), and, including the 2 cases presented here, have found 22 cases. In 17 of these, the bezoar was in the stomach, in 3 it was in the small intestine, and no information about the site was given in the remaining 2 patients.

DISCUSSION

Aetiology.—After gastric resection the majority of bezoars are found in the small intestine (Olivier and others, 1966), probably because of the rapidity of gastric emptying. This is in striking contrast to our finding that after vagotomy operations bezoars are most commonly found in the stomach. It may be presumed that this is related to the effect of vagotomy on gastric motility, and it is therefore of interest that Kuiper (1971) described a bezoar in the stomach of a patient with generalized myotonic dystrophy which he attributed to gastric retention.

Vagotomy has two important effects on the stomach:—

1. Decreased secretion of hydrochloric acid with a reduced peptic activity contributing to thickening of the gastric contents.
2. Decreased gastric motility so that the stomach is an atonic bag with a more or less flaccid antrum which does not accomplish its mixing, grinding, and propulsive actions effectively. Drainage procedures, i.e., gastrojejunostomy or pyloroplasty, or limited resections sometimes fail to relieve these disturbances of motility. This failure is because the motor disturbances of the stomach following vagotomy are occasionally so serious that it is not able to empty its contents adequately, even through a large and patent anastomosis. Slow emptying can also be due to narrowing of the anastomosis. Prolonged retention of food in a slowly emptying stomach, especially if the food contains large amounts of indigestible vegetable fibres, facilitates the formation of a bezoar. Gastritis resulting from retention of food produces an abundant quantity of gastric mucus, which enhances bezoar formation. The resection associated with vagotomy is often of limited extent and may include no more than the gastric antrum. The motor disturbances caused by vagotomy are probably more serious in the distal part of the stomach so that the more limited the resection is the worse the gastric retention may be.

Clinical Picture and Diagnosis.—The site of a bezoar determines the clinical picture. It is worth

Table I.—SUMMARY OF THE DETAILS OF CASES OF BEZOAR FORMATION AFTER VAGOTOMY REPORTED IN THE LITERATURE

AUTHOR	AGE AND SEX	INITIAL DISEASE	INITIAL OPERATION	INTERVAL (mth.)	METHOD OF DIAGNOSIS	SITE	TREATMENT
Bert (1966)	—	—	Vagotomy and gastric resection	—	—	—	—
Borg and others (1966)	—	—	Vagotomy, gastric resection, and Billroth-I anastomosis	—	—	Stomach	—
Collins and Miller (1966)	46 F.	Duodenal ulcer	Vagotomy and antrectomy	—	—	—	—
Olivier and others (1966)	28 M.	Duodenal ulcer	Gastric resection and then vagotomy	11	Laparotomy	Stomach	Larger resection with Billroth-II-Braun anastomosis
Riegel (1966)	62 F.	Duodenal ulcer	Vagotomy, gastric resection, and Billroth-II anastomosis	48	Laparotomy	Jejunum	Removed by jejunotomy
Moseley (1967)	67 M.	Duodenal ulcer	Vagotomy and pyloroplasty	2½	Laparotomy	Stomach	Gastrojejunostomy
Cain and others (1968)	60 F.	Duodenal and gastric ulcers	Vagotomy, antrectomy, and Billroth-I anastomosis	3	Radiography and gastroscopy	Stomach	Conservative
Pollard and Block (1968)	52 M.	Duodenal ulcer	Vagotomy, antrectomy, and Billroth-I anastomosis	48	Radiography	Stomach	Conservative
Sparberg and others (1968)	43 M.	Gastric ulcer	Vagotomy, antrectomy, and Billroth-I anastomosis	3	Radiography	Stomach	Conservative
Szemes and Amberg (1968)	62 M.	Duodenal ulcer	Vagotomy, gastric resection, and Billroth-I anastomosis	½	Radiography	Stomach	Conservative
	46 M.	Duodenal ulcer	Vagotomy, gastric resection, and Billroth-I anastomosis	1	Routine radiography	Stomach	—
	44 M.	Duodenal ulcer	Vagotomy, gastric resection, and Billroth-I anastomosis	26	Routine radiography	Stomach	Removed by gastrotomy
	43 M.		Vagotomy, gastric resection, and Billroth-I anastomosis	3	Routine radiography	Stomach	Refused
	53 M.	Malignant pre-pyloric ulcer	Vagotomy, gastric resection, and Billroth-I anastomosis	36	Radiography and gastroscopy	Stomach	
Rigler (1970)	36 M.	—	Vagotomy, gastric resection, and Billroth-II anastomosis	12	Radiography and gastroscopy	Stomach	Conservative
	45 M.	—	Vagotomy, gastric resection, and Billroth-II anastomosis	36	Radiography	Stomach	Conservative
Benoit and others (1971)	63 M.	Duodenal ulcer	Vagotomy and pyloroplasty	10	Radiography and gastroscopy	Stomach	Conservative for 5 recurrences
	41 M.	Duodenal ulcer	1. Vagotomy and gastrojejunostomy 2. Pyloroplasty	26	Gastroscopy	Stomach	
Sanderson and others (1971)	37 F.	Duodenal and gastric ulcers	1. Gastric resection and Billroth-II anastomosis 2. Vagotomy and Braun anastomosis 3. Billroth-I anastomosis	37	Radiography	Stomach	Conservative, then pyloroplasty
	50 M.	Recurrent hiatus hernia, then gastric ulcer	Vagotomy and pyloroplasty for recurrent hiatus hernia. Gastric resection and Billroth-I anastomosis for gastric ulcer	14	Radiography	Stomach	Conservative
Mir and Mir (1973)	41 M.	Duodenal ulcer	Vagotomy and gastrojejunostomy	30	Laparotomy	Ileum	Removed by ileotomy
	45 M.	Duodenal ulcer	Vagotomy and gastrojejunostomy	36	Laparotomy	Jejunum	Removed by jejunotomy

noting that a bezoar in the stomach may be completely symptomless and has been found in 3 patients submitted to routine postoperative radiographic examination (Szemes and Amberg, 1968). More interesting still is the fact that in some patients the surgical removal of the bezoar or successful medical treatment leading to its dissolution has not eliminated all the symptoms attributed to the presence of the bezoar (Benoit, Fays, and Hoeffel, 1971). It seems that many of the symptoms are in fact nothing more than the signs and symptoms of delayed gastric emptying.

When the bezoar is located in the stomach the patient suffers from early satiety, a gradual onset of epigastric fullness, especially of a postcibal type, nausea, and vomiting. Emaciation and weight-loss due to malnutrition follow. The bezoar in the stomach sometimes produces a ball-valve mechanism; it causes intermittent obstruction of the anastomosis leading to severe gastric retention and then is suddenly disimpacted to allow gastric evacuation.

In the majority of the patients the bezoar has been discovered by radiographic examination (*Table I*). The characteristic radiological findings are well described by Szemes and Amberg (1968) and Rigler (1970). Barium-meal examination shows one or more spherical masses in the stomach around which the barium flows readily. Careful examination will show that the mass is movable and not attached to gastric mucosa. A delayed radiograph reveals some residual barium covering the surface or imprisoned inside the bezoar. A plain radiograph taken in the upright position sometimes shows the dome-shaped superior surface of the floating bezoar contrasting with the gastric air-bubble.

Treatment.—When the bezoar is in the small intestine the patient presents the picture of acute intestinal obstruction, and emergency laparotomy should be performed in all cases. An attempt should be made to fragment or to squeeze the bezoar gently into the caecum. According to Vernon (1969) this procedure is successful in 38 per cent of cases. Removal of the bezoar by enterotomy should be performed if these measures fail.

The treatment of a bezoar in the stomach is never an emergency surgical procedure. The case should be treated conservatively at first and this is often successful. A phytobezoar is formed of vegetable fibres with a small quantity of protein and much gastric mucus. It is possible to disorganize the bezoar by the administration of papain, a powerful proteolytic enzyme, which acts in an acid as well as in an alkaline medium. Experience has shown that papain is more efficient when used in association with sodium bicarbonate. According to Sanderson, Ibberson, and Fish (1971) this is because sodium bicarbonate is a mucolytic substance which splits the mucus involved in the formation of the bezoar and facilitates the action of papain on the protein constituent of the bezoar. Some authors advise the use of ananase, another proteolytic enzyme. Pollard and Block (1968) proposed the administration of a mixture of enzymes, such as pepsin, pancreatic enzymes, cellulase, and dehydrocholic acid, of which cellulase seemed to be the most effective. Schlang (1970) advocated the use of a solution containing 15 ml. of acetyl cysteine in 50 ml. of normal saline instilled into the stomach three or four times. Some authors, including Sanderson and others (1971), have had good results with intensive gastric lavage. Rigler (1970) advised a liquid regimen and reported 2 patients in whom this treatment was successful in dissolving the bezoar in 2 weeks. These conservative measures are not sufficient to dissolve the bezoar completely in all cases, but may make it smaller or fragment it sufficiently to be vomited or eliminated via the intestine. When conservative treatment proves successful the patient should be advised to avoid unripe fruits and uncooked vegetables. Adequate chewing and proper dietary management prevent the recurrence of the condition in many cases but not in all (Sanderson and others, 1971).

Failure of conservative treatment or frequent recurrences after successful treatment require operation for removal of the bezoar and, if possible, correction of the factor which led to its development. In planning operative treatment it is worth noting that owing to long-standing malnutrition the majority of these patients are in a poor general condition and sometimes are a poor operative risk. Corrective operations have two objectives:—

1. Reconstruction of a new anastomosis if it is defective.

2. More extensive resection of the distal part of the stomach whose motor function is most affected by vagotomy. This should be followed by a gastrojejunal anastomosis.

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BRIT. J. SURG., 1973, Vol. 60, No. 11, NOVEMBER

A NEW VENOUS THROMBECTOMY TECHNIQU

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SUMMARY

This paper describes a new technique whereby a specially designed thrombectomy catheter can be passed distally in the venous tract without trauma to or hindrance by the venous valves. The catheter is advanced distally on the end of a guide-wire which has been threaded proximally along the vein to be thrombectomized. The technique enlarges the scope of surgery in relation to deep-vein thrombosis. A possible use in arterial thrombo-embolectomy is discussed.

THE use of balloon catheters for removal of intravascular thrombus is well established (Edwards, Sawyers, and Foster, 1970; Mavor, Galloway, and Karmody, 1970; Fogarty, Daily, Shumway, and Krippaehne, 1971). However, thrombectomy of the venous tree presents a technical difficulty not encountered on the arterial side, i.e., the venous valves interfere with distal passage of the catheter. Thus, although an arterial catheter may readily be passed from the groin to the ankle it is not possible to do this in the venous tract. Despite the flexible tip of the venous thrombectomy catheter and other manœuvres recommended to negotiate the valves (Fogarty and Krippaehne, 1965) the farthest distally the catheter can usually be advanced is to the popliteal fossa. At times the valves in the femoral vein cannot be negotiated and venous thrombectomy in the lower limb is then confined to the iliofemoral segment and the superficial femoral vein is ligated (Browse, 1970; Mavor, 1971).

This paper describes a technique of lower-limb venous thrombectomy which makes it possible to clear the main deep veins of thrombus as far as the lower third of the leg. For this purpose a guide-wire is introduced into the deep veins above the ankle and advanced to the groin. Then a specially designed thrombectomy catheter is fitted end to end to the tip of the guide-wire (*Fig.* 1) and passed distally. The guide-wire leads the catheter through the valve commissures.

In principle and in practice the technique has proved to be simple and effective. Following a detailed study in cadaveric limbs the technique has been applied in the clinical condition of extensive whole-limb deep-vein thrombosis. In these instances distal passage of the catheter and thrombectomy have been achieved without difficulty. In particular, no snagging in valves was encountered.

TECHNIQUE

With the patient systemically heparinized the common femoral vein is exposed through a vertical groin incision and its branches controlled. A venotomy is made and a standard iliofemora
is carried out.

To achieve distal thrombectom
materials are needed: (1) a 0·024-in. S
100 cm. in length, of medium flexib
core; (2) a disposable guest cannula,
Braunula or a 19G Butterfly needle,
a suitable vehicle for introduction o
(3) a specially designed thrombecton
an open tip to receive the guide-wir

To facilitate assembly and disc
catheter guide-wire 'line' it is imp
preliminary bed in the open tip of t
the hard non-flexible end of the
soft or flexible end of the guide-w
easily introduced into and discon
catheter when in use. A light hold
by the catheter is all that is necessa

A 5-cm. vertical incision is mad
aspect of the lower leg, centred at t
middle and lower thirds, in the gr
Achilles tendon and the deep flex
posterior compartment is entered a
tibial vessels are exposed by dividi
crural fascia. The guide-wire is intr
through a muscular or perforating br
up one of the tibial veins until it arri
venotomy.

It is advisable to fix the venepu
needle in position while the guide-
protects the venepuncture from shr
advance and withdrawal of the gui
of the guide-wire is delivered into
and lightly impacted into the open t
ectomy catheter. With one hand t
draws the guide-wire from the
simultaneously advancing the cathet
tract with the other hand. The fir
catheter is to the level of the knee-j
is carefully inflated and the cat
thrombectomizing the femoropopli
the catheter is withdrawn the guide
is still connected comes up to the g
the guide-wire–catheter 'line' is ass
passage of the catheter down the dee
as far as the level of the distal vene
passages as necessary are made s
intimal trauma.

Following thrombectomy of on
vein and with the balloon at the
disconnected by gently twisting
the direction which tightens its spira
it from the catheter. The second p
is entered and thrombectomized in

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* Present address: Bon Secours Hospital, Cork, Ireland.

* The thrombectomy catheter is
Eschmann Brothers & Walsh Ltd.,
Shoreham-by-Sea, Sussex.

In this instance before disconnecting the 'line' a tight Esmarch bandage is applied to the limb in an attempt to squeeze thrombus from the branches into the main deep veins. This thrombus is then brought out after removal of the bandage.

The peroneal veins are less accessible than the posterior tibial veins. Although they can be approached through the same medial leg incision the exposure is limited, especially in a swollen leg. A better but still limited exposure of the peroneal veins is afforded by a lateral leg incision diametrically opposite the medial one at the anterior border of the soleus muscle. The posterior compartment is entered, the transverse crural fascia incised, and the flexor hallucis longus fibres detached from their fibular origin throughout the length of the incision. When this muscle is retracted away from the fibula the peroneal vessels are brought into view from under the medial aspect of this bone. There are no suitable branches for the introduction of the guide-wire and therefore direct peroneal venepuncture is necessary. Otherwise the technique of thrombectomy is the same as for the posterior tibial veins, with a further application of the Esmarch bandage before disconnecting the peroneal 'line'.

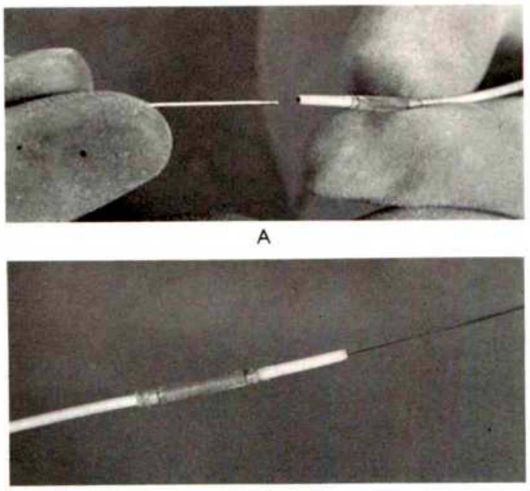

Fig. 1.—A, The specially designed, tapered, open-ended thrombectomy catheter about to be fitted on to the end of a 0·024-in. diameter guide-wire. B, The catheter connected to the guide-wire.

Although in practice it has not been found necessary, it is advisable to have alternative 0·024-in. diameter guide-wires available, e.g., one of soft flexibility or a J-shaped guide-wire with a movable core. Should passage of the straight, fixed-core, medium-flexibility guide-wire be obstructed this could be replaced with one of the alternative types indicated above. Such guide-wires have been found to be enormously effective in negotiating irregular and tortuous arteries and ought readily to pass up the smooth straight venous tract. It would be unwise to use the J-shaped guide-wire without prior proximal control of the femoral vein because of the danger of dislodging thrombus. In addition, with this guide-wire the core should not be withdrawn until the tip has reached a vessel of sufficient diameter to accommodate curling of the tip, i.e., the popliteal vein.

RELEVANT ANATOMY

There are some anatomical facts relating to the superficial femoral vein which need to be mentioned.

While there is usually one main channel there are accompanying medial and lateral comitans femoral veins of varying size. These join the superficial femoral vein below the profunda and as they also communicate with the popliteal vein the guide-wire may side track through one of these vessels only to reappear in the common femoral venotomy (*Fig.* 2A). This was observed in one cadaveric limb. Unrecognized in the clinical situation it could have meant failure to thrombectomize the main femoral vein. Awareness of the possibility and failure to produce the expected amount of thrombus should alert the operator to check that the guide-wire is traversing the main superficial femoral vein. If it is not, the guide-wire should be withdrawn and reintroduced if necessary using a different entry vessel. In this situation the J-shaped guide-wire may also be useful.

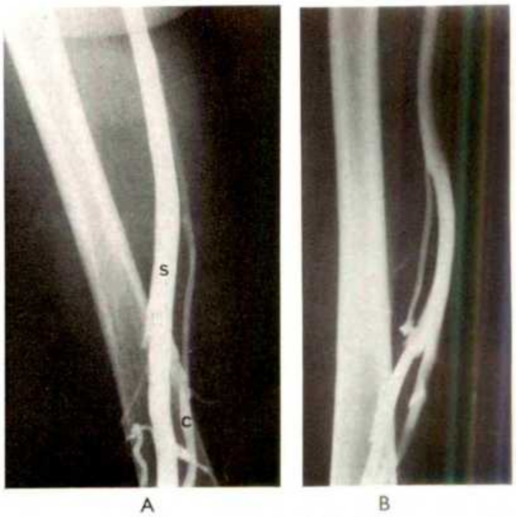

Fig. 2.—A, A phlebogram of the thigh showing a secondary femoral vein (c) coursing beside the main superficial femoral vein (s). B, A phlebogram of the thigh showing loops at the lower end of the superficial femoral vein.

There may be a loop on the femoral vein (*Fig.* 2B). It is quite likely that both limbs of such a loop can be successfully cleared especially when repeated passage of the guide-wire is undertaken.

Operative radiographic facilities are likely to be helpful, as in iliofemoral thrombectomy (Mansfield, 1972). In addition, a suction autotransfusion-linked system would be a valuable adjunct.

USE IN ARTERIAL THROMBECTOMY

When an arterial thrombectomy catheter is passed distally into the leg via a femoral or popliteal arteriotomy there is no control over which of the leg vessels it enters. Because of the angle of take-off the anterior tibial artery is by-passed. As the peroneal artery is the most direct continuation of the popliteal artery it is a common route taken by the catheter in the leg. It is likely that in a significant number of cases thrombectomy of the posterior tibial artery is not achieved. Consequently it is a recommended procedure to expose the posterior tibial artery at the ankle and perform an anteriotomy to achieve clearance from below. The technique described here is an alternative in this situation. The posterior tibial artery is exposed, and the guide-wire is introduced and threaded up the arterial tree to receive the thrombectomy catheter. Once the catheter has entered the posterior tibial artery the guide-wire is disconnected and removed so that the catheter can be advanced beyond the site of arterial puncture to achieve complete thrombectomy.

Acknowledgements.—I should like to thank Mr. Lawson Lyon of Eschmann Brothers & Walsh Ltd., for his invaluable assistance in producing the thrombectomy catheter. I am grateful to Professor G. W. Taylor for his helpful advice, and to the staff of the Department of Medical Illustration, St. Bartholomew's Hospital, London.

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EXTENSIVE CERVICAL LAMINECTOMY

LONG-TERM RESULTS

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Summary

It has been possible to follow up 5 patients who underwent complete cervical laminectomy for cervical spondylotic myelopathy between 12 and 17 years ago. The operation was described by Rogers in 1961. Clinical examination findings, together with the radiological appearances, indicate that this procedure does not predispose to instability of the cervical spine. This relatively simple procedure achieved long-lasting improvement in the patients examined.

Extensive cervical laminectomy in the treatment of cervical spondylotic myelopathy was described by Rogers in 1961. An attempt has been made to follow up the 33 cases described in his paper, from 12 to 17 years after their original operations.

Full records were available in 21 cases. It is assumed that the remaining 12 cases had undergone operation at establishments other than the major hospitals in the Cardiff area. A postal search revealed that 5 of the 21 patients had died from unknown causes and 3 had died from malignant disease which may or may not have been related to the underlying factor in their spondylotic myelopathy. Seven patients had moved from the district and could not be traced. Of the remaining 6 patients, 1 could not be traced owing to demolition in the area of the patient's original address and therefore 5 patients were followed up. These 5 patients have been re-examined and radiographs of the cervical spine have been repeated in order to assess the long-term results of Rogers's procedure.

CASE REPORTS

Case 1.—In 1955 a 55-year-old woman fell downstairs and became rapidly quadriplegic. She developed severe flexor spasms within hours of the injury. After 3 weeks it was observed that the degree of quadriplegia and flexor spasm remained constant. The initial radiographs showed only degenerative changes in the cervical column and the same feature was recorded in the films of the lumbar spine. Films at 4 weeks confirmed the earlier radiological appearance and it is noteworthy that at this time apart from a moderate degree of cervical spondylosis seen particularly at C.V. 5/6/7 there were no fractures and no marked displacement of one vertebra on another. At 5 weeks there was no sign of improvement and myelography was then performed from above and below. A break in the myodil column at C.V. 3/4 and to a lesser extent at C.V. 4/5 was observed. Within 2 months of her cervical laminectomy the patient was able to stand unsupported. Examination in 1972 found her to be walking with a normal gait and with minimal sensory loss in the lower limbs. Neck movements were full and normal. The plantar response remained extensor. A hard boggy mass was readily palpated deep to the laminectomy scar. The radiographs showed a cervical spine with normal alinement.

Case 2.—A 47-year-old man presented in 1956 with a history of left lower-limb weakness of gradual onset following a minor colliery accident the year before. Examination demonstrated atrophy of the small muscles of both hands, fasciculation of the forearm extensors, and exaggerated upper-limb reflexes. There was bilateral lower-limb weakness, the left greater than the right, clonus at both knees and ankles, and bilateral extensor plantar responses. Cervical spondylosis was clearly seen on the plain films and myelography demonstrated a partial block to flow at C.V. 4/5 and C.V. 5/6.

Following complete cervical laminectomy 8 months after the original injury the patient made slow but steady improvement and when examined in 1972 no abnormalities, with the exception of slight limitation in neck movements, were noted. There was a slight fullness deep to the scar. Radiographs showed normal alinement (*Fig.* 1). The patient has continued to work since 1957 and is in full employment.

Case 3.—A 40-year-old woman was admitted in 1956 following a fall downstairs and was noted on admission to have a marked sensory loss below C.V. 5. She became quadriplegic over a period of 3 weeks and a full picture of compressive cervical myelopathy was recorded. At this stage plans were being made for her transfer to a long-stay rehabilitation unit but in view of the success with *Case* 2 further investigations were considered. Eight weeks after the original injury her clinical picture showed no improvement and myelography from above and below demonstrated a block at C.V. 5.

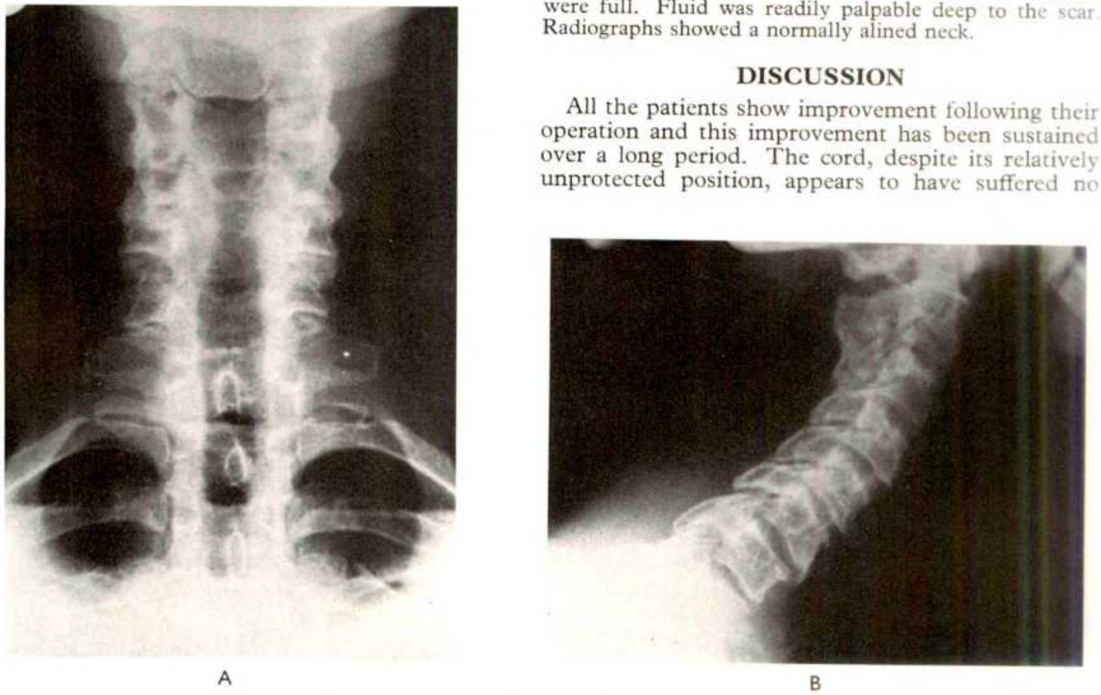

FIG. 1.—*Case* 2. Two views of the cervical spine 14 years after cervical laminectomy.

Following operation the patient made a fair recovery and in 1972 she was able to walk unsupported but with an obvious spastic gait. All neck movements were limited to about half the normal range and there was a fluid collection, presumed to be cerebrospinal fluid, deep to the scar. Radiographs showed no evidence of any abnormality other than marked osteophytosis and the absence of laminae and spines of all the cervical vertebrae.

Case 4.—A 38-year-old man developed numbness and weakness in the left index finger and thumb 3 weeks after a fall at work in 1954. Later, all the digits of both hands became similarly affected. Three months after the original fall he presented with these symptoms in addition to hesitancy of micturition and a dragging left foot. A mild degree of spondylosis was seen on the plain films and the myelogram showed a narrow canal at C.V. 4/5 level.

Following operation the patient had no further urinary difficulty and was back at work within 3 months. He remains in work in 1972 and has no complaints other than clumsiness of fine hand movements. He has full neck movements and the scar is normal. Radiographs show normal alinement.

Case 5.—A 50-year-old man was admitted to hospital in 1960 with a 3-year history of a 'dead' sensation in the hands and dragging of the right foot. Bilateral, generalized upper-limb paraesthesia and flexor fasciculation were present and he was unable to perform fine manual tasks. Despite his complaint no lower-limb weakness was demonstrated, although his reflex responses were exaggerated and he had a bilateral extensor plantar response. Plain films showed degenerative changes throughout the whole spine and there was persistent hold-up of the myodil column at the body of C.V. 5.

Following operation the patient regained a normal gait and power returned to the hands. In 1972 he still had some difficulty with fine movements of the hands, although handwriting comparisons showed there to be a marked improvement from the 1960 picture. Neck movements were full. Fluid was readily palpable deep to the scar. Radiographs showed a normally alined neck.

DISCUSSION

All the patients show improvement following their operation and this improvement has been sustained over a long period. The cord, despite its relatively unprotected position, appears to have suffered no damage in any case. All the spines remain fully mobile with the exception of *Case* 3, which had marked osteophytosis on the 1972 radiographs.

Since the cord and its blood-supply are affected by minor contusions from the prolapsed disk or osteophytic bars protruding into the canal during neck movements, repeated minor injury may be important in the development of cervical myelopathy (O'Connell, 1956). This, together with the established fixation of the cord by the dentate ligaments (Bedford, Bosanquet, and Russell, 1952), justifies the wide exposure and freeing of the cord. But does the threat to neck stability justify such an exposure? The stability of the cervical spine depends on the intervertebral joints, the laminae, spinous processes, ligamentum flavum, interlamina ligaments, and paraspinal muscles and ligaments. Scoliosis and kyphosis have been described following multiple laminectomies in the lumbar and thoracic spine in children (Tachdjian and Mason, 1965), and following cervical laminectomy in 3 children (Cattell and Clark, 1967). Adolescent kyphosis and anterior subluxation has also been described (Bette and Englehardt, 1955). In the adult no such postoperative deformities have been recorded, and Rogers's early confidence in his operation appears to be well justified by the long-term follow-up presented here. During growth structures other than intervertebral joints may be primarily responsible for spinal stability but at maturity the major stabilizing factors may well be the joints themselves, leaving other structures in a position of secondary importance. If the laminae and spinous processes become redundant structural factors, then their removal should produce no defect in stability and movement. This is, in fact, the case.

It is suggested that Rogers's operation, which by comparison with other surgical procedures popularly adopted in the treatment of cervical spondylotic myelopathy is relatively simple, has particular merit not only on the grounds of technique but also in the lack of long-term complications.

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BASAL OSTEOTOMY OF THE FIRST METACARPAL IN THE TREATMENT OF ARTHRITIS OF THE CARPOMETACARPAL JOINT OF THE THUMB

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SUMMARY

This is a preliminary report of 8 cases of osteo-arthritis of the carpometacarpal joint of the thumb treated by a basal abduction osteotomy of the first metacarpal.

Follow-up from 6 months to 9 years has shown a relief of pain and an increased function of the hand.

Although the osteotomy has been designed to correct the adduction deformity of the first metacarpal, in 2 cases this correction was not achieved and it is possible that a transverse osteotomy might be just as effective.

OSTEOTOMY has been advised in the treatment of osteo-arthritis of a number of joints. It has been shown to be successful in the relief of pain in osteo-arthritis of the hip (McMurray, 1935; Osborne and Fahrni, 1950; Harris and Kirwan, 1964), and more recently good results have been reported in the use of osteotomy for the treatment of arthritis of the knee (Benjamin, 1969; Jackson, Waugh, and Green, 1969). Pain relief in these cases has often occurred without any other functional improvement and without any regression of the disease process. Osteo-arthritis of the carpometacarpal joint of the thumb is not only painful but is very often associated with an adduction deformity of the first metacarpal—a deformity which can be worsened by the operation of excision of the trapezium or base of the metacarpal. Fusion of the joint, although it corrects the adduction deformity and relieves pain, is sometimes difficult to achieve. It was because of the disadvantages of the standard methods of treatment that a basal osteotomy of the first metacarpal was first carried out 9 years ago. Only severe cases which have not responded to conservative measures have been submitted to surgery. In the author's experience the indication for operation in this condition is relatively infrequent and a large personal series of cases cannot be expected. This paper is therefore a preliminary communication and describes the results of 8 cases which have been followed up for periods varying from 6 months to 9 years.

OPERATION

Osteo-arthritis of the first carpometacarpal joint is nearly always associated with radial subluxation of the base of the metacarpal and subsequent adduction deformity of the shaft of the bone (*Fig.* 1). The aim of the operation is to carry out an abduction osteotomy at the proximal end of the first metacarpal by removing a wedge of bone based radially and closing the defect by abducting the distal fragment. The operation is performed through a 4-cm. incision sited over the proximal half of the metacarpal and in line with the shaft (*Fig.* 2). The extensor tendon of the thumb is retracted to one side and the proximal third of the metacarpal is exposed subperiosteally (*Fig.* 3). The site of the osteotomy, which should be about 1 cm. distal to the carpometacarpal joint, is marked with an osteotome; the size of the wedge necessary to produce an abduction of the metacarpal shaft of 20–30° is approximately 5 mm. at its base. Before bone is removed the wire for fixing the osteotomy must be inserted (*Fig.* 4). Transverse holes are drilled through the proximal and distal fragments about 6 mm. from the base section and 26-gauge wire is threaded into position. The wedge of bone is removed piecemeal using an osteotome and small bone cutters and the cortex on the far side is weakened by two drill holes. The empty wedge left in the bone can then be closed by fracturing the osteotomy and tightening the ends of the wire which are twisted together to maintain the position of the bone (*Fig.* 5). A forearm plaster is applied with the thumb in wide abduction and this position is maintained for 6 weeks (*Fig.* 6).

CLINICAL MATERIAL

The patients under review consisted of 7 women and 1 man. The youngest patient was 54 at the time of operation and the oldest 67. There were no true rheumatoid cases, but in 1 case the E.S.R. was elevated to 24 mm. per hour.

RESULTS

All the patients have been completely relieved of pain and are entirely satisfied with the result of the operation. Powerful grasp action has been restored

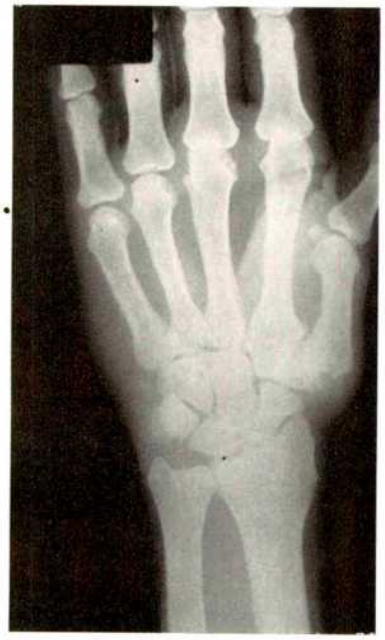

FIG. 1.—Adduction deformity of the first metacarpal typical of osteo-arthritis of the carpometacarpal joint of the thumb.

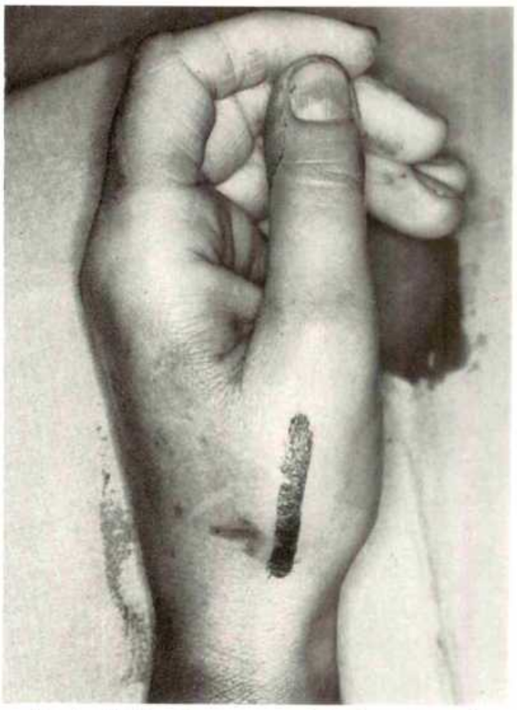

FIG. 2.—Incision for osteotomy of the first metacarpal.

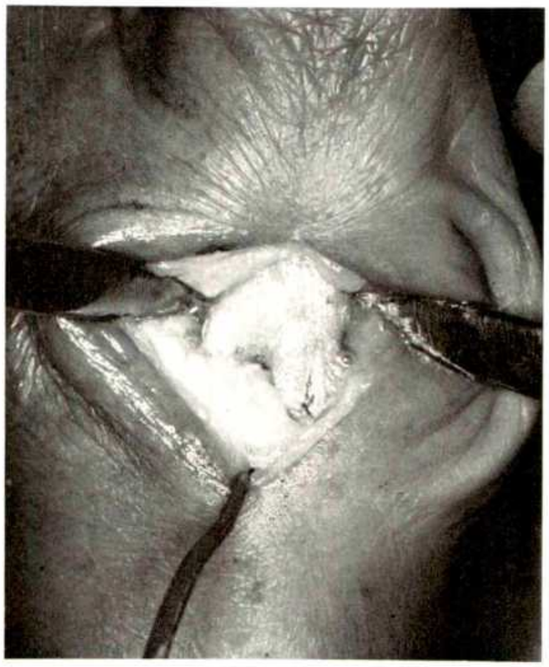

FIG. 3.—Subperiosteal exposure of the lower third of the first metacarpal.

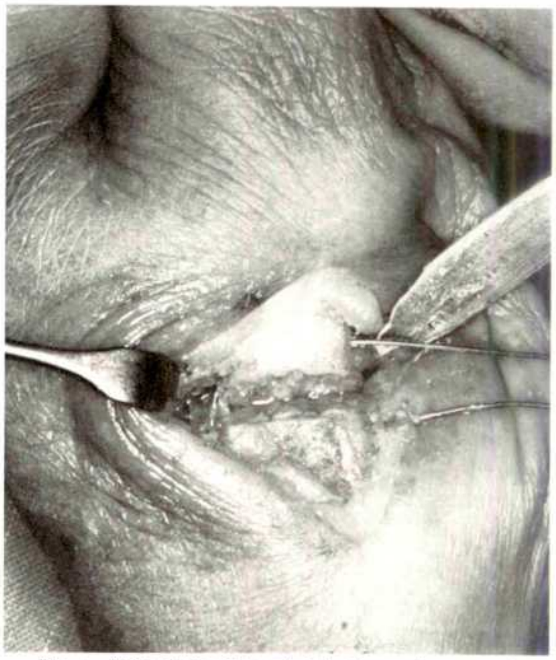

FIG. 4.—Wires in position and abduction wedge removed.

and the improved spread of the hand allows the patients to grip large objects without difficulty (*Fig.* 7). In 2 cases the osteotomy did not correct the adduction deformity of the metacarpal, but despite this there was a complete resolution of symptoms and the thumb-to-finger grasp for large objects was regained by hyper-extension at the metacarpophalangeal joint. There has been no evidence

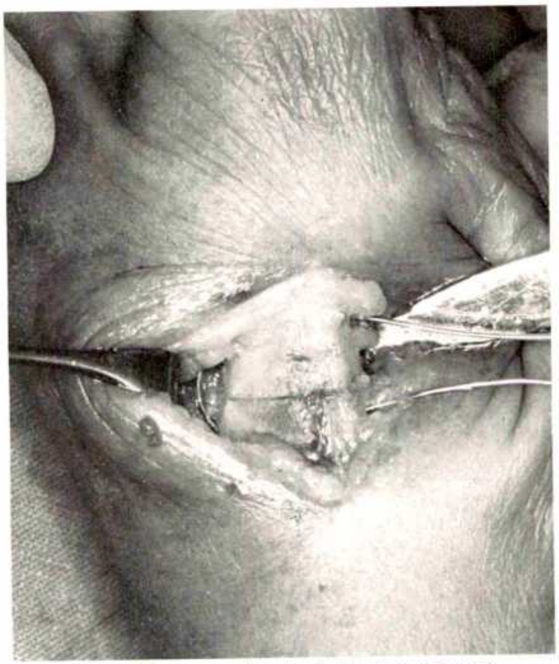

FIG. 5.—Osteotomy closed and wire loop tightened.

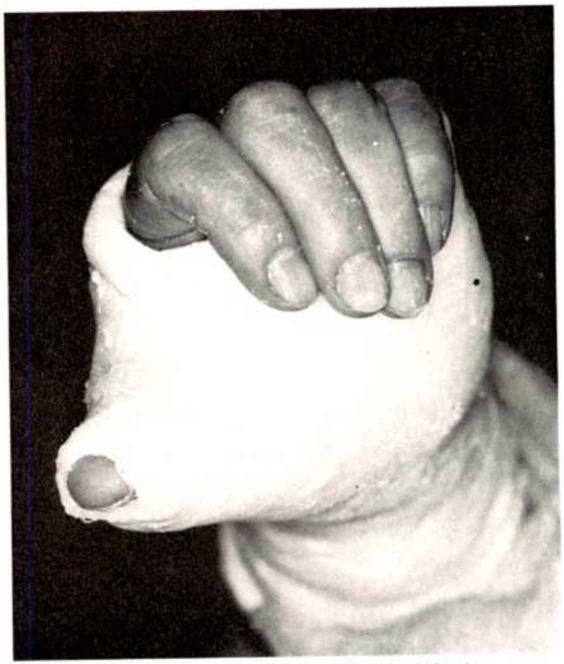

FIG. 6.—Plaster immobilization in wide abduction.

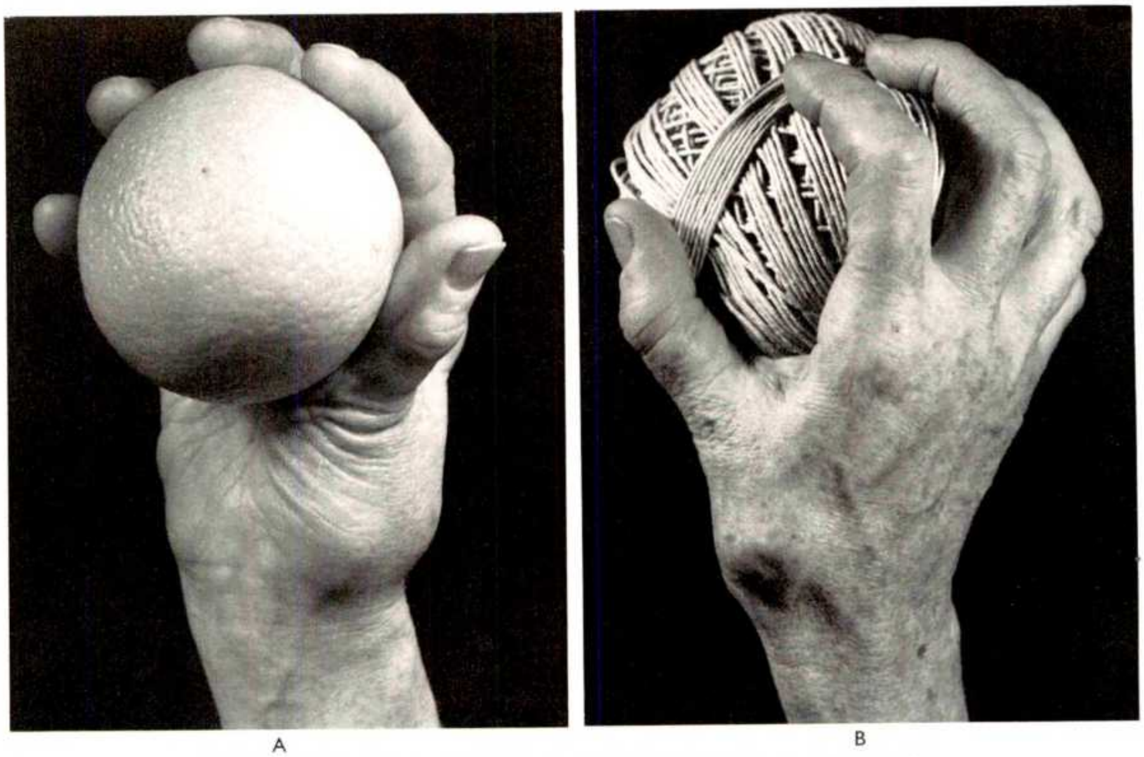

FIG. 7.—A, The ability to grasp before operation. B, The grasp 3½ years after operation.

radiologically of further deterioration in the joint after osteotomy, but no improvement in joint appearance has been demonstrated. One patient with bilateral disease had the opposite side treated by excision of the base of the metacarpal, but although this resulted in a painless thumb the patient much preferred the side on which the osteotomy had been carried out because of the restoration of a powerful thumb grasp.

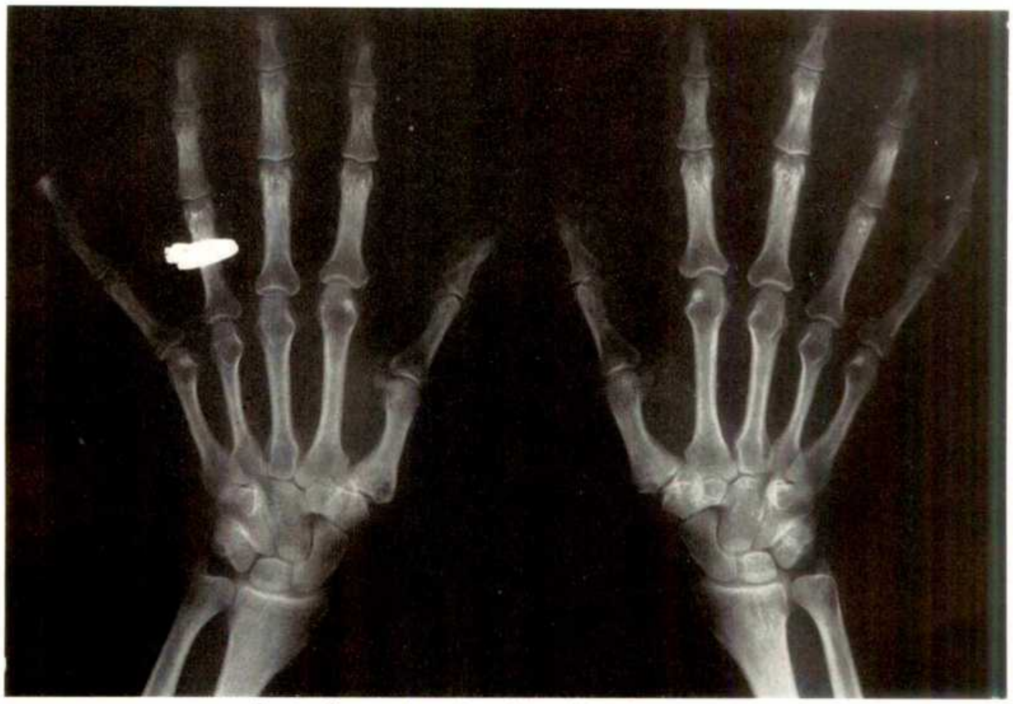

FIG. 8.—Preoperative radiograph in a bilateral case (W. K.).

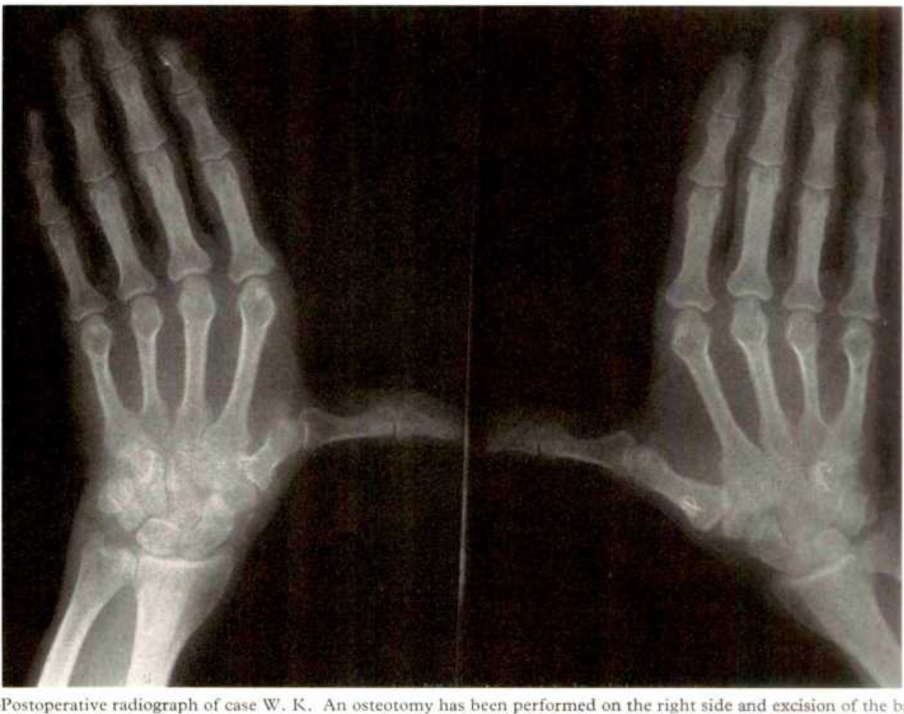

FIG. 9.—Postoperative radiograph of case W. K. An osteotomy has been performed on the right side and excision of the base of the metacarpal on the left side.

CASE REPORT

W. K., a 59-year-old woman, had a history of carpometacarpal arthritis of both thumbs for 10 years (*Fig.* 8). In 1962 an excision of the base of the left first metacarpal was carried out, but although pain was relieved the patient developed increased adduction deformity and did not regain a satisfactory grasp. In 1964 she had a 20° abduction osteotomy through the base of the metacarpal on the right side. At the time of review 9 years later the patient was free of pain on both sides but the adduction deformity of the first metacarpal on the left side had increased, whereas on the side of the osteotomy a normal spread of the thumb had been regained (*Figs.* 9 and 10). The difference in grasp power of the two thumbs is illustrated in *Fig.* 11.

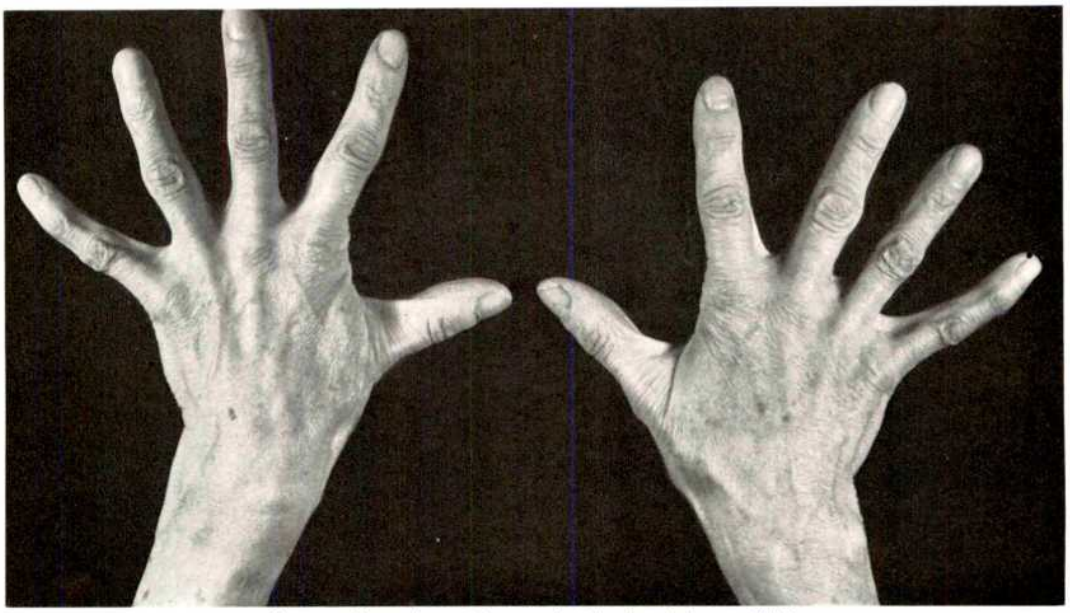

FIG. 10.—Comparison of the spread of the thumbs in case W. K.

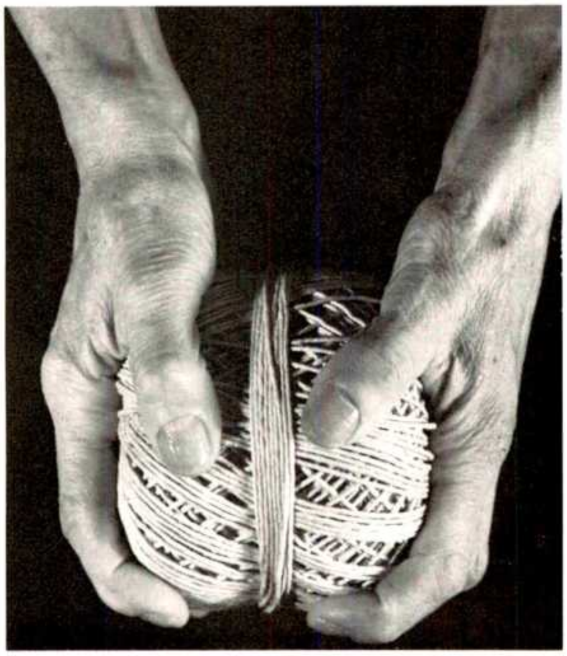

FIG. 11.—Comparison of the grasp in case W. K.

COMPLICATIONS

In no case has there been any significant complication. All the osteotomies have been radiologically united within 3 months, and although the wire fixation has broken in 1 case this has not caused any disability. In 1 patient there was a minor loss of sensation at the tip of the thumb, presumably owing to involvement of a branch of the digital nerve, but this has proved to be no disability.

Acknowledgements.—I am grateful to Mr. R. J. Whitley of the Photographic Department, Institute of Orthopaedics, for reproduction of the photographs and radiographs, and to my secretary, Miss Doreen Fox, for preparation of the manuscript.

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SUBCAPITAL FRACTURES OF THE NECK OF THE FEMUR TREATED BY DOUBLE-DIVERGENT FIXATION

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SUMMARY

A method of fixation of femoral neck fractures which involves double-divergent fixation using two Watson-Jones nails is described. The method has been compared against nail and autogenous fibular graft fixation and gave results which were better. The method has also been compared against single-nail fixation and has given much better results. There seems to be little place for single-nail fixation of displaced femoral neck fractures.

A clinical series of 90 cases of displaced fractures treated by double-divergent fixation is presented. Failure of fixation occurred in 12 cases (13·3 per cent).

The technique of double-divergent fixation prevents femoral neck collapse or resorption.

THE intracapsular fracture of the femoral neck has often been referred to in the past as the 'unsolved fracture' (Dickson, 1953), but nowadays there are some grounds for a more optimistic view.

There is considerable uncertainty about the ideal treatment, but the incidence of this fracture is high and some scheme of management is necessary. Over the years a vast literature has accumulated. Internal fixation by a trifin nail was introduced in 1931 (Smith-Petersen, Cave, and Van Garder, 1931), since when various series and many modifications have been described: nail and autogenous bone-graft, trans-articular nailing, the use of compression screws, nail plates, sliding nails and plates, multiple pins, cross-screws, etc. (Moore, 1937; Brittain, 1942; Patrick, 1949; Jewett, Albee, Powers, and Stanford, 1952; Pugh, 1955; Schumpelick, 1955; Charnley, Blockey, and Purser, 1957; Massie, 1958; Deyerle, 1959; Hargadon and Pearson, 1963; Brown and Abrami, 1964; Burton, 1964; Garden, 1961a, b; Jarry, 1964; Smyth, Ellis, Manifold, and Dewey, 1964; Metz, Sellers, Feagin, Levine, Onkey, Dwyer, and Eberhard, 1970). The variety in style and complexity of the devices is clear evidence of the lack of a uniformly satisfactory method. Because of the dissatisfaction which surrounds internal fixation it is not surprising that immediate prosthetic replacement of the head of the femur has become an alternative method of management, but this technique has a significant incidence of complications and the patients are not all free from symptoms at a later stage (Hinchey and Day, 1964; Thomson, 1968; Rush, 1971).

Reports of the success of early weight-bearing after internal fixation (Abrami and Stevens, 1964; Gibson, 1964) have led to a renewal of interest in internal fixation as a primary treatment. To allow early weight-bearing the fixation device should be mechanically capable of sustaining the loads imposed (Frankel, 1959). This leads to increasing technical complexity, considerably increased operation time, or liability to technical failure.

This paper describes a method of fixation which has been used in Edinburgh since 1964 (McQuillan, 1966, 1968). The method uses two standard Watson-Jones nails. A pilot study of 12 cases was carried out and the results were satisfactory. Further work was done by random testing of the method of double-divergent fixation by two Watson-Jones nails against two other methods.

CASE MATERIAL

The method has been used in the treatment of patients with displaced femoral neck fractures. Garden's classification has been used in the assessment of the degree of displacement (Garden, 1964). Fractures with displacement of Garden's grades 1 and 2 have been treated where no difficulty has been encountered, the results being satisfactory. Other methods are equally satisfactory in these types of fracture (Fielding, Wilson, and Zekel, 1962; Bentley, 1968).

The cases to be reported here are all displaced fractures of Garden's grade 3 or 4. The patients were aged 45 years or over with displaced fractures of the femoral neck, either subcapital or transcervical (Watson-Jones, 1955; Klenerman and Marcuson, 1970), who were able to walk before their fracture, which was not itself pathological other than as a result of osteoporosis.

METHOD OF REDUCTION AND DOUBLE-DIVERGENT FIXATION

In the treatment of displaced fractures a satisfactory reduction is important (Watson-Jones, 1955; Garden, 1964).

Vigorous or formal manipulation of the fracture has not been used. It is believed to be unnecessary and possibly harmful. The method of reduction has been to apply gentle traction with the patient under general anaesthesia on a Charnley table, the leg being held in a neutral position in the first instance. Radiographs are then taken. In about 60 per cent of cases the fracture is seen to be in an anatomical position provided that the leg is immobilized in *neutral* and *not* in abduction and internal rotation. In 30 per cent of cases adjustment of the position is required—usually some increase in internal rotation. In the remaining 10 per cent of cases these measures may not be sufficient to produce an acceptable reduction and the procedure may need to be repeated. In a tiny percentage an open reduction may be required when failure to achieve reduction by simple measures is seen to be due to local mechanical problems, e.g., a spike of bone piercing the capsule.

An anatomical or near anatomical reduction is necessary before proceeding further. The operative steps to be undertaken must be carried out in a precise and regulated way or problems will ensue.

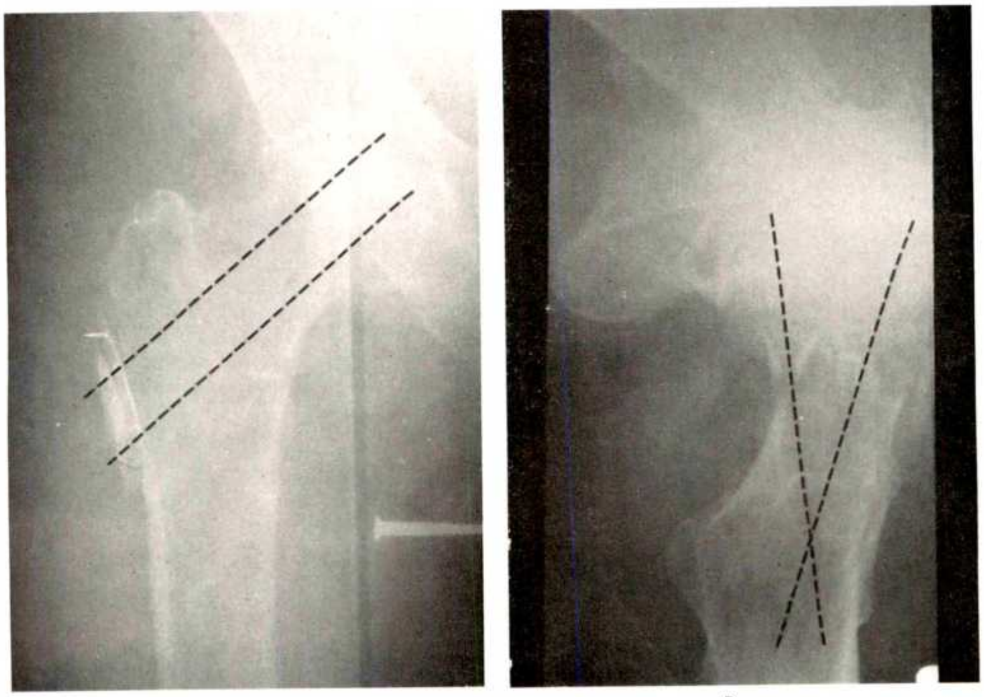


FIG. 1.—Radiographs illustrating the technique of insertion of guide-wires. The fracture has been reduced as described in the text. Lines are drawn on the post-reduction radiographs in the positions in which it is desired to place the nails. On the anteroposterior view (A) the distances from the vastus ridge can be estimated together with the angle to the shaft. (The angles are not changed materially by X-ray distortion and the distances are increased.) On the lateral view (B) the angles to the horizontal can be estimated. The upper wire normally passes forwards so that the drill hole preparatory to insertion of the wire usually lies behind the midpoint of the shaft. The lower wire will pass backwards into the head and the drill hole thus is usually forward of the midline of the shaft.

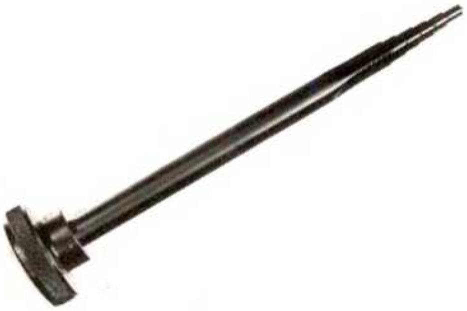


FIG. 2.—The Ritchey starter provides a clean trifin cut around the guide-wire. A plastic mallet is a useful addition. When used properly the starter locks in the guide-wire and makes an ideal starting hole in the shaft without fragmentation. This is the only 'new' instrument necessary.

Operative Details.—The lateral side of the thigh is exposed through a curved incision. This incision reduces the need for forceful retraction and gives better exposure than a straight incision. The vastus lateralis is reflected from its ridge, exposing the lateral side of the femur. The vastus ridge is used as a landmark. On the post-reduction films guide-lines can be drawn as shown in *Fig.* 1 from which it is possible to estimate the angles and the directions of the guide-wires to be inserted through preparatory drill holes. Two guide-wires only are used. Protractors and a ruler corrected for the radiographic magnification are helpful, but with increasing experience these aids do not prove necessary.

When the desired position has been achieved the guide-wires are driven across the head of the femur into the acetabulum to prevent tilting of the head as the nails are inserted. The Ritchey starter (*Fig.* 2) provides a clean trifin cut and does not fragment the cortex, a problem which can result from the use of some other instruments. The nails are introduced one at a time, the nails being driven alternately. The guide-wires are withdrawn and the position of the nails is checked by radiographs. Traction should be released at this stage and an additional tap given to each nail. Formal impaction is not carried out as it will not achieve any advantage with the desired nail position.

Preservation of the integrity of the lateral cortex is important, and allowed for by the use of the Ritchey starter.

Position of the Nails.—The optimum position of the nails is as shown in *Fig.* 3. In the anteroposterior view a parallel or minimally divergent position of the nails is chosen, while in the lateral view the upper nail can be seen to pass into the centre or anterior aspect of the head and the lower nail is positioned posteriorly, clear divergence of the nails being obtained. It should be noted that with this type of fixation further impaction is not possible.

It may appear radiologically that a great deal of metal is present. The radiological appearances do not allow for the trifin section of the nails.

The nails will be contained easily within the neck of the femur as illustrated in *Fig.* 4.

POSTOPERATIVE MANAGEMENT

Early weight-bearing is encouraged with whatever assistance (Zimmer aid, crutches, or sticks) is required by the patient for comfort and security. Some patients have walked on the day after operation while others have not until 1 week later but all the patients in the present series have been encouraged towards full weight-bearing as soon as possible.

Routine anticoagulation can give problems in elderly patients (McQuillan, 1964). In this series the measures used to reduce the incidence of thrombo-embolism have been:—

1. *Early operation*: Where possible, surgery has been carried out within a few hours of admission and rarely later than 24 hours after injury.
2. *Speedy operation*: This procedure can be carried out within ¾–1 hour, the time being greatly reduced with experience.
3. *Early mobilization and ambulation.*

These measures appear to have been very satisfactory in the prophylaxis of deep venous thrombosis and pulmonary embolism.

RESULTS

Pilot Study.—The traditional method of treatment of displaced fractures of the femoral neck by a single trifin nail has given results which were less than satisfactory (Welch, 1966). The nail-and-graft procedure as reported by Patrick (1949) was used as an alternative for a time but without a great improvement in the results. The use of the graft raised the question as to whether the fibular graft acted as a bone graft or whether its value was purely mechanical, so that better fixation was achieved than with one nail alone. Clearly one method of determining whether the fibular graft acted as a mechanical aid or whether it acted biologically could be determined by carrying out a comparative study using two mechanical devices without osteogenic properties. A preliminary study was carried out in which 12 patients were treated by double-nail fixation. This showed the technical feasibility of the operation and its relative simplicity as compared with the nail-and-graft operation. The results were entirely satisfactory in that all 12 patients had good results although there were many variables in these cases.

Controlled Surgical Trial.—It seemed important to evaluate double-divergent fixation against the nail-and-graft procedure (*Fig.* 5) by a controlled surgical trial.

Patients (*vide supra*) with displaced fractures of the femoral neck of Garden's grade 3 or 4, the fracture not being pathological, who were otherwise fit for operation and who had walked before the incident, were included in this trial.

A random index was produced prospectively for operation by two nails or nail and graft. As patients were admitted to the unit the index was consulted to determine the procedure to which they should be submitted, i.e., the next one listed. Fifty-four cases were dealt with in this fashion. The results are shown in *Table I*.

Table I.—RESULTS OF A CONTROLLED TRIAL OF DOUBLE-DIVERGENT FIXATION COMPARED WITH NAIL AND GRAFT IN 54 PATIENTS

	NAIL AND GRAFT	DOUBLE-DIVERGENT FIXATION
Total number of cases	27	27
United	10	17
Held. ? union	3	2
Failed	6*	1
Total number of deaths	8	7
Up to 1 mth.	2	1
Fracture failure	1	0
1 mth.–2 yr.	6	6
Fracture failure	1	1
Total number of failures	8	2
Late complications, avascular necrosis	3	2

* Infection occurred in 1 case.

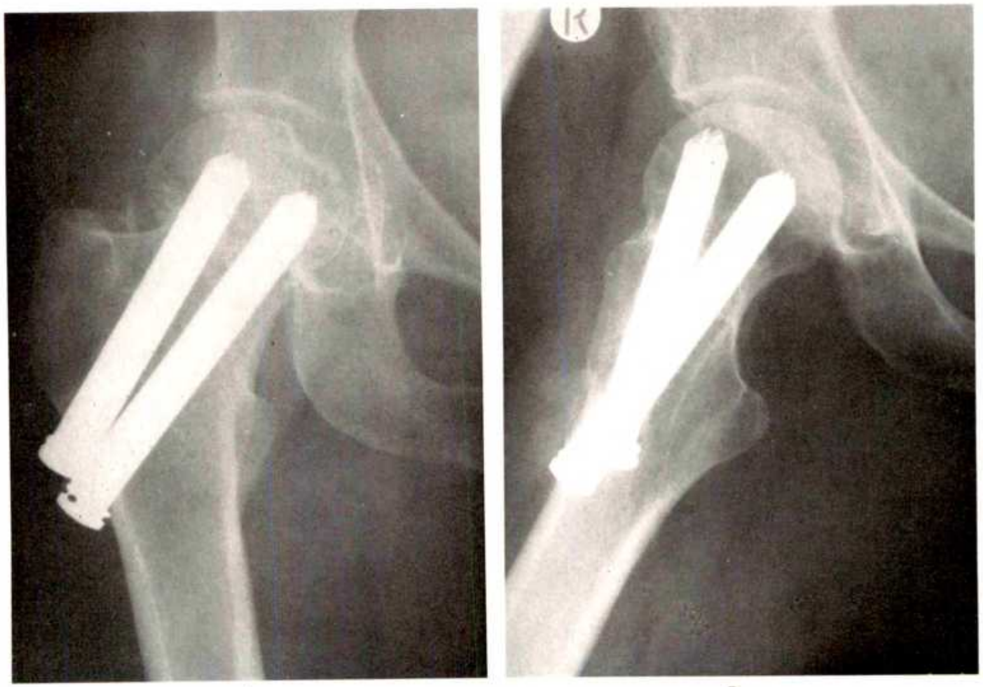
It seems clear from this evidence that two-nail fixation has advantages over the nail-and-graft procedure. It commends itself by virtue of the results of fixation and, just as importantly, because it is technically easier, it does not involve a second operative procedure on the same patient for removal of the graft, and it produces a satisfactory clinical result. The method allowed early walking with pain relief in the vast majority of patients.

Second Clinical Trial.—Although the published results of single-nail fixation are much poorer than the results obtained by double-divergent fixation there is no firm evidence to justify the conclusion that double-divergent fixation is superior to single-nail fixation if the latter procedure is carefully carried out. It was therefore decided to conduct a trial of two-nail against single-nail fixation in which an experienced surgeon would carry out all the operations.

A second clinical trial was therefore carried out on patients with displaced fractures, this time the random index selecting patients for single- or two-nail fixation. A further 50 hips in 49 patients were treated during the process of this controlled trial. One patient provided the ideal controlled situation (*Fig.* 6).

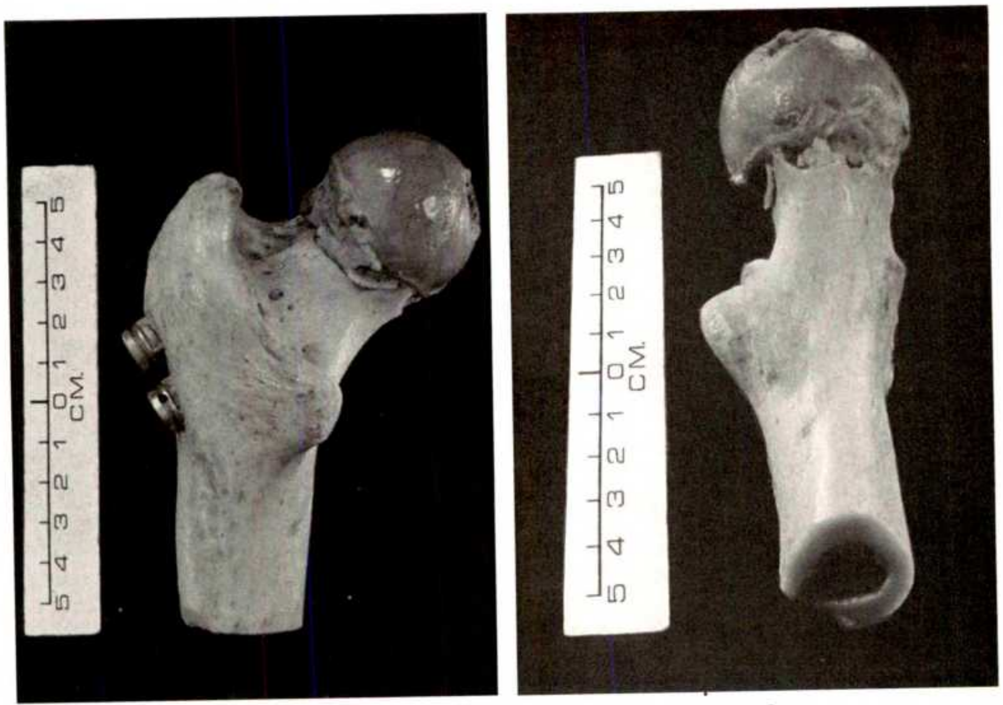
In this trial full consideration was given to achieving the best reduction and fixation by each method. The procedures were carried out by the same surgeon. The results are as shown in *Table II*.

The failure rate of single fixation in displaced fractures was almost 50 per cent, a figure similar to that found in a much larger series (Welch, 1966) and unacceptably high for clinical practice.



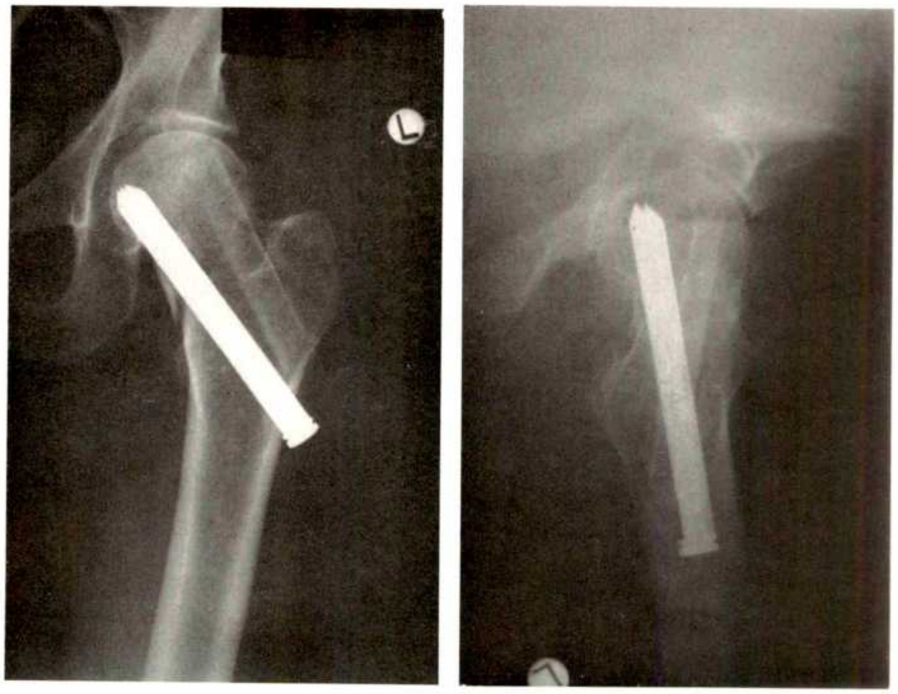
A B

FIG. 3.—The nails should be parallel or slightly divergent in the anteroposterior view (A). It is easier to converge the nails but this is less satisfactory. In the lateral view (B) the nails can be seen to diverge, the lower nail strutting across the commonly found posterior comminution while the anterior nail passes forwards into the head.



A B

FIG. 4.—These photographs are of a specimen removed at autopsy from a female patient who died 2 weeks after operation. This femoral neck is small but the nails are easily contained. (The fixation obtained has defied many attempts to disrupt it by manual force.)



A B

FIG. 5.—The position of fixation in the nail-and-graft procedure. The positions are similar to those already described in the technique of double-divergent fixation, with the graft taking the upper and anterior position.

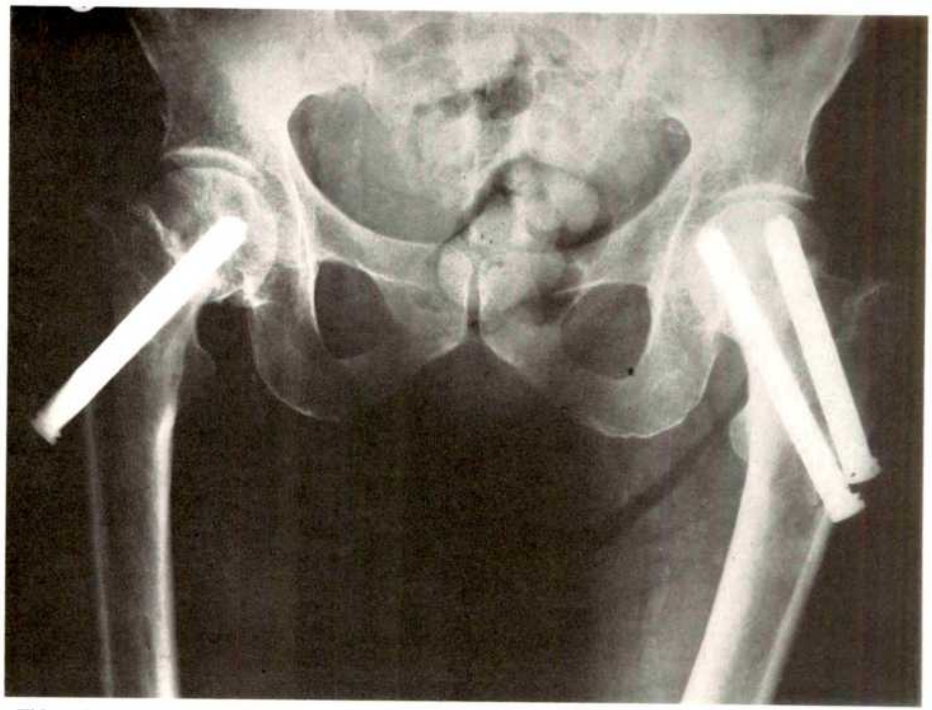


FIG. 6.—This patient sustained two fractures during the time of the trial. The left hip was treated initially by two-nail fixation. Four months later she was readmitted having fractured the right hip and had a single nail inserted (according to the random index). At 10 weeks there is failure of fixation and non-union of the right hip.

At this stage the second clinical trial was abandoned as it seemed clear that no further purpose could be served in continuing it, the results showing that double-divergent fixation is superior in all aspects to single-nail fixation in patients with displaced femoral neck fractures.

Further Clinical Experience.—It was decided to increase the experience of double-divergent fixation and in particular to extend its use so that the operation could be evaluated when performed by a less experienced staff. A further 90 operations have been carried out of which the majority have been done by registrars in training. (It is probable that in routine clinical practice the majority of operations for elderly patients with femoral neck fractures are done by junior staff.)

Although mechanically simple, the method will give rise to technical difficulties unless it is carried out properly and precisely. After adequate experience of simple hip operations, registrars have been given careful instruction and supervision in the method of double-divergent fixation before operating without immediate supervision.

These criteria having been met, the majority of the operative procedures on the 90 patients in this group have been carried out by a considerable number of registrars and senior registrars of varying grades of experience.

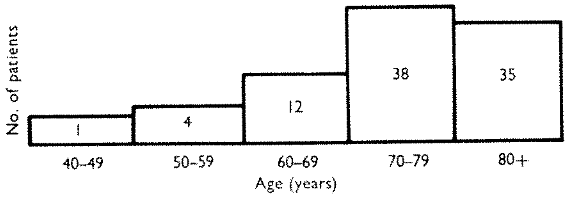


FIG. 7.—Age distribution of 90 patients (average age, 79·8 years) who were operated on by junior hospital staff.

Table II.—RESULTS OF A CONTROLLED TRIAL OF DOUBLE-DIVERGENT FIXATION COMPARED WITH SINGLE-NAIL FIXATION IN 50 PATIENTS

	DOUBLE-DIVERGENT FIXATION ($n = 25$)	SINGLE-NAIL FIXATION ($n = 25$)
Failure	2	12
Death within 1 mth.	2	6
Death 1 mth.–1 yr.	3	4
Fracture failure	1	2
Total No. of failures	3	14

Table III.—RESULTS OF DOUBLE-DIVERGENT FIXATION IN 90 PATIENTS

Result	*No. of Cases**
Firm radiological union	61
Position held	17
Failure of fixation	12

* There were 35 fractures of Garden's grade 3 and 55 of Garden's grade 4.

Fig. 7 details the age distribution of these patients, while the length of their follow-up at the time of this review is shown in *Fig.* 8. A general analysis of these cases is given in *Table III.* This analysis includes the results of treatment in cases which ultimately proved fatal, i.e., where a patient died soon after operation or during the period of follow-up.

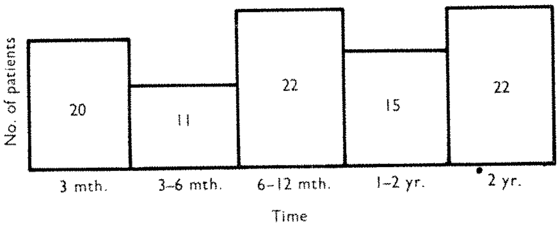


FIG. 8.—Length of follow-up of 90 patients who were operated on by junior hospital staff.

Table IV.—MORTALITY-RATE IN 90 PATIENTS AFTER DOUBLE-DIVERGENT FIXATION

Time	*No. of Deaths*
1 wk.	4 (4·4 per cent)
1 wk.–6 mth.	17
6–12 mth.	4
Total at 1 yr.	25 (27·7 per cent)

Total in-patient deaths 9 (10 per cent).

Table V.—INCIDENCE OF AVASCULAR NECROSIS IN 90 PATIENTS AFTER DOUBLE-DIVERGENT FIXATION

	No. of Cases
Total number of cases	13
Fracture union	9
Non-union	4
Total head necrosis	7
Segmental necrosis	6

Table VI.—ANALYSIS OF FAILURE OF FIXATION IN 90 PATIENTS AFTER DOUBLE-DIVERGENT FIXATION

1. Failure *v.* delay in surgery
    5 under 24 hours
    7 over 24 hours
2. Failure *v.* type of fracture
    8 type 4
    4 type 3
3. Failure *v.* reduction/fixation
    6 good reductions and good nails (1 syphilis)
    1 good reduction and poor nails
    3 fair reductions and poor nails
    2 fair reductions and accurate nails
4. Failure *v.* age
    3, 60–70 years age-group
    9, over 70 years
5. Associated pathology
    3 associated bone pathology
    2 rheumatoid arthritis
    1 syphilis
    All failed

The assessment of the mortality-rate in hip fractures is a controversial problem and many different rates are described which are meaningless unless specified precisely. In this series (*Table IV*) the mortality-rate is given at 1 week and at 1 year and the arbitrary figure of the in-patient mortality-rate is included. The in-patient mortality-rate of 10 per cent compares favourably with reported results using other methods.

Some controversy exists as to whether fractures which have failed to unite have failed because of avascular necrosis of the femoral head or because of failure of fixation. The results for avascular necrosis (*Table V*) include 4 cases where union did not occur. These are also included in the group of failures where histological analysis of the head removed at subsequent reoperation showed total necrosis of the femoral head. The incidence of avascular necrosis in the fractures which united was 9 cases, of which 6 developed segmental necrosis and 3 had late total head necrosis after fracture union. A total figure for avascular necrosis in patients of this age-group is difficult to obtain, but it should be remembered that segmental necrosis in elderly patients is not a major complication and may not require further surgical treatment.

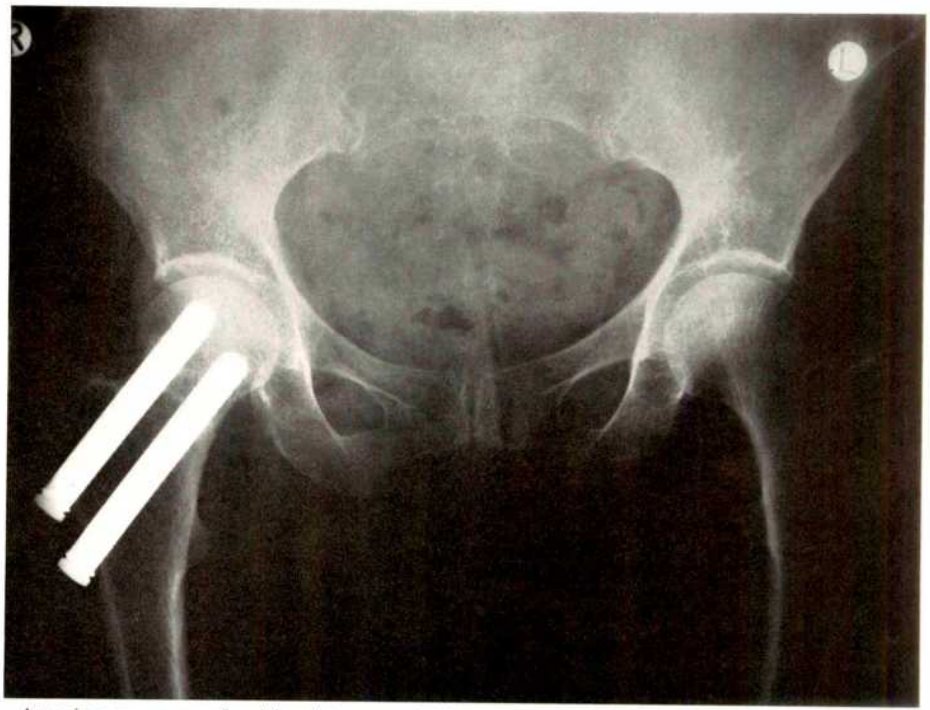


FIG. 9.—A precise measurement of neck length is extremely difficult to obtain. This radiograph illustrates the type of case classified as showing no neck resorption. There is union, maintenance af Shenton's line, and a normal calcar femorale, and the lesser trochanter occupies a normal position as compared with the uninjured side.

Table VI details the cases where there was failure of fixation. No firm conclusions can be drawn but it is of interest that in 6 of the 12 failures there were 3 cases with associated bone pathology, 2 cases of rheumatoid arthritis, and 1 syphilitic case. There were 6 failures amongst the patients who were classified as having good reductions with good fixation, one of these being the syphilitic case already referred to.

DISCUSSION

Evidence from the literature supports strongly the concept of multiple fixation of femoral neck fractures rather than single fixation (Moore, 1937; Deyerle, 1959; Schumpelick, 1955; Strange, 1971). The results of our trial of double fixation compared with single fixation show that the technique of double-divergent fixation is superior. The percentage success in our larger series of 'routine' cases reflects firmly the advantage of two-nail fixation over the traditional single-nail technique.

The study of two-nail fixation against nail and autogenous graft is also in favour of the two-nail method. This does not invalidate the nail-and-graft method *per se* in certain cases. The case material of the present series was largely confined to elderly females in whom a prepared fibular graft is neither ideal as a bone-graft nor does it provide rigid mechanical fixation. The method may have a place in younger patients or where delay has occurred before hospitalization, but we believe that in elderly patients the nail-and-graft method has no advantages over two-nail fixation.

Table VII.—INCIDENCE OF NECK RESORPTION IN 61 PATIENTS WITH A UNITED FRACTURE AFTER DOUBLE-DIVERGENT FIXATION

Neck Resorption	*No. of Cases*
None	42
Avascular necrosis	4
Minimal	10
Avascular necrosis	1
Marked	9
Avascular necrosis	4

There are some additional findings of great interest in this series. It was noted clinically that neck resorption was not an inevitable accompaniment of healing, although it is often alleged that this is so and indeed sliding devices are designed in the belief that some movement is necessary to maintain firm contact at the fracture site (Brown and Abrami, 1964).

Table VII gives an analysis of our cases where union occurred and shows clearly that neck resorption is not inevitable (*Fig.* 9); indeed, it occurred only in a minority of these cases. It is tempting to infer that neck resorption is a reflection of inadequate fixation. If this were so, then clearly sliding devices are constructed on a false premiss and are designed to deal with pathology which is secondary to the mechanical inadequacy of the device.

This paper reports a clinical study and detailed mechanical studies are without its compass. An assessment by the Department of Mechanical Engineering, University of Edinburgh, suggests that double-divergent fixation is mechanically sound (Barr, 1971) and our results would support this view.

The results of any series are always open to discussion as to what constitutes mortality-rate, union rate, etc., and whether cases which are ultimately fatal should be excluded from the results. In this series a full analysis of the results in all the cases has been given without exclusions. The figures of the mortality-rate, union rate, and late complications justify the continued use of the technique and support the firm clinical impression that the method is sound and eminently practical.

Acknowledgements.—We wish to thank the consultants at the Royal Infirmary of Edinburgh who have kindly referred cases for treatment, successive senior registrars and registrars who have operated on many of the cases, successive house surgeons who have documented the cases and contributed to their management, and Mrs. E. Wilson for secretarial help.

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CARCINOMA OF THE DUODENUM: COMPARISON OF SURGERY, RADIOTHERAPY, AND CHEMOTHERAPY

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SUMMARY

Three cases of infra-ampullary carcinoma of the duodenum are presented, and in each case the management was different.

A new method of reimplantation of the common bile-duct and pancreatic duct is described.

One hundred and twenty-six cases from reports in the past decade have been reviewed, and the distribution, sex ratio, clinical features, investigations, management, and prognosis are discussed.

In polyposis investigation of the upper gastrointestinal tract is advised.

The use of radiotherapy and chemotherapy is discussed and advocated.

CARCINOMA of the duodenum is an uncommon condition and most of our knowledge is based on necropsy studies in overseas literature. In the past decade a small number of individual cases and short series have been reported, but in most reports the data are meagre and incomplete.

Increased awareness of the condition, improvement in diagnostic techniques, and a more aggressive surgical approach have combined to change this disease from a post-mortem curiosity to a condition that can be treated with satisfactory results.

Three new cases are presented here, and are discussed with 123 cases reported in the literature in the past 10 years.

CASE REPORTS

Case 1.—V. G., a female aged 51 years, gave a history of anorexia, lassitude, weakness, and weight-loss of 13 kg. over a period of 6 months, followed by severe colicky lower abdominal pain for 1 week. She had vomited twice, bringing up bile, but gave no history of dysphagia, haematemesis, melaena, or jaundice.

She was a known diabetic since 1964 and was controlled with tolbutamide. In 1965 she underwent a laparotomy for acute abdomen and was found to have a papillary cyst adenocarcinoma of her ovary, which was initially treated with salpingo-oophorectomy, followed by total hysterectomy. There was no evidence of recurrence on regular follow-up.

Examination showed the patient to be pale, and her weight was 60·5 kg. There was an epigastric mass approximately 4 cm. in diameter and fixed to the posterior abdominal wall.

Investigations showed the haemoglobin to be 9·6 g. per 100 ml. and there was occult blood in her stools. Barium-meal examination showed the abdominal mass to correspond with a stenotic area in the third part of the duodenum (*Fig.* 1).

A laparotomy was performed in the first week of June, 1971, and the tumour was found to be in the infra-ampullary part of the duodenum. It was adherent to the pancreas, aorta, and left renal vein. It also involved the mesentery of the small intestine and the transverse colon, where some moderately enlarged lymph-nodes were palpable. The liver was free from metastases, and there was no evidence of recurrence of the previous carcinoma of the ovary in the pelvis.

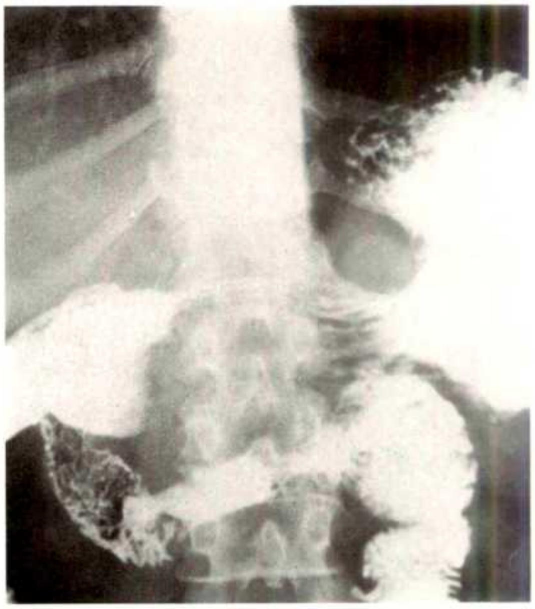

FIG. 1.—*Case* 1. Barium-meal film showing the stenotic tumour and ulcer in the third part of the duodenum.

The tumour mass was dissected from the middle colic vessels and portal vein, and was shaved off the aorta, the left renal vein, and the head of the pancreas. It was necrotic, friable, and microscopically incompletely excised. A segmental resection of the duodenum was carried out with a 1·5-cm. clearance of normal mucosa at the proximal end and an 8-cm. clearance at its distal end. Proximally the duodenum was divided above the ampulla and it was found that a separate common bile-duct and pancreatic duct were coursing for about 1·5 cm. along the posterior wall of the duodenum. These were dissected free and reimplanted through a stab incision in the duodenal wall in order to free about 1 cm. of duodenum for anastomosis (*Fig.* 2). The common bile-duct and the pancreatic duct were re-embedded in the duodenal lumen around a plastic tube splint, and the continuity of the bowel was restored with a conventional two-layer continuous chromic catgut end-to-end anastomosis.

The pathology report confirmed the operative finding of a necrotic friable tumour. A malignant ulcer measuring 7 × 7 cm. completely encircled the lumen of the bowel and extended to 1·5 cm. of the cut edge.

Microscopy showed a well-differentiated adenocarcinoma which appeared to be arising in the mucosa (*Fig.* 3).

Postoperative management was with intravenous fluids, nasogastric suction, and a sliding scale of intramuscular soluble insulin. Progress was uneventful and the patient made a rapid recovery.

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In view of this patient's remarkable progress and the knowledge that the resection had not completely removed all the tumour tissue it was decided to give her a course of 5-fluoro-uracil; 500 mg. were given intravenously, nightly, under haematological control for 1 week, then weekly in the out-patients' department for 3 months.

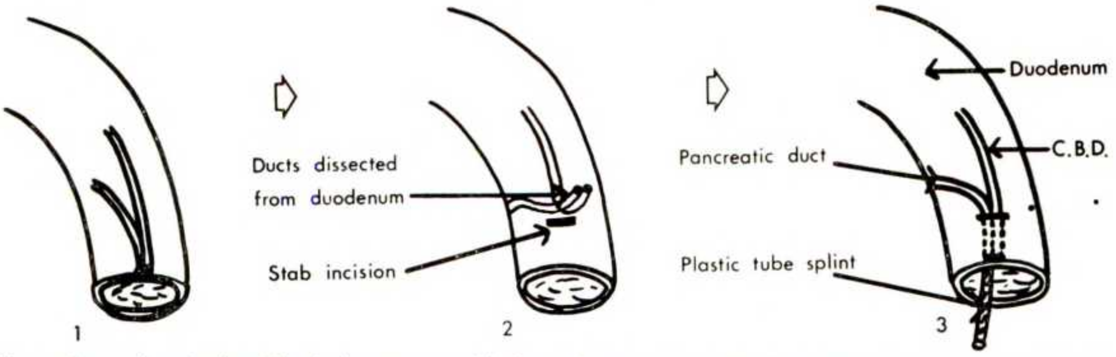

FIG. 2.—*Case* 1. Posterior view of the duodenum, common bile-duct, and pancreatic duct. The ducts were dissected free from the posterior wall of the second part of the duodenum and reimplanted through a stab incision in the duodenal wall around a plastic splint.

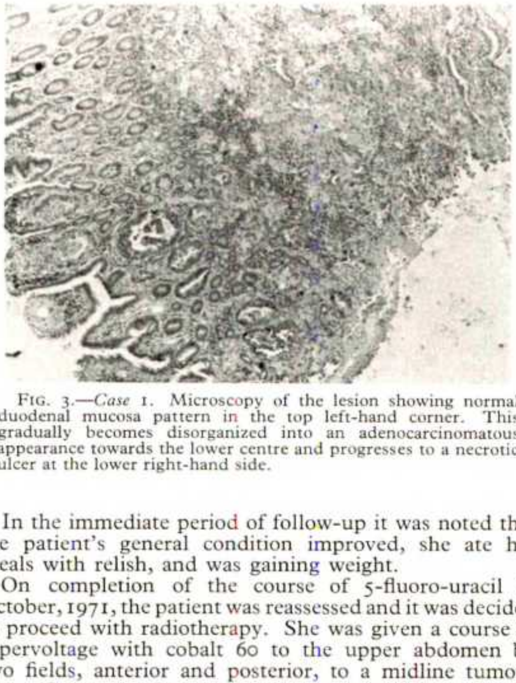

FIG. 3.—*Case* 1. Microscopy of the lesion showing normal duodenal mucosa pattern in the top left-hand corner. This gradually becomes disorganized into an adenocarcinomatous appearance towards the lower centre and progresses to a necrotic ulcer at the lower right-hand side.

In the immediate period of follow-up it was noted that the patient's general condition improved, she ate her meals with relish, and was gaining weight.

On completion of the course of 5-fluoro-uracil in October, 1971, the patient was reassessed and it was decided to proceed with radiotherapy. She was given a course of supervoltage with cobalt 60 to the upper abdomen by two fields, anterior and posterior, to a midline tumour dose of 5000 r with thirty treatments over a period of 43 days.

She progressed well, was asymptomatic, and when last seen, 22 months after her operation, had gained 10 kg. in weight.

Case 2.—R. B., a female aged 74 years, complained of dyspnoea, epigastric pain, and vomiting for 5 months. These symptoms were temporarily relieved by alkalis, but 2 months later were followed by weakness, weight-loss, anorexia, nausea, and continuous vomiting.

Examination showed a thin woman with a vague mass in the left hypochondrium.

Investigations showed her haemoglobin to be 11·7 g. per 100 ml. with a white-cell count of 8000 per mm.^{3} A repeat barium-meal examination showed a stricture at the distal end of the third part of the duodenum (*Fig.* 4).

At operation an encircling tumour causing a complete obstruction was found at the distal end of the third part of the duodenum. It was invading the peritoneum and retroperitoneal structures and was unresectable. A gastro-jejunostomy was performed and the biopsy taken was reported as 'fat infiltrated by columnar cell, mucus-secreting adenocarcinoma of gastro-intestinal origin'.

The patient's postoperative progress was uneventful and she was treated with a course of radiotherapy to a total tumour dose of 5000 r, and chemotherapy with 5-fluoro-uracil intravenously over a period of 3 months was also given. She progressed well and was alive 2 years after her first attendance at hospital, but she died shortly afterwards.

Case 3.—W. J., a male aged 65 years, complained of indigestion, anorexia, vomiting, abdominal discomfort, and marked weight-loss over a period of 12 months.

Examination showed an emaciated dehydrated man, with right-sided abdominal guarding and visible peristalsis.

Investigations showed his haemoglobin to be 10·8 g. per 100 ml. with a white-cell count of 10,000 per mm.^{3} Barium-meal examination showed a grossly distended first and second part of the duodenum proximal to a stenosing lesion (*Fig.* 5).

At operation a tumour was found encircling the third part of the duodenum and invading the superior mesenteric artery. It was unresectable and a duodenojejunostomy was performed. A biopsy was taken and was reported as 'fragments invaded by moderately differentiated adenocarcinoma'. No further treatment was given.

The patient's postoperative progress was uneventful. However, he developed severe anaemia with obstruction and died 3 months after the operation.

DISCUSSION

Incidence.—The incidence of carcinoma of the duodenum is approximately 0·01–0·04 per cent in necropsy studies (Jefferson, 1917; Eger, 1933; Willis, 1948). It comprises 0·3 per cent of all gastro-intestinal carcinomas (Eger, 1933), and 45–47 per cent of carcinomas of the small intestine (Eger, 1933; Hoffman and Pack, 1937; Hancock, 1970).

Site.—The distribution within the duodenum is described with reference to the ampulla (Jefferson, 1917; Mateer and Hartman, 1932), and the figures have varied mainly because of the controversy and difficulty in the determination of the tissue of origin of the periampullary lesions. Earlier authors (Eger, 1933; Berger and Koppelman, 1942) have quoted 60 per cent of the lesions to be periampullary, with the remainder being more common above than below the ampulla. By contrast, more recent authors (Resnik and Cooper, 1958) have quoted 17 per cent as periampullary, the remainder being evenly distributed above and below the ampulla. In this review of 126 cases the distribution was 9·5 per cent supra-ampullary, 48·4 per cent periampullary, and 42·1 per cent infra-ampullary (*Table I*).

Age and Sex.—The age distribution has its peak, as one would expect, in the sixth and seventh decades. The sex distribution shows a marginally increased incidence in women, with a ratio of 3 : 2 (*Table II*), contrary to the high male predominance reported by other authors (Hoffman and Pack, 1937; Serrano and McPeak, 1966).

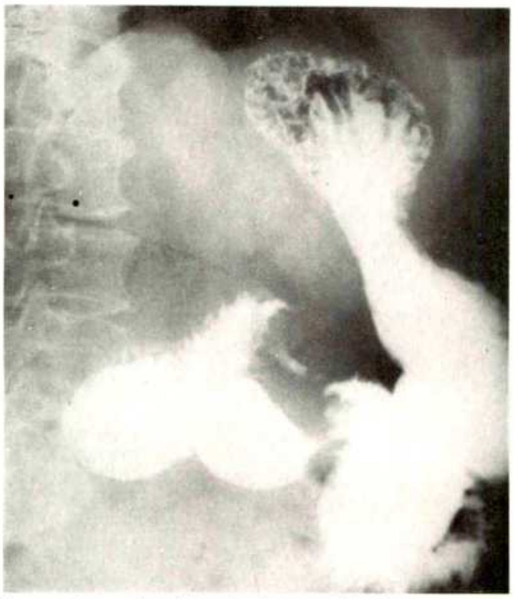

FIG. 4.—*Case* 2. An oblique barium-meal film showing obstruction in the third part of the duodenum.

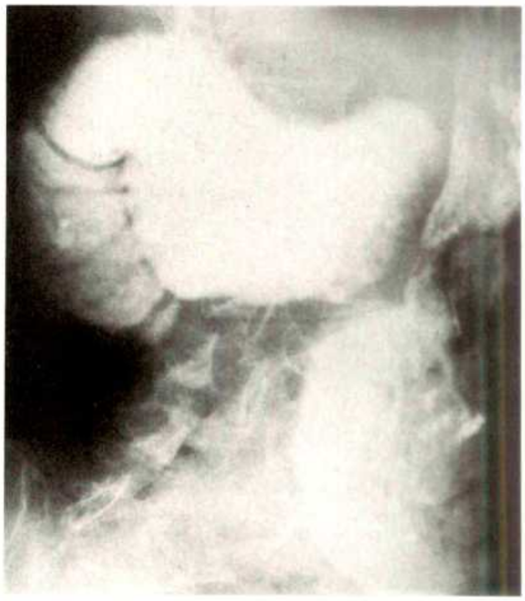

FIG. 5.—*Case* 3. An oblique barium-meal film showing a grossly distended first part of the duodenum with obstruction at the distal end of the second part of the duodenum.

Table I.—DISTRIBUTION OF CARCINOMA OF THE DUODENUM IN REPORTED SERIES

AUTHOR	NO. OF CASES	SITE OF TUMOUR (related to the ampulla)		
		Supra	Peri	Infra
Aagaard, Andreassen and Lindenberg (1961)	5	2	2	1
Iovine and Tsangaris (1961)	4	—	1	3
McNeill (1961)	1	—	—	1
Benson (1963)	4	1	2	1
Innes (1963)	1	—	1	—
Spinazzola and Gillesby (1963)	8	1	5	2
Austin (1964)	1	—	—	1
Andersen and others (1965)	3	—	1	2
Hunt and Ragaz (1965)	1	—	—	1
Reid (1965)	1	—	1	—
Warren and others (1965)	1	—	1	—
Williams and Knudsen (1965)	1	—	—	1
Fawcett (1966)	1	1	—	—
Lewis (1967)	3	2	—	1
Devlin and others (1968)	5	1	3	1
Everett (1968)	1	—	1	—
Hentschel and others (1968)	1	—	—	1
Kreel and MacIntosh (1968)	4	1	—	3
Bosse and Neely (1969)	21	1	9	11
Craig (1969)	4	—	2	2
Stassag and Klingensmith (1969)	25	—	15	10
Bennett (1970)	1	—	1	—
Boquist and Bergdahl (1970)	1	—	—	1
Cleator (1970)	1	—	—	1
Hancock (1970)	17	1	11	5
McCluskey (1970)	1	1	—	—
Simon and Elbaz (1970)	1	—	—	1
Kenefick (1972)	5	—	5	—
Present series (1973)	3	—	—	3
Total Per cent	126	12 9·5	61 48·4	53 42·1

Presenting Symptoms and Signs.—The most common presenting symptoms and signs are those of gastro-intestinal obstruction, abdominal discomfort and pain, weight-loss, and chronic blood-loss leading to anaemia. This was the presentation in the 3 cases described here. Occasionally biliary obstruction or a palpable abdominal mass, as in *Cases* 1 and 2, may be present, but these are late features. Early diagnosis must be based on a high degree of suspicion (Devlin, Platten, and Corrin, 1968). Analysis of 126 cases shows that when these symptoms and signs are clearly manifest there is no significant correlation between duration of symptoms prior to diagnosis and the ultimate prognosis, which probably depends mainly on the biological behaviour of the tumour itself (*Table III*).

Hunt and Ragaz (1965) described a case where the presenting symptoms and signs were those of large-bowel obstruction. Investigations and later operation failed to demonstrate a large-bowel lesion but a duodenal carcinoma was discovered and resected. A similar case was described by Cleator (1970), who considered this to be the result of involvemen of the autonomic nerves around the superior mesenteric artery.

Predisposing Factors.—It is difficult to determine what factors play a part in the development of this disease. The past history of carcinoma of the ovary in *Case* 1 tended to confuse the issue initially. One can only speculate on the significance of this in the aetiology and ultimate prognosis.

The presence of diabetes mellitus in *Case* 1 is also of interest. Diabetes is not associated with a higher incidence of cancer, except for that of the pancreas, where the incidence is tripled or even quadrupled (Karmody and Kyle, 1969). This patient's diabetic state was stable and caused no complications during the operation and in the postoperative period. Control of her diabetes became difficult after radiotherapy but settled with time.

Table II.—AGE AND SEX DISTRIBUTION

AGE (yr.)	MALE	FEMALE	TOTAL
Under 30	2	1	3
31–40	3	1	4
41–50	3	8	11
51–60	9	13	22
61–70	9	13	22
Over 70	4	9	13
Unstated	3	3	6
Total	33	48	81

Table III.—DURATION OF SYMPTOMS PRIOR TO DIAGNOSIS COMPARED WITH LENGTH OF SURVIVAL

DURATION OF SYMPTOMS PRIOR TO DIAGNOSIS	LENGTH OF SURVIVAL					
	0	6 mth.	1 yr.	2 yr.	3 yr.	+4 yr.
3 mth.	6	9	7	3	3	2
6 mth.	6	7	3	2	1	2
1 yr.	3	—	2	—	1	2
More than 1 yr.	3	2	2	3	—	4
Total	18	18	14	8	5	10

Table IV.—RESULTS OF BARIUM-MEAL EXAMINATION

Result	*No. of Cases*	*Percentage*
Correct diagnosis	31	64·6
Indefinite report	6	12·5
Negative report	7	14·6
Reported as duodenal ulcer	1	
Reported as cancer of pancreas	2	
Total	47	

Despite the frequency of duodenal ulceration only 7 fully substantiated cases of ulcer cancer of the duodenum have been reported (Fawcett, 1966). This contrasts remarkably with the incidence of ulcer cancer of the stomach.

Polyposis of the upper gastro-intestinal tract, unlike that of the large bowel, has always been considered unlikely to undergo malignant change. However, this complacency is unfounded. Twelve cases have been found in a search of the literature where adenocarcinoma had developed directly in or in close association with polyps; of these, 5 occurred in cases of Peutz-Jeghers syndrome (Barclay and Kent, 1962; Horn, Payne, and Fine, 1963; Reid, 1965; Warren, Kune, and Poulantzas, 1965; Williams and Knudsen, 1965). Three cases occurred in siblings with familial polyposis (Ungar, 1949). Two developed as adenocarcinomatous change in benign polyps (Benson, 1963; Andersen, Iversen, and Ostberg, 1965), while the remaining 2 cases were suggestive of adenocarcinomatous change in benign polyps (Devlin and others, 1968).

A recent report suggests that duodenal polyposis in Gardner's syndrome is more common than is realized (Melmed and Bouchier, 1972). They reported 2 cases and from their review of the literature found 4 more. Of these 6 cases, 4 were associated with periampullary adenocarcinoma. The tissue of origin of malignant change, however, was not definitely established.

In view of the above findings it would be interesting and advisable to investigate the upper gastro-intestinal tract of all patients with polyposis.

Diagnosis.—Early diagnosis is extremely difficult for many reasons and relies entirely on suspicion and awareness of this condition. Initial symptoms are vague and are often passed off by the patients without consulting their medical practitioners. Later, more severe symptoms are often confused with those of peptic ulceration, and a period of conservative management with alkalis follows.

A conventional barium-meal examination may not help in the diagnosis as its accuracy is limited and this causes further delay. Where this was recorded in the 126 cases reviewed only 64·6 per cent were diagnosed correctly on a routine barium-meal examination (*Table IV*). All 3 cases in this report were diagnosed late.

The first barium-meal examination in *Case* 2 was reported as normal, but a repeat examination 1 month later, with special posturing, showed the lesion (*Fig.* 4). This emphasizes the difficulty in making an early diagnosis by the conventional barium-meal study, as some areas, especially the third part of the duodenum, are difficult to visualize and may need special posturing. Even so, small lesions can be very difficult to distinguish from the normal mucosal pattern and require special techniques, such as hypotonic duodenography or even coeliac and superior mesenteric angiography (Bosse and Neely, 1969).

The development of duodenoscopy should help greatly in the early diagnosis as it allows direct visualization, photography of the lumen of the duodenum, and biopsy to be performed.

All these sophisticated investigations may be required to distinguish carcinoma of the duodenum from pancreatic carcinoma, ampullary carcinoma, and secondary tumours from adjacent organs. Carcinoid and lymphoma of the small bowel are not rare and Crohn's disease and malignant melanoma have been described in the duodenum. Congenital abnormalities such as diverticula and annular pancreas may confuse the diagnosis.

Management.—A change of attitude in the management of this condition has occurred in the past decade, following the criticism: 'the unusual reticence to attack this lesion aggressively' (Resnik and Cooper, 1958). Operability has increased from 50 per cent a decade ago (Resnik and Cooper, 1958) to 93·4 per cent, and resectability from 43 per cent (Serrano and McPeak, 1966) to 61·7 per cent (*Table V*). Of the present 3 cases, only 1 was resectable and in the remaining 2 a by-pass operation was performed.

In *Case* 1 a segmental resection of the duodenum was carried out even though the tumour extended beyond the confines of the bowel wall and total clearance was not possible. This was done with the hope that reduction in the tumour mass would result in a better response to chemotherapy and radiotherapy. The anatomical anomaly of a separate common bile-duct and pancreatic duct entry into the duodenum increased the difficulty of reimplantation of these ducts. Dissecting them from the duodenum to allow room for anastomosis left the posterior duodenal wall thinned out. This, however, did not produce any difficulties in establishing a conventional two-layer anastomosis. The expected difficulties with reimplantation of the ducts did not occur and at no time in the postoperative period was there any evidence of leakage.

Table V.—TYPES OF OPERATION PERFORMED FOR CARCINOMA OF THE DUODENUM

Operation	*No. of Cases*	*Percentage*
Palliative by-pass	19	31·7
Local resection of lesion	4	61·7
Segmental resection	18	
Pancreaticoduodenectomy	15	
Terminal	4	
Total	60	

In the choice of operation there seems to be little to choose between a local resection and the more radical operation of pancreaticoduodenectomy (*Table VI*). However, a radical resection is strongly advocated, no matter how large or how extensive the tumour might be (Benson, 1963), even if total clearance is not possible. This is good palliation and may bring favourable results when combined with radiotherapy and chemotherapy, as in *Case* 1.

Chemotherapy and radiotherapy have rarely been used in this condition. Apart from *Cases* 1 and 2 there are only 3 other recorded cases in the recent literature.

The lesson learned by Sir Thomas Dunhill in 1927 (Dunhill, 1952), who inserted radium needles in an open operation for a recurrence, has been forgotten until now. The initial response was good, but his patient finally succumbed after 6 months.

It is most interesting to note the prolonged survival of 4 patients who had palliative by-pass operations followed by radiotherapy and chemotherapy (*Table VI*). Two survived for more than 2 years (Spinazzolla and Gillesby, 1963), 1 for 2 years (*Case* 2), and 1 for 4½ years (Serrano and McPeak, 1966). This contrasts markedly with the 15 patients who had by-pass operations alone, as 13 did not survive for more than 1 year and 2 were not followed up adequately (*Table VI*). The good response to radiotherapy seems to indicate that carcinoma of the duodenum is amenable to this form of treatment, contrary to popular belief, and that reluctance in its use is unfounded. With modern radiotherapeutic technique a large dose may be delivered accurately and safely to the area of involvement.

Table VI.—MORTALITY AND SURVIVAL PATTERN COMPARED WITH TYPE OF TREATMENT

TREATMENT	LENGTH OF SURVIVAL						TOTAL
	0	6 mth.	1 yr.	2 yr.	5 yr.	More than 5 yr.	
Laparotomy							
Dead	4	—	—	—	—	—	4
Alive	—	—	—	—	—	—	
By-pass							
Dead	9	1	3	—	—	—	13
Alive	1	1	—	—	—	—	2
By-pass with deep X-ray therapy and chemotherapy							
Dead	—	—	1	2	1	—	4
Alive	—	—	—	—	—	—	—
Local resection							
Dead	—	1	1	—	—	—	2
Alive	—	—	2	—	—	—	2
Segmental resection							
Dead	3	—	1	3	1	—	8
Alive	3	2	1	—	1	2	9
Segmental resection with deep X-ray therapy and chemotherapy							
Dead	—	—	—	—	—	—	—
Alive	—	—	—	1	—	—	1
Pancreaticoduodenectomy							
Dead	2	1	1	—	2	—	6
Alive	3	1	2	1	1	1	9
Total							
Dead	18	3	7	5	4	—	37
Alive	7	4	5	2	2	3	23

There have been no reports on the postoperative use of radiotherapy and chemotherapy following resection, apart from the present *Case* 1. The patient in this instance has done well and only with increasing use can the full benefit of this procedure be evaluated.

Prognosis.—It is difficult to determine the real prognosis because this series is relatively small and the follow-up of cases has been poor or for too short a period. For this reason a 5-year survival rate would be invalid, but the pattern of mortality and survival

(*Table VI*) may give some guidance in assessing the progress of this disease in relation to its management. There was a 22·2 per cent immediate mortality-rate, i.e., survival of less than 3 months, which accounts mainly for the terminal cases. Most subsequent deaths occurred within the first 2 years, and there were 4 deaths after this period. Three patients survived for more than 5 years, and the speculative assessment of *Table VI* would make the 5-year survival rate much lower than the 22 per cent quoted from the Mayo Clinic in a series of 41 patients (Pagtalunan, Mayo, and Dockerty, 1964).

CONCLUSIONS

Study of the 3 cases presented here together with reports in the recent literature show that carcinoma of the duodenum is slow-growing, late to metastasize and, in a small number of cases, may arise from, or in close association with, intestinal polyps and polyposis.

There does not seem to be any correlation between duration of major symptoms prior to diagnosis and the length of survival. Hence, the emphasis is on early diagnosis and utilization of modern diagnostic techniques to achieve this, as conventional barium-meal examination is only about 65 per cent accurate.

Aggressive surgical management produces the best results even when resection is incomplete, and radiotherapy has a definite place, as in the few cases reported the effect was beneficial and the tumour appeared to be more amenable to radiotherapy than has previously been considered.

Acknowledgements.—We would like to thank Mr. B. S. Ashby for his advice and permission to publish his case. We are grateful to Dr. D. Caldwell for *Fig.* 3 and comments on microscopy of the tumour, and to Mr. J. Wood and the Photography Department of Southend General Hospital for the other photographs. We would like to thank Mrs. J. Bramley for typing the manuscript.

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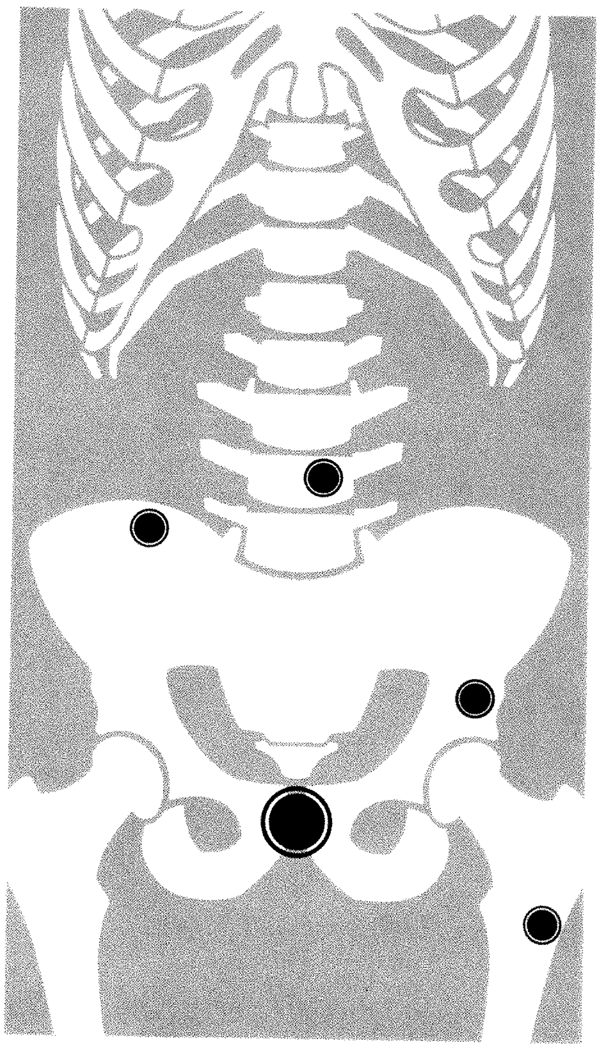

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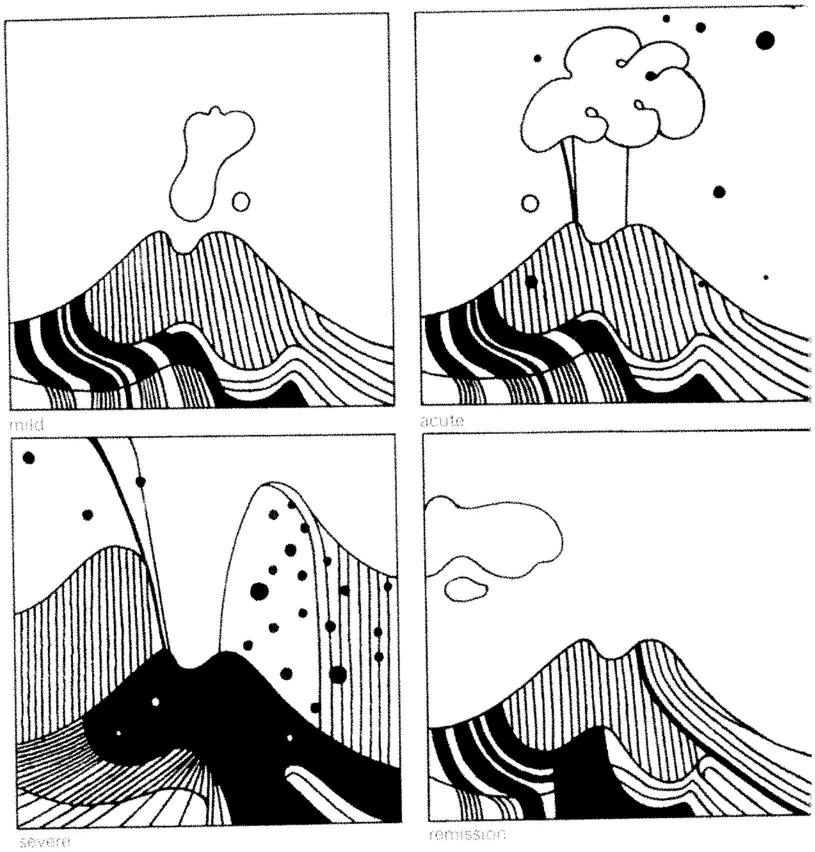

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CIGARETTE CONSUMPTION AND ATHEROSCLEROSIS

THEIR RELATIONSHIP IN THE AORTA AND ILIAC AND FEMORAL ARTERIES

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SUMMARY

The relationship between cigarette consumption and stenotic and occlusive atherosclerotic disease of the lower abdominal aorta and iliac and femoral arteries has been investigated by means of lumbar aortography. Cigarette smoking appears to be associated with atherosclerosis of these vessels. This association seems to be quantitatively related in the lower abdominal aorta, but the relationship is less marked for the iliac vessels and the severity of the disease in the femoral arteries does not appear to be related quantitatively to cigarette consumption. The failure to show a quantitative association in the more peripheral vessels could either be due to limitations and artefacts produced by the method of measurement, or suggest that the atherosclerotic lesions at different levels in the arterial tree are not necessarily homogeneous in nature.

THERE is now a considerable body of information relating to tobacco consumption and atherosclerosis of the coronary arteries. Doyle, Dawber, Kannel, Heslin, and Kahn (1962), Auerbach, Hammond, and Garfunkel (1965), and Strong, McGill, Richards, and Eggen (1966) were among the first to note that the frequency and severity of coronary artery disease were directly related to cigarette consumption. Less has been documented about the relationship of peripheral atherosclerotic vascular disease and cigarette consumption, although Begg (1965), Gomes, Bernatz, and Juergens (1967), and Oldham (1964) have demonstrated that there is a relationship between cigarette consumption and atherosclerotic vascular disease. However, Doll and Hill (1964) were not able to show a heightened risk of arterial disease other than coronary heart disease among British doctors who smoked cigarettes. This contrasts with the findings of Widmer, Hartmann, Duchosal, and Plechl (1969), who reported that arterial occlusions of the limbs and coronary arteries were associated with the same risk factors.

Coran and Warren (1966) have shown that symptoms alone cannot provide reliable information on either the type or the extent of peripheral arterial lesions. Kingsbury (1966) noted that when the disease was considered in terms of arterial lesions, rather than symptoms and signs, there appeared to be some division in the type of disease as well as in its extent, and suggested that atherosclerotic lesions at different sites could not necessarily be considered homogeneous in nature. Study of the radiographs of the aorta and iliac and femoral arteries can allow precise diagnosis and anatomical localization of peripheral atherosclerotic disease and this lends itself to objective reproducible measurement. It would therefore seem possible to compare the lesions of atherosclerotic peripheral vascular disease as seen on radiographs with cigarette consumption and to determine their overall association as well as attempting to define their relationship at different sites in the arterial tree.

MATERIAL AND METHODS

All the patients in this series were referred by clinicians because of symptoms of impaired vascular supply. The series was composed of 41 males and 13 females whose mean ages were 60·3 and 60·2 years respectively. Lumbar aortography was performed by direct needle puncture and consecutive films were obtained using the Garrow Box film changer. Diagnostic films from the aorta to the popliteal artery were obtained. The height of the X-ray tube above the films was constant in all the cases and magnification factors may be considered to be constant. Patients known to have diabetes, hypertension, or polycythaemia were excluded from the series, as were patients who had already undergone vascular surgery and patients in whom there was any doubt that the occlusive or stenotic lesion was primarily due to atherosclerosis. Patients who presented with atherosclerotic abdominal aneurysms were likewise excluded since their condition was not essentially that of occlusive arterial disease. Otherwise, the series consisted of consecutive referrals, and in the patients who later underwent surgery the diagnosis of atherosclerosis was confirmed. All the patients were interviewed before aortography and their smoking habits were recorded as to whether they were cigarette, pipe, cigar, or mixed smokers. The quantity of cigarettes consumed was recorded in four groups: non-smoker, 1–19, 20–29, and over 30 per day. Dramatic changes in consumption within the previous 3 years were ignored, the objective being to obtain as far as possible accurate figures of the patient's lifelong smoking habits. The radiographs were analysed and a series of measurements was taken. Previous workers have described techniques for the analysis of arteriograms but none was considered suitable for this investigation and a new system of analysis was introduced. Routine lumbar aortography only allows appreciation of the arterial system in the postero-anterior plane. It is appreciated that because the vessels are only visualized in one plane, occasional errors of interpretation could occur. However, this procedure has gained general acceptance as a precise means of accurately showing the arterial tree, and findings at operation or autopsy compare well with aortography. An artery which has a minimum cross-sectional diameter equal to half of its maximum cross-sectional diameter has its calibre reduced by half in the postero-anterior plane and has a minimum : maximum ratio of 0·5. This minimum : maximum ratio is equivalent to the 'available' artery remaining, and a severely stenosed artery would thus have a low reading whilst an unaffected artery would have a reading approaching 1·00. An occluded artery has a reading of zero. Measurements of the internal diameters of the vessels were taken at their minimum and maximum cross-sectional diameters for each artery. The lower abdominal aorta was considered to be too long a segment to be treated as one artery and two arbitrary lines were drawn at the lower border of the second lumbar vertebra and at the lower border of the third lumbar vertebra. One set of minimum and maximum diameters of the aorta was taken between the lower border of the second lumbar vertebra and the lower border of the third lumbar vertebra. This is referred to as the aorta opposite lumbar vertebra 3. A second set of minimum and maximum diameters of the aorta was taken between the lower border of the third lumbar vertebra to the aortic bifurcation. This is referred to as the aorta opposite lumbar vertebra 4. An example of the method used is illustrated in *Fig.* 1. The radiographs of a random sample of the cases were examined 'blind' by a second person who was unaware of the age or tobacco consumption of the patients in order to determine the reproducibility of the measurements.

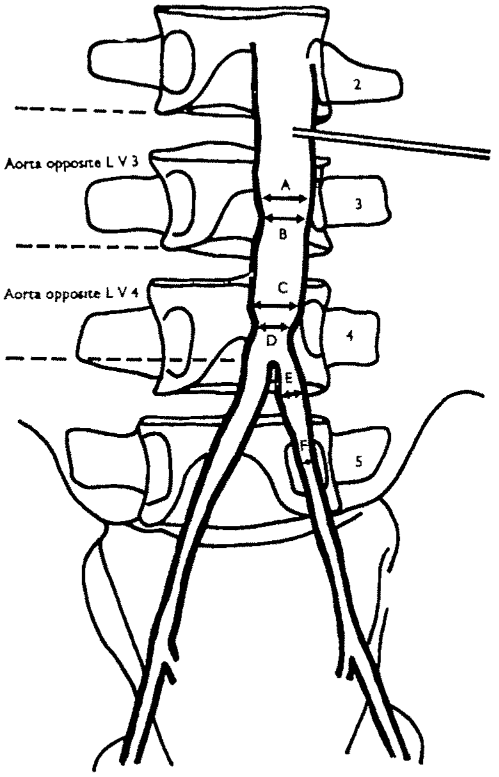

FIG. 1.—An illustrative example of the method used to determine measurements and ratios described in the text. For the aorta opposite L.V.3, A = maximum aortic measurement = 26 mm. and B = minimum aortic measurement = 20 mm., therefore the minimum : maximum ratio opposite L.V.3 is 20 : 26 or 0·77. For the aorta opposite L.V.4, C = maximum aortic measurement = 22 mm. and D = minimum aortic measurement = 16 mm.; therefore the minimum : maximum ratio opposite L.V.4 is 16 : 22 or 0·73. For the left common iliac artery, E = maximum measurement = 11 mm. and F = minimum measurement = 7 mm.; therefore the minimum : maximum ratio is 7 : 11 or 0·64. The ratios for the right common iliac, the external iliac, common femoral, and superficial femoral arteries are obtained in the same manner.

RESULTS

A total of 56 patients was studied, consisting of 41 males and 15 females. All the male patients smoked cigarettes and 6 of these also smoked cigars or pipes or both. Two of the females were life-long non-smokers and were not included in the quantitative assessment since this additional group would have been too small to give valid data for study. *Table I* shows a paucity of relatively light smokers (1–19 cigarettes per day) in the youngest age-group, and it seems that, in general, the heaviest smokers (over 20 cigarettes per day) were younger. *Table II* shows the expected minimum : maximum ratio measurement at the mean age for each group of cigarette smokers. The statistical technique used to estimate and test the ratios in *Table II* was analysis of covariance. The results for both groups of aortic measurements are significant ($P < 0·01$) and show that when related to age the heaviest smokers have the most severe atheromatous stenotic lesions. The ratios for the common iliac artery also show that the heaviest smokers have the most severe stenoses, but the significance level is lower ($P < 0·05$). The ratios for the external iliac artery show the same general trend of increasing severity of disease with increasing cigarette consumption but this finding is not statistically significant. The ratios in the common and superficial femoral artery appear to be entirely random in distribution and are not related quantitatively to

Table I.—NUMBER OF PATIENTS CLASSIFIED BY NUMBER OF CIGARETTES SMOKED PER DAY AND BY AGE

AGE (yr.)	NO. OF CIGARETTES SMOKED PER DAY			TOTAL NO. OF PATIENTS
	1–19	20–29	30+	
Under 50	0	5	3	8
50–59	4	5	6	15
60–69	8	7	9	24
70–79	4	1	2	7
Average age	65·2	59·1	57·1	54

Table II.—EXPECTED MINIMUM : MAXIMUM RATIO MEASUREMENT AT THE MEAN AGE (60·26 YEARS) CLASSIFIED BY NUMBER OF CIGARETTES SMOKED PER DAY AND BY SITE

SITE	NO. OF CIGARETTES SMOKED PER DAY			SIGNIFICANCE
	1–19	20–29	30+	
Aorta opposite L.V.3	0·87	0·78	0·71	$P < 0·01$
Aorta opposite L.V.4	0·93	0·78	0·67	$P < 0·01$
Common iliac artery (left and right)	0·68	0·53	0·46	$P < 0·05$
External iliac artery (left and right)	0·75	0·66	0·64	N.S.
Common femoral artery (left and right)	0·72	0·66	0·79	N.S.
Superficial femoral artery (left and right)	0·37	0·28	0·32	N.S.

N.S., Not significant.

increasing use of cigarettes. A standard statistical program (B.M.D. X64: Bio-medical Computer Programs, X-series Supplement, University of California Press, 1970) was used to do the computation. The radiographs of 5 patients (the sample chosen by using tables of random numbers) were analysed and measured by a second person 'blind' to the figures obtained by the first. This involved 100 measurements at 50 sites. A comparison of the results showed disagreement by a margin of over 0·10 in only 6 per cent of cases, and in 60 per cent of the measurements the margin of disagreement was not more than 0·03. The area of greatest disagreement was in the measurements in the more distal arteries.

DISCUSSION

The consecutive referrals consisted of 41 males and 15 females, of whom only 13 were included in this quantitative assessment. The male : female ratio is under 3 : 1. This compares with the larger series of Gomes and others (1967) where a 4 : 1 ratio was encountered. The invariable consumption of cigarettes by the male patients has been well documented by Oldham (1964) and Begg (1965), and this compares with the findings of Todd (1969), who noted that only 61 per cent of all men in the United Kingdom were cigarette smokers. Several studies concerned with the relationship of cigarette smoking and atherosclerosis have been carried out on autopsy material by Auerbach and others (1965), Strong and others (1966), and Sackett, Gibson, Bross, and Pickren (1968), for it is difficult to assess the amount of atherosclerosis in living patients (Kingsbury, 1969). It has been suggested by Mainland (1953) that there may be inherent disadvantages in this type of study where there may be strong selective factors that tend to make autopsy series non-representative of the general public. In addition, historical information desired for comparison with autopsy findings may be unavailable.

Other work has been concerned with the follow-up of patients presenting with claudication or gangrene (Oldham, 1964; Begg, 1965), but not all patients had lumbar aortography to assess aorto-iliac disease as well as femoral artery disease. Also, there may have been some patients who were not primarily affected by atherosclerosis. During the collection of the present series, patients were excluded on the grounds of emboli, aortitis, thrombo-angiitis obliterans, and fibromuscular arterial disease. It is not suggested that the appearance of this group of patients with non-atherosclerotic arterial disease is in any way representative other than reflecting clinician interest. Diabetic, hypertensive, and polycythaemic patients were also excluded from the series since these patients have been shown by Gomes and others (1967) to be associated with increased risk factors in peripheral vascular disease. Steinberg, Archer, and Steinberg (1965) were the first to attempt systematic measurements of the normal and diseased aorta. Morton, Ehrenfeld, and Wylie (1967) devised a scoring system based on arterial blocks. Kingsbury (1969) showed that it was not possible to group atherosclerotic plaques naturally into representative shapes or sizes and he attempted to grade the severity, type, and extent of atherosclerotic peripheral disease also on a scoring system. However, it was felt that these methods of scoring were not acceptable in this study in that each artery was not individually measured, and also it was thought that the previous scoring systems could not be as accurate for this particular study as the method devised. Kingsbury (1969) suggested that there might be differences in extent and type of atheroma and he noted that blood-sugar concentrations (but not plasma-cholesterol levels) differed according to the distribution of the main arterial lesion, being higher in aorto-iliac disease than in femoropopliteal disease. Studies of both the epidemiology and pathology by Morris (1951) and Mitchell and Schwartz (1965) suggested that atherosclerosis is not necessarily a uniform disease.

There are a number of areas in this study where error in data collection or assessment might have occurred. First, there is possible bias through case selection. In general, surgeons are now less prepared to operate on stenotic or occlusive lesions below the inguinal ligament and will tend to refer for aortography only the patients whose disease clinically is predominantly in the aorto-iliac region. There might be some factors in these patients which differ from those whose disease is more peripheral. Secondly, there is possible bias in smoking assessment. All the patients were examined by the same person and a formal questionnaire was used. Thirdly, the measurements might be inaccurate, but from the sample of radiographs examined 'blind' by a second person there was little disagreement in the figures obtained for the proximal arteries although some disagreement occurred in the more distal arteries. This suggests that any inaccuracies of measurement are only of importance in the more peripheral arteries. In the smaller arteries, measurement differences of 1 mm. may have a profound effect on the minimum : maximum ratio, and it is therefore possible that this ratio is a much better measure of disease (and hence its smoking association) in larger arteries and that the smaller peripheral arteries are not capable of being assessed accurately by the method used here. However, it is difficult to see any modification which might allow more accurate assessment. It is also possible that the apparent absence of an association between smoking and disease of the superficial femoral artery might be because of gross end-stage disease and that an earlier effect is obliterated as the artery becomes blocked. Although this is probably the case, it was noted that there was no apparent quantitative association between atherosclerosis in the common femoral artery and smoking. This artery was only rarely occluded and had a relatively high ratio. A fourth possibility which could affect the assessment of the results is the effect of proximal stenosis on distal calibre. It is not always possible to know whether the whole lumen of an artery distal to an obstruction has been filled by contrast material. Where there is a tight proximal stenosis with a big pressure drop the contrast material often does not fill out the entire arterial lumen. This factor clearly could affect the measurements obtained. It is stressed, however, that it is not suggested that the diameters measured or the ratios obtained are in any way related to flow or pressure. In spite of all these errors which might occur during the collection of the results it is thought probable that the figures obtained reflect the quantitative association of atherosclerosis with smoking. This association appears to be maximal in the aorta and becomes less apparent distally, either because of inaccuracies in measurement hiding a true association or, less likely, because of differences in the homogeneity of atherosclerosis.

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THE 'ICED-GLOVE' METHOD OF TREATMENT OF PARAPHIMOSIS

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SUMMARY

A new method of reduction of paraphimosis, using a rubber glove filled with iced water, is described. The method is simple to carry out and causes little discomfort to the patient. Successful reduction was performed in 9 out of 10 cases, often when manual reduction had failed. Reasons for the single failure are put forward, and alternative treatment is suggested for such complicated cases.

PARAPHIMOSIS may occur at any age. The patient usually presents for treatment before venous engorgement of the glans has resulted in anoxic ulceration and infection. Early reduction is necessary to prevent these changes.

Manual reduction by compression of the oedematous tissues and manipulation of the constricting band over the glans penis (Schenck, 1930) is often successful but without a general anaesthetic is extremely painful. This method may be facilitated by lubrication with Vaseline and the application of ice packs to lessen the oedema. If the method fails other procedures which can be tried include the injection of hyaluronidase to dissipate oedema (Ratcliff, 1954), drainage of oedema by Southey's tubes (Barry, 1954), a dorsal slit of the constricting band (Schenck, 1930), immediate circumcision (Cletsoway and Lewis, 1957), excision of the constricting band (Cumston, 1920), or reduction of the constricting band with Babcock clamps (Skoglund and Chapman, 1970). All these methods require skin puncture or incision into, or application of clamps on to, an oedematous area which will increase inflammation in damaged tissues. A general anaesthetic is often required because operative techniques are painful.

In this paper a simple method is described to reduce the paraphimosis without incising or puncturing the skin using local pressure and ice.

METHOD

The glans penis and oedematous fold of foreskin are coated with anaesthetic jelly (e.g., xylocaine gel), both to lubricate and to anaesthetize the area. After 2 minutes surface anaesthesia is complete. A disposable No. 8 rubber glove is half filled with ice and water and a knot is tied in the cuff to prevent the contents from escaping (just as one would tie off the spout of a toy balloon). The fingers may also be tied so that the contents are confined to the body of the glove. The prepuce is fully retracted, and the glans is placed into the thumb of the glove which is held invaginated by the operator (*Fig.* 1). The distended glove is pressed on to the pubis by the surgeon and held in place for 5 minutes, or until the oedema has resolved (*Fig.* 2). A combination of ice cooling together with compression from the thumb of the glove causes a reduction of oedema. The paraphimosis can usually be reduced without difficulty by pushing the constricting band over the contracted glans. Reduction can often be performed through the glove as a 'closed' procedure, but if this fails it is carried out as soon as the glove is removed.

RESULTS

The 'iced-glove' method of reduction of paraphimosis has been performed on 10 consecutive cases presenting at the Radcliffe Infirmary. Their ages ranged from 8 to 91 years and the duration of the paraphimosis varied from 8 hours to 4 weeks (*Table I*).

In 9 cases painless reduction was successfully performed. In 6 of these patients attempts at the standard manual reduction by a general practitioner or casualty officer had failed.

In 1 case the patient had chronic balanitis, which was complicated by a paraphimosis of 3 days' duration. There was severe ulceration of the glans and adhesions between the constricting band and the penile sulcus. These changes made it impossible to reduce the paraphimosis by conservative means, and the 'iced-glove' method failed. A dorsal slit with division of the adhesions under general anaesthetic was successfully performed.

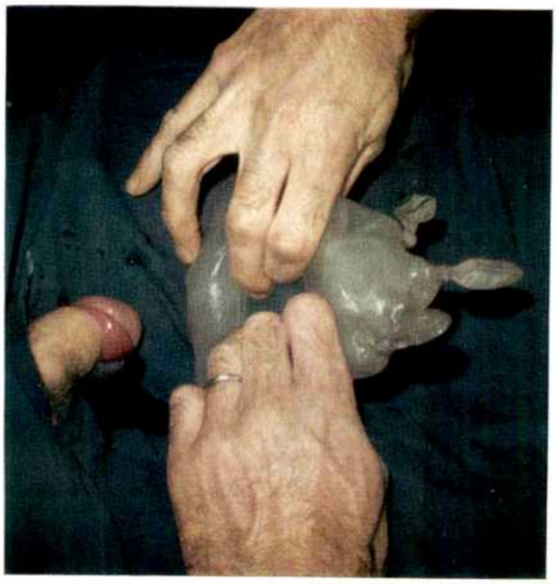

FIG. 1.—Invaginated thumb of the glove about to be stretched over the paraphimosis.

Table I.—SUMMARY OF THE CASES IN THE PRESENT SERIES

CASE No.	AGE (yr.)	DURATION	PREVIOUS ATTEMPTS AT REDUCTION	'ICED-GLOVE' METHOD
1	78	12 hr.	None	Success
2	8	16 hr.	None	Success
3	88	4 d.	Manual reduction failed	Success
4	81	1 d.	Manual reduction failed	Success
5	18	30 hr.	Manual reduction failed	Success
6	23	36 hr.	Manual reduction failed	Success
7	91	4 wk.	Manual reduction failed	Success
8	68	3 d.	None	Failed
9	42	2 d.	None	Success
10	17	3 d.	Manual reduction failed	Success

DISCUSSION

The success of the 'iced-glove' method of reduction of paraphimosis depends upon both pain relief and dissipation of oedema. Surface anaesthesia is established by the local application of xylocaine gel to the glans penis and oedematous foreskin. A gauze swab wrapped around the oedematous tissues ensures that the melting gel remains in place for 2 minutes, by which time surface anaesthesia is usually well established.

Application of the glove is a painless procedure, and it is greatly facilitated by the lubricant action of the gel. Anaesthesia is potentiated by the ice and subsequent reduction of the paraphimosis can be carried out with little discomfort.

As the ice is enclosed within a glove the patient is not distressed by ice-cold water dribbling over the perineum and thighs, which is unavoidable if plain ice packs are applied.

However, in the case with a badly scarred and ulcerated paraphimosis the 'iced-glove' method caused discomfort and failed to cure the condition. In a long-standing and scarred paraphimosis it may be impossible to effect reduction by manipulation, owing to fibrous adhesions between the constricting band and the penile sulcus. In such cases the 'iced-glove' technique is contra-indicated and operative reduction such as a dorsal slit should be immediately undertaken.

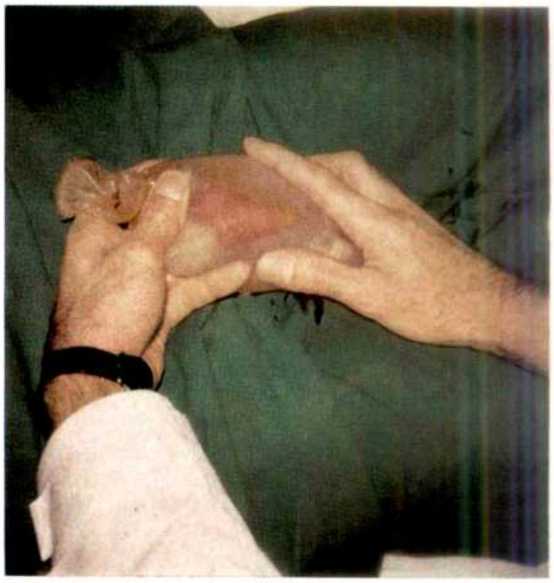

FIG. 2.—Glove in place during compression of the glans.

CONCLUSION

The 'iced-glove' method of reduction of paraphimosis is a successful and painless procedure. It is superior to the standard methods of reduction, but is not recommeded in the presence of ulceration and scarring of the glans.

Acknowledgement.—I am very grateful to Mr. Emanoel Lee for his advice and critical reading of the manuscript.

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LUMBAR SYMPATHECTOMY

A RETROSPECTIVE STUDY OF 142 OPERATIONS ON 100 PATIENTS

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SUMMARY

A retrospective survey of 142 lumbar sympathectomies has shown that this operation is of value in the treatment of rest pain and ischaemic ulceration, especially in the 61–70 age-group. It is of less value in claudication. Diabetics fare only slightly less well than non-diabetics. Two cases of ureteric injury are described. Neuralgia occurred in 12·6 per cent of patients.

LUMBAR sympathectomy is one of the commonest operations performed for ischaemia of the feet. The rationale is that there is a high level of vasoconstrictor tone in the circulation of the skin of the foot in contrast to that of the muscle of the calf (Myers and Irvine, 1966b), and that sympathetic denervation results in marked vasodilatation in the foot in the experimental animal (Lövsing and Mellander, 1956) and in man (Walker, Lynn, and Barcroft, 1950).

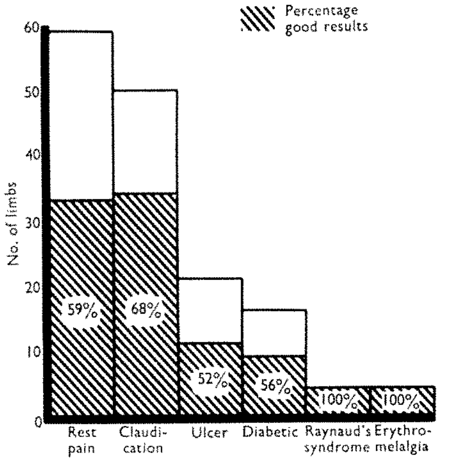

FIG. 1.—Response to lumbar sympathectomy compared with the indications for operation.

The rationale of sympathectomy for intermittent claudication is more obscure (Myers and Irvine, 1966a). Sympathectomy is, however, often performed for the relief of claudication, although its value is disputed (Taylor and Calo, 1962). The main arguments for its use are that some cases in which direct arterial surgery is contra-indicated seem to gain considerable relief of symptoms, and that if done early in the progress of arterial disease it may defer the onset of rest pain and gangrene.

Experienced vascular surgeons generally regard sympathectomy as a safe and simple operation which is relatively free from serious complications. It must be remembered, however, that complications do occur, and that the success of the operation depends upon its proper execution. The present study examines the success of sympathectomy in a London teaching hospital over a period of 5 years with particular reference to the indications, age of patients, complications, subsequent amputation, diabetes, and histology of the sympathetic chain removed at operation.

INDICATIONS

Of the 142 sympathectomies performed, 59 were for rest pain, 20 for ischaemic ulceration, and 51 for claudication. The remainder were for Raynaud's syndrome (4), erythromelalgia (4), acrocyanosis (2), traumatic ulcer (1), and undiagnosed foot pain (1).

OPERATIONS

Fifty-four operations were performed by consultants and 88 by registrars. That sympathectomy is an operation so often entrusted to junior staff is a further, perhaps unsaid, advantage of the procedure.

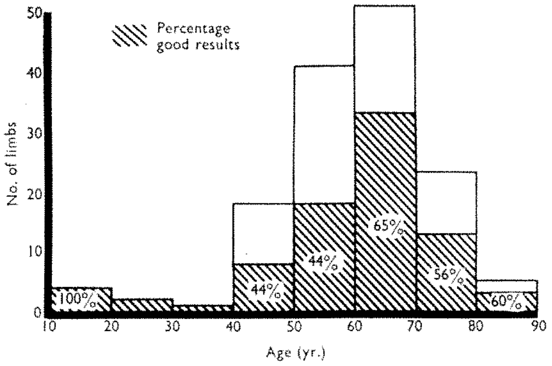

FIG. 2.—Response to lumbar sympathectomy compared with age.

RESULTS

Results of the operation were classified as 'good' or 'bad'. Good results were those in which the patient stated unequivocally that he was improved after the procedure or in which skin lesions were seen to heal. All other responses were classified as bad, since anything but obvious success must be regarded as failure for an elective operation for a specific symptom. In *Figs.* 1 and 2 response is related to the indications and age. Fifty-nine per cent of the patients with rest pain were relieved. This figure falls at the upper end of the usually quoted range of success in rest-pain relief (Berry, Flotte, and Coller, 1955; Gillespie, 1960). An unusually high success rate of 68 per cent was obtained in patients treated in this series for intermittent claudication. The quoted incidence of improvement varies from 13 per cent (Gillespie, 1960) to 75 per cent (Smithwick, 1957). Taylor and Calo (1962) found that 39 per cent of untreated cases improved compared with 41 per cent of cases treated by sympathectomy.

Ischaemic ulceration improved in just over half of the patients treated.

Diabetics fared only slightly less well than the non-diabetic patients.

The response in Raynaud's syndrome and erythromelalgia was excellent, although the numbers involved do not give results of significance.

Age appeared to have a significant effect upon the response to sympathectomy. The 61–70 age-group had a higher success rate than other age-groups over 40 years, in spite of a similar distribution of the various indications. The small number of patients treated for vasospastic as distinct from degenerative disease occurred mainly in the under 40 age-group and had excellent results.

COMPLICATIONS

Post-sympathectomy neuralgia was the most troublesome complication, occurring after 12·6 per cent of operations in this series. Martin, Lynn, Dible, and Aird (1956) stated that the incidence was about 12 per cent, and Tracy and Cockett cited 18 per cent (1957). Four patients with bilateral sympathectomy suffered from neuralgia in only one limb. In a review by Cooley and Herman (1963) the range of incidence of neuralgia is quoted as 2–100 per cent, depending on how thoroughly it is sought. Those authors stated that ligation of the cut ends of the sympathetic chain abolished post-sympathetic neuralgia in 50 cases. Litwin (1962) has reviewed the theories of aetiology of neuralgia, and Silverstein and Jacobson (1967) have discussed the neurological findings. However, no satisfactory explanations have emerged. The clinical findings can largely be explained by postulating a chemical stimulation of somatic afferent fibres by the degenerating myelin of severed fibres of the white rami communicantes. This would explain the delayed onset, spontaneous resolution, and upper lumbar distribution.

Ureteric injury occurred in 2 cases. In one patient with extensive scarring due to an old psoas abscess the injury was recognized at the time of operation and was successfully repaired. The other case presented with ureteric bleeding 1 week after sympathectomy and required nephrectomy.

Ileus occurred in 4 patients, 2 of whom had had bilateral sympathectomy at the same operation.

One deep-vein thrombosis and one myocardial infarction occurred.

There was 1 death in an elderly patient.

HISTOLOGY

The histology of the removed sympathetic chain proved negative in 9 cases (7 performed by registrars and 2 by consultants). The response to surgery was good in 55 per cent of these cases (58 per cent overall), suggesting either the unreliability of subjective responses or that the sympathetic chain was removed but not seen on microscopy.

SUBSEQUENT AMPUTATION

Major amputation following sympathectomy was required in 15 per cent of the limbs in this series. Amputation was usually a relatively early event, being required within 6 months of sympathectomy in most cases. The possible explanation for this is that sympathectomy has little effect on rapidly progressive arterial disease or established gangrene (Taylor and Calo, 1962), but that it significantly reduces the risk of development of gangrene (Edwards and Crane, 1961).

CONCLUSIONS

Lumbar sympathectomy retains an important place in the treatment of ischaemia of the feet, and is of undoubted value in the relief of rest pain and the promotion of healing of ischaemic ulceration. It probably delays the development of gangrene, but has little value in the treatment of established gangrene, those limbs requiring amputation coming quickly to this procedure. In this series, sympathectomy appeared to improve intermittent claudication, even taking into account the natural tendency for this symptom to improve in some instances.

The complication rate is low, although neuralgia causes appreciable postoperative disability. However, although this is difficult to treat, it is self-limiting. The mortality and incidence of serious cardiorespiratory complications are low.

Two cases of ureteric injury in 100 patients highlight the dangers of sympathectomy and are a reminder of the necessity to identify the ureter and to check its integrity before closure of the wound (Higgins, 1967).

Diabetes has little adverse influence on the effectiveness of sympathectomy.

Acknowledgement.—I should like to thank Mr. H. H. G. Eastcott for his interest and advice in the preparation of the text.

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EFFECT OF CORPORAL AND ANTRAL GASTROJEJUNOSTOMY ON CANINE GASTRIC EMPTYING OF SOLID SPHERES AND LIQUIDS

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SUMMARY

Gastric emptying of solids and liquids was measured in 12 dogs with and without corporal or antral gastrojejunostomy. Both types of stoma hastened the onset but did not alter the time from onset to complete emptying of 40 small plastic spheres. Corporal gastrojejunostomy slowed the emptying of 400 ml. of 154 mM NaCl but not of 500 mM glucose, whereas antral gastrojejunostomy slowed the emptying of both.

GASTRO-ENTEROSTOMY has been used by surgeons to alter gastric emptying for almost 100 years (Wölfler [1881], 1962). The assumption often made is that the operation speeds the discharge of gastric content from the stomach. However, no quantitative assessment of gastric emptying of solids and liquids after gastro-enterostomy has been done.

We tested the effect of corporal and antral gastrojejunostomy on gastric emptying of solid spheres and liquids in conscious dogs and found that the rate of emptying was not increased. In fact, gastric emptying of iso-osmolar NaCl was slowed.

MATERIALS AND METHODS

Twelve mongrel female dogs, weighing 8–15 kg., were divided into two groups. Four dogs underwent immediate gastrojejunostomy under sodium pentobarbital anaesthesia using sterile technique, and 8 were not operated on. The stomach and jejunum were exposed through a ventral midline upper abdominal incision. In dogs 1 and 2 a longitudinal gastrotomy was made through the anterior wall of the stomach parallel to the greater curvature and 1 cm. from it; the incision began 16 cm. orad to the gastroduodenal junction and extended aborad 4 cm. A longitudinal jejunotomy was next made through the antimesenteric border of the proximal jejunum; the incision began 15 cm. distal to the ligament of Treitz and extended aborad 4 cm. An antecolic anastomosis was then performed between the stomach and the jejunum at the enterotomy sites using a single layer of non-inverting, interrupted, 000 Dacron sutures. The stomach and jejunum were joined so that the orad limits of the gastrotomy and jejunotomy were apposed, as were the aborad limits. Thus, an isoperistaltic, antecolic, anterior, corporal gastrojejunostomy resulted, with a circumference of 8 cm. and a diameter of about 2·5 cm. The most distal limit of the anastomosis was 12 cm. from the gastroduodenal junction. Silver clips were placed at the anastomosis to facilitate its later fluorographic identification.

Identical techniques were used in dogs 7 and 8 to fashion an antral gastrojejunostomy, with the distal limit of the anastomosis 2 cm. from the gastroduodenal junction.

The dogs that underwent operation were allowed 2 weeks to recover, after which emptying tests were begun. Each dog was fully conscious during every test and had been fasted for 18–24 hours. The stomach was aspirated using an oral gastric tube and then washed with 200 ml. of water 30 minutes before the start of any test. If gross amounts of food or particulate matter were found in the aspirate or wash the dog was not used on that day. If small amounts were found the stomach was washed with 100-ml. aliquots of water until it was clear, and the dog was allowed to rest for at least 3 hours before testing.

Gastric emptying of solids was measured five times in each dog, using 40 radio-opaque solid spheres made of polypropylene, each with a diameter of 7 mm. and a specific gravity of about 1·02. The spheres were placed into the stomach via an oral gastric tube, which was then removed. The number of spheres that emptied from the stomach was counted fluoroscopically every 20 minutes, until all the spheres had emptied or 8 hours had passed. The pattern of gastric and intestinal contractions was also noted, and, on some occasions, cinefluorography was performed to obtain films of the movements. The use of spheres by our laboratory to monitor gastric emptying of solids has been described previously (Schlegel, Coburn, and Code, 1966).

Gastric emptying of liquids was assessed on four or five occasions in each dog. The dogs stood or rested comfortably in a Pavlov sling. An oral gastric tube was inserted, and 400 ml. of 154 mM NaCl with 0·00035 per cent of 1,2-^{14}C-polyethylene glycol (^{14}C-PEG; New England Nuclear) of specific activity 0·6 μc. per g. were instilled into the stomach during a period of 20–30 seconds. The tube was then removed. When administered the instillate was at 37·5° C. and had a pH of approximately 6·5. Fifteen minutes after instillation the gastric tube was reinserted and the gastric content was removed by siphoning and gentle aspiration with a syringe. The stomach was washed with 100 ml. of NaCl, and the wash was aspirated to recover any residual instillate.

At the completion of each test the volume of gastric aspirate and gastric wash recovered was measured. The specific activities of 5-ml. samples of aspirate, wash, and original instillate were determined using a liquid scintillation spectrometer (Packard TriCarb 3375). The volume of the instillate remaining in the stomach after 15 minutes was then calculated using the following formula:—

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$$V_R = V_A\left(\frac{SA_A}{SA_I}\right) + V_W\left(\frac{SA_W}{SA_I}\right),$$

in which V_R is the volume (ml.) of the original instillate remaining in the stomach after 15 minutes, V_A is the volume (ml.) of the gastric aspirate, V_W is the volume (ml.) of the gastric wash, and SA_I, SA_A, and SA_W are the specific activities of the instillate, gastric aspirate, and gastric wash, respectively.

A third set of experiments performed four or five times in each dog was done in an identical fashion, except that a 400-ml. instillate of 500 mM glucose was used instead of the NaCl instillate, and the stomach was washed with 100 ml. of distilled water.

In a final set of tests, serum gastrin was measured by use of a radio-immunoassay technique (Yalow and Berson, 1970) in 4 dogs without stomas, in 2 with corporal gastrojejunostomy, and in 2 with antral gastrojejunostomy before and 15 minutes after instillation of 400 ml. of 154 mM NaCl.

Usually only one test of gastric emptying was performed on a dog per day. However, on some occasions, two tests a day were done. At least 3 hours separated the two tests when a liquid instillate preceded the administration of spheres or when two saline instillates were given, and at least 5 hours separated the two tests when glucose instillates were given.

After the initial experiments were completed the dogs with gastro-enterostomy were reoperated on, the stomas, which were well healed, patent, and had a diameter of at least 2·5 cm., were removed, and the enterotomies were closed. The dogs who had not been previously operated on then underwent corporal gastrojejunostomy (dogs 3–6) or antral gastrojejunostomy (dogs 9–12). Beginning 2 weeks after operation, the tests of the gastric emptying of solids and liquids were repeated.

RESULTS

All the dogs survived the operations without complications and were well healed after 2 weeks. The dogs with corporal gastrojejunostomy, however, ate poorly, often vomited, and 3 of the 6 dogs lost weight (dogs 3, 4, and 6). They carried a bile-stained, thick, gastric residue of about 100 ml. after an 18-hour fast. Dogs 3 and 6 became very weak, vomited, and aspirated gastric content, and died 5 weeks after the construction of the stoma. The remaining 4 dogs survived until sacrificed 4–6 months later.

The dogs with antral gastrojejunostomy remained healthy and maintained their weight throughout the experiment.

Dogs without a Stoma.—The pattern of emptying of solid spheres and liquids in dogs without a stoma was the same whether the dogs were investigated after the removal of the stoma (dogs 1, 2, 7, and 8) or before the construction of the stoma (dogs 3–6 and 9–12). Therefore, the data on all the dogs without a stoma are considered together.

Gastric Emptying of Spheres.—The overall pattern of gastric movement of spheres in dogs without a stoma was one of retention of the spheres in the antrum, with continuous mixing and grinding interspersed between periodic bursts of emptying (*Fig.* 1).

The spheres passed through the oral gastric tube directly into the fundus and proximal corpus of the stomach. They were then promptly moved into the distal corpus and antrum, where they usually remained for long periods. The overall mean interval (± S.E.) from insertion to onset of discharge of the spheres from the stomach was 77 ± 13 minutes.

While in the distal stomach the spheres were continuously mixed and ground by peristalsis and the terminal antral contraction. An advancing peristaltic wave propelled the spheres up against the gastroduodenal junction. The spheres were then squeezed by the forceful terminal antral contraction until, unable to pass into the duodenum, they suddenly shot back into the more proximal antrum and distal corpus. This propulsion, squeezing, and retropulsion occurred many times, thoroughly triturating the spheres.

At certain times as a peristaltic wave approached the terminal antrum, bunches of spheres would be moved rapidly from the terminal antrum through the gastroduodenal junction into the duodenum. Sometimes, all 40 spheres would be emptied within a 20-minute period (*Fig.* 1, dogs 1, 7, 8, 9, and 10). However, the overall mean time from onset to completion of gastric emptying was 125 ± 26 minutes.

Once in the small intestine the spheres were usually quickly moved from the duodenum into the jejunum. The caudad rate of movement of the spheres then slowed in the jejunum. Rhythmic jejunal contractions oscillated the spheres back and forth, while moving them gradually and progressively caudad. The spheres never re-entered the stomach from the small intestine.

Gastric Emptying of Liquids.—Iso-osmolar NaCl emptied rapidly from the stomach of dogs without a stoma. Almost half of the 400-ml. instillate had left the stomach after 15 minutes (*Table I*). In contrast, hyperosmolar glucose emptied slowly, so that only about 50 ml. had emptied 15 minutes after instillation (*Table I*).

The gastric aspirates in dogs without a stoma were almost always colourless and were not stained with bile (*Fig.* 2). The mean ratio of disintegrations per minute (dpm) from the ^{14}C-PEG in the aspirate over that in the instillate for 12 randomly selected samples was 0·93 ± 0·02 when NaCl was instilled and 0·92 ± 0·02 when glucose was instilled, showing that the marker had been slightly diluted by gastro-intestinal contents.

Serum Gastrin.—The mean fasting concentration of gastrin in the serum of 4 dogs without a stoma was 194 pg. per ml., and it had not increased 15 minutes after the instillation of 400 ml. of 154 mM NaCl, when it was 192 pg. per ml.

Dogs after Gastro-enterostomy.—The patterns of emptying of solid spheres and liquids after gastro-enterostomy were almost identical whether the stoma was constructed in the corpus or in the antrum.

Gastric Emptying of Spheres.—The overall pattern of emptying of spheres after gastro-enterostomy was that of a rapid onset and steady gradual discharge of spheres from the stomach, in contrast to the retention, then burst-of-emptying pattern noted in dogs without a stoma (*Fig.* 1).

The spheres were promptly moved from the fundus and corpus into the antrum of the dogs with both types of gastrojejunostomy, just as when the dogs had no stoma. Vigorous peristaltic waves and terminal antral contractions then commenced, and these effectively propelled and retropelled the spheres in spite of the presence of the large stoma.

Table I.—EFFECT OF CORPORAL AND ANTRAL GASTROJEJUNOSTOMY ON GASTRIC EMPTYING OF LIQUIDS

DOG	MEAN VOLUME (ml.) REMAINING AFTER 15 MINUTES			
	NaCl (154 mM) $n = 5$*		Glucose (500 mM) $n = 4$†	
	Without Stoma	With Stoma	Without Stoma	With Stoma
Corporal gastrojejunostomy				
1	199	323‡	364	386‡
2	201	333‡	341	375
3	213	286‡	350	349
4	199	188	375	343
5	183	344‡	339	401‡
6	235	246	343	415‡
Overall mean	205	287§	352	378
Antral gastrojejunostomy				
7	143	219‡	348	363
8	169	232‡	347	369
9	239	338‡	353	407‡
10	221	242	338	373
11	235	220	331	373
12	214	303‡	345	366
Overall mean	203	259§	344	375§

* Except dog 1 with stoma and dog 10 without stoma, in which $n = 4$. S.E. are between 11 and 28, except in dog 2 with stoma in which it was 8.

† Except dogs 1, 3, 6, 11, and 12 with stoma and dogs 3, 5, 6, 11, and 12 without stoma, in which $n = 5$. S.E. are between 4 and 16, except in dogs 2, 3, 10, 11, and 12 with stoma in which they were between 19 and 30.

‡ Differs from value without stoma ($P < 0{\cdot}05$, unpaired t-test).

§ Differs from value without stoma ($P < 0{\cdot}05$, paired t-test).

However, in contrast to dogs without a stoma, those with a stoma began almost immediately to empty the spheres from the stomach. The mean interval from insertion to onset of emptying was 13 ± 2 minutes which is much quicker than the 77 minutes required when the dogs had no stoma ($P < 0{\cdot}01$, paired t-test).

The spheres were discharged from the stomach in three different ways. First, the spheres moved from the gastric lumen through the stoma and into the efferent limb of the gastrojejunostomy. When the spheres took this route, they did so not in a burst pattern but in a slow, one-by-one sequence.

Secondly, bunches of spheres also periodically shot through the gastroduodenal junction into the duodenum just as they did when the dogs had no stoma. Once in the duodenum the spheres were swept rapidly around into the proximal jejunum which formed the afferent limb of the gastro-enterostomy. The spheres then either re-entered the stomach via the stoma, completing a full circular movement, or moved past the stoma into the efferent limb of the jejunum and thence caudally into the small intestine. On occasions when the spheres were re-entering the stomach through the stoma, the number of spheres counted in the stomach at a given point was sometimes greater than had been found in the preceding period. The phenomenon occurred at least once in 8 of the 12 dogs with gastro-enterostomy (*Fig.* 1), but happened on only one occasion in dogs without a stoma (dog 4).

Thirdly, the spheres occasionally passed from the stomach through the stoma and into the afferent jejunal limb, moving a very short distance orad in the afferent limb. They then would be quickly propelled back again to the stoma and thence into the stomach or into the efferent limb.

Thus, the emptying of spheres from the stomach was the net result of discharge from the stomach through the stoma and through the gastroduodenal junction, as well as of movement back into the stomach from the jejunum through the stoma. (A film documenting the movement of spheres with and without gastrojejunostomy is available from the authors' laboratory.)

Although the onset of emptying of the spheres occurred sooner after both corporal and antral gastrojejunostomy than when the dogs had no stoma, the time from onset to completion of emptying of the spheres was not altered by either stoma (*Fig.* 1). The overall mean time from onset to complete emptying after gastro-enterostomy of 164 ± 26 minutes did not differ significantly from the mean of 125 minutes found when the dogs had no stoma ($P > 0{\cdot}05$, paired t-test). However, none of the dogs with gastro-enterostomy emptied all 40 spheres from the stomach in 20 minutes as they sometimes did when no stoma was present (*Fig.* 1).

The movement of the spheres in the small intestine distal to the stoma in the dogs with gastrojejunostomy, as in those without, was that of slow, rhythmic, back-and-forth oscillation with progressive caudad migration. Once in the efferent jejunal limb, the spheres did not re-enter the stomach.

Gastric Emptying of Liquids.—Corporal gastrojejunostomy slowed the gastric emptying of iso-osmolar NaCl but not of hyperosmolar glucose (*Table I*). The emptying of glucose was slowed in 3 of 6 dogs with a corporal stoma, but when the group was considered as a whole the difference was not significant. Antral gastrojejunostomy slowed gastric emptying of both NaCl and glucose (*Table I*).

Glucose continued to empty more slowly than NaCl in dogs after both types of gastrojejunostomy, just as it did when the dogs had no gastrojejunostomy (*Table I*, $P < 0{\cdot}01$, paired t-test).

The gastric aspirates from dogs with gastrojejunostomy were always, or nearly always, heavily stained with bile, while aspirates from the same dogs without a stoma were almost always colourless (*Fig.* 2). The mean ratio of dpm in the aspirate to dpm in the instillate for 12 randomly selected samples in dogs with slower gastric emptying of NaCl or glucose after gastro-enterostomy was 0·85 ± 0·02, compared with 0·95 ± 0·02 in identical tests in the same dogs without a stoma. Thus, greater dilution of the marker occurred in these dogs after gastro-enterostomy ($P < 0{\cdot}01$, paired t-test). In contrast, in dogs with unaltered gastric emptying after gastro-enterostomy the mean ratio of dpm in the aspirate to that in the instillate was unchanged at 0·93 ± 0·02.

Serum Gastrin.—The mean serum-gastrin concentration during fasting in dogs with gastro-enterostomy was 189 pg. per ml. and was not greater than that in dogs without a stoma. The mean serum gastrin was not increased 15 minutes after the instillation of NaCl in dogs with a stoma, when it was 187 pg. per ml.

Autopsy Findings.—At autopsy the stomas in the 8 dogs with intact gastro-enterostomy were well healed, patent, and not kinked, showed no ulcers, and had a diameter of 2·5 cm. or more (*Fig.* 3). In the 4 dogs in which stomas had been removed, the sites of closure in the stomach and jejunum were smoothly healed, and no evidence of gastric or intestinal stenosis or obstruction was present.

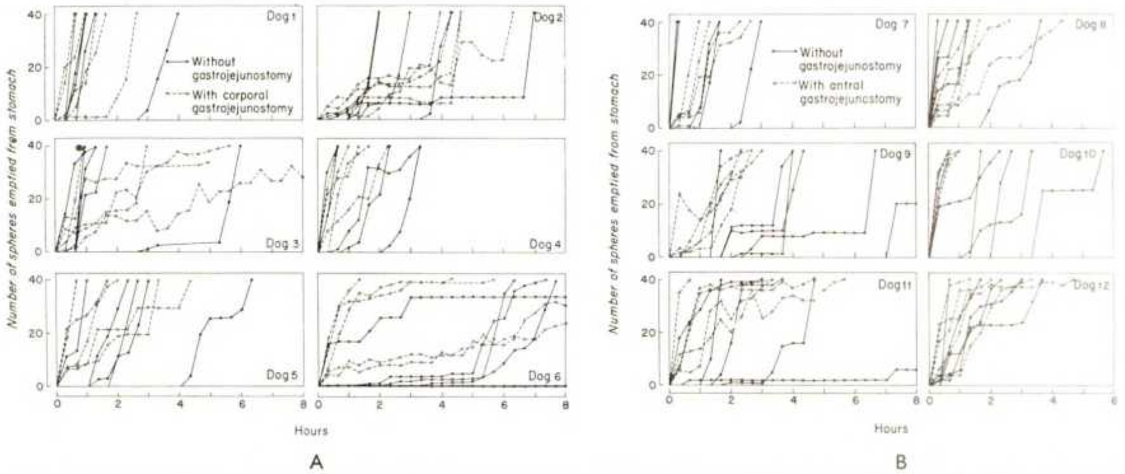

FIG. 1.—Gastro-enterostomy hastens the onset but does not alter the time from onset to complete emptying of 40 plastic spheres. Five tests were done in 6 dogs with and without corporal gastrojejunostomy (A) and in 6 dogs with and without antral gastrojejunostomy (B).

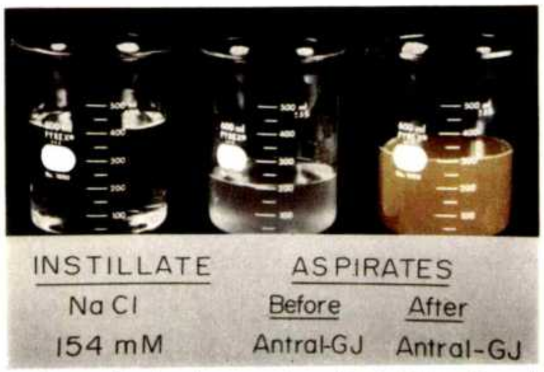

FIG. 2.—Gastric aspirates 15 minutes after instillation of 400 ml. of iso-osmolar NaCl are colourless in dogs without gastro-enterostomy but are bile-stained in dogs with antral (or corporal) gastro-enterostomy. Volume of instillate remaining is greater after gastro-enterostomy (*Table I*).

DISCUSSION

Our experiments have shown that gastro-enterostomy in the dog does not speed gastric emptying of solid spheres and liquids but that it actually slows the emptying of iso-osmolar NaCl.

Cannon and Blake (1905) fed starch gruel or canned salmon mixed with bismuth subnitrate to cats that had corporal or antral gastro-enterostomy, after which they studied gastric emptying fluoroscopically. They found that gastric content, especially the more solid salmon, usually emptied via the gastroduodenal junction rather than via the stoma. They also noted that chyme circulated from the stomach to the duodenum and then back into the stomach again through the stoma. Cannon and Blake, however, did not measure the rate of gastric emptying in their experiments.

Johnston and Ravdin (1935) measured gastric emptying of liquids in dogs with gastro-enterostomy. They instilled solutions of glucose into the stomach and killed their animals 1 hour later. They found greater volumes of fluid in the stomachs of dogs with gastro-enterostomy than in those without. Their instillates were hypertonic, however, and no unabsorbable marker was used. Thus, Johnston and Ravdin could not determine what portion of the volume remaining was instillate and what portion was of gastric or small intestinal origin.

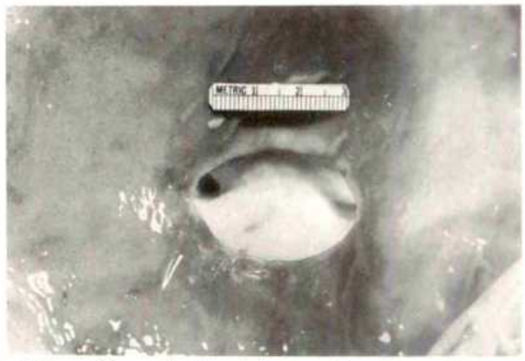

FIG. 3.—Dog 5. A view of the stoma from the gastric lumen at autopsy shows a well-healed gastro-enterostomy with no ulceration or kinks, and a stomal diameter of about 2·5 cm.

In contrast, Gianturco (1934), studying dogs, and Buckler (1967), studying humans, did not find that gastro-enterostomy consistently altered gastric emptying. Neither worker, however, compared gastric emptying in the same subjects before and after gastro-enterostomy.

Our experiments have shown that gastro-enterostomy did not alter the rate of gastric emptying of spheres, but that it did slow the emptying of iso-osmolar NaCl. It is striking that, in spite of the presence of a stoma with a diameter about four times that of the spheres, the net rate of emptying of spheres from the stomach did not differ from that of the controls. We had anticipated, as did Armitage and Dean (1963), that the great pressure generated by gastric contractions, especially in the antrum, would quickly propel the spheres through the large stomas into the jejunum and speed gastric emptying. But this did not happen. The rate of gastric emptying of spheres was not altered by gastro-enterostomy.

An incoordination between gastric and jejunal contractions may have impeded the exit of spheres through the stoma. Weisbrodt, Wiley, Overholt, and Bass (1969) have shown that gastric emptying is impaired if the co-ordinated sequence of gastric contraction–duodenal relaxation is disturbed.

Some spheres did empty in a slow one-by-one sequence through the stoma, and this may account for the earlier onset and the gradual steady pattern of emptying of spheres in dogs with gastro-enterostomy. However, the number of spheres leaving the stomach via the stoma must have been balanced by the number re-entering the stomach, because the overall time of emptying of spheres was unchanged after gastro-enterostomy.

Both corporal and antral gastrojejunostomy slowed gastric emptying of iso-osmolar saline, but only antral gastrojejunostomy slowed emptying of hyperosmolar glucose. However, glucose emptied so slowly in dogs with either type of stoma that the differences were very small.

Since gastrin slows gastric emptying of saline solutions (Hunt and Ramsbottom, 1967), we wondered at first if the slowed emptying of similar solutions that we observed after gastro-enterostomy was partly due to the release of gastrin from the antrum by bile-salts (Bedi, Debas, Gillespie, and Gillespie, 1971; Nahrwold, 1972). Bile was consistently present in the gastric lumen after gastro-enterostomy. However, there was no difference in the amount of gastrin in the serum between dogs with gastro-enterostomy and those without. Thus, bile-salts were not bathing the antral mucosa in concentrations great enough to cause the release of increased amounts of gastrin.

Our experiments show that gastric emptying of liquids is slower after gastro-enterostomy because of the circular movement of gastric content from the stomach to the duodenum and jejunum and back into the stomach again via the stoma. The dilution of the gastric marker, the presence of bile in the aspirated content, and the circular movement of the spheres seen at fluoroscopy after gastro-enterostomy support this interpretation. Thus, the slow emptying is a net result of two opposing fluxes: (1) the discharge of gastric content through the pylorus and through the stoma, and (2) the re-entry of this content into the stomach via the stoma.

It is possible that duodenal content re-entered the stomach by refluxing through the pylorus rather than by passing through the stoma in dogs with gastro-enterostomy. This seems unlikely, however, since we never observed duodenal spheres re-entering the stomach through the pylorus whereas we frequently saw them do so via the stoma.

The braking mechanisms for gastric emptying brought into play by the duodenal osmoreceptors (Hunt, 1963) are still effective after gastro-enterostomy. The emptying of hypertonic glucose remained slower than that of isotonic NaCl in dogs with a stoma. A similar conclusion was reached by Gianturco (1934) and Johnston and Ravdin (1935).

It has been stated that antral gastrojejunostomy leads to more rapid gastric emptying than does corporal gastrojejunostomy (Cannon and Blake, 1905). However, we found little difference in the patterns of emptying between the two types of stomas. The dogs with corporal gastrojejunostomy had a greater gastric residual, vomited more often, and were poorer eaters than those with an antral stoma. Furthermore, 2 of the 6 dogs with a corporal stoma died of aspiration pneumonitis in the post-operative period. We have no satisfactory explanation for these findings. We did not find kinks at the site of the anastomosis, as Cannon and Blake (1905) described.

Gastrojejunostomy has been commonly used in the treatment of duodenal ulcer in the past (Mayo, 1905) and is still employed by some in patients with low outputs of acid (Small, Falconer, Smith, McManus, and Sircus, 1971). The healing effect of the operation, however, has never been explained adequately. The present experiments indicate that the operation may aid the healing of duodenal ulcers by (1) slowing the net rate of emptying of corrosive gastric juices and (2) allowing small intestinal content to enter the stomach where it can buffer and neutralize hydrogen ions.

It should be emphasized that our dogs had no obstruction at the gastroduodenal junction and had intact vagal innervation. When pyloric obstruction or truncal vagotomy has already slowed gastric emptying, gastro-enterostomy may then speed the discharge of gastric content. However, in dogs with a normal stomach the operation does not speed gastric emptying.

Acknowledgements.—Thanks are expressed to Dr. C. F. Code for advice and to Dr. V. L. W. Go who performed the analyses for gastrin.

This investigation was supported in part by Research Grant AM-2015 from the National Institutes of Health, Public Health Service.

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References: 1 *British Journal of Cancer* (1971), 25, 270.
2 *British Medical Journal* (1973), 1, 13.

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RUPTURED NON-TRAUMATIC ANEURYSMS OF THE DESCENDING THORACIC AORTA

By T. G. J. BRIGHTMORE and C. E. DREW
THORACIC SURGICAL UNIT, WESTMINSTER HOSPITAL, LONDON

SUMMARY

Two cases of ruptured non-traumatic aneurysm of the descending thoracic aorta and a third in which rupture was imminent are discussed with regard to two simple operative techniques, both of which were employed with success. Partial aneurysmectomy was employed in one case and a temporary to permanent shunt graft in the other two. The simplicity of the techniques is such that they may be used in hospitals which are not equipped for extracorporeal perfusion.

THE most common site of aortic aneurysms after the infra-renal abdominal aorta is the descending thoracic aorta (Joyce, Fairbairn, Kincaid, and Juergens, 1964; Bloodwell, Hallman, Beall, Cooley, and De Bakey, 1966; Austen, 1967). The poor prognosis of untreated aneurysms of the thoracic aorta is well documented (Boyd, 1924; Colt, 1927; Kampmeier, 1938; Cranley, Herrmann, and Preuninger, 1954). Their natural history is enlargement and eventually rupture (Groves, 1961) and survival mainly depends on the mode of aneurysm rupture and whether the adjacent tissues, especially the mediastinal pleura, are strong enough to contain the haemorrhage (Bromley, Hobbs, and Robinson, 1965; Valiathan, Weldon, Bender, Topaz, and Gott, 1968).

In dissecting aneurysms rupture is the major cause of death (Hirst, Johns, and Kime, 1958; Wheat, Palmer, Bartley, and Seelman, 1965). Rupture is the cause of death in approximately one-third to one-quarter of patients with syphilitic and arteriosclerotic aneurysms of the thoracic aorta (Cranley and others, 1954; Joyce and others, 1964). In 25 per cent of ruptured syphilitic aneurysms of the thoracic aorta the patient lived for over 6 hours after rupture and 15 per cent of these cases lived for over 25 hours (Cranley and others, 1954). With the more common arteriosclerotic aneurysm death is probably quicker following rupture possibly because of widespread vascular disease.

Factors which have an adverse effect on survival include size of the aneurysm, advanced age, diastolic hypertension, and generalized arteriosclerotic disease (De Bakey, Cooley, Crawford, and Morris, 1958; Joyce and others, 1964). Ching and Hughes (1967) in a clinical series observed an increased incidence of arterial obstructive lesions affecting the brain, heart, and kidneys in patients with arteriosclerotic aneurysm of the thoracic aorta and they concluded from necropsy studies that there was a higher death-rate from causes other than the aneurysm. They recommended a thorough clinical and arteriographic investigation, and because many patients died from myocardial infarction during or after aneurysm

Table I.—DETAILS OF EMERGENCY OPERATIONS FOR RUPTURED ANEURYSMS OF THE DESCENDING THORACIC AORTA REPORTED IN THE LITERATURE

AUTHOR	AGE AND SEX OF PATIENT	SITE OF RUPTURE	TYPE OF SHUNT EMPLOYED	TYPE OF GRAFT	RESULT
Barnard and Schrire (1963)	38 M.	Left lung	Left atriofemoral with moderate hypothermia	Teflon	Died 6 days postoperatively from pulmonary and renal complications and insulin hypersensitivity
	59 M.	Left lung	Left atriofemoral	Teflon	Recovered
Garrett, Ricks, Lewis, Howell, and De Bakey (1965)	62 M.	Left upper lobe bronchus	Left subclavian-femoral	Dacron	Recovered after 2 days' transient hemiparesis
Bryant, Bowlin, Malette, and Danielson (1968)	68 M.	Left main bronchus	Left atriofemoral	Dacron	Died during operation
	61 M.	Left main bronchus	Left atriofemoral	Dacron	Recovered
Valiathan and others (1968)	71 M.	Right chest	Left subclavian-femoral	Dacron	Died 3 weeks postoperatively from myocardial infarction and with ischaemic damage to spinal cord
	55 F.	Left pulmonary artery and left main bronchus	Left subclavian artery to distal thoracic aorta	—	Died during operation
Crawford and others (1970)	65 M.	Not stated	No shunt, aortic cross-clamping	Dacron	Died 2 days postoperatively from cerebrovascular insufficiency
	66 M.	Not stated	No shunt; aortic cross-clamping	Dacron	Died 9 days postoperatively from pulmonary emboli and with paraplegia

resection advised myocardial revascularization, if indicated, prior to aneurysm surgery.

Whatever the merits of advising surgery for intact aneurysms the treatment of ruptured aneurysms is of the utmost urgency. Few patients survive to reach hospital and, of these, only a very few will respond to resuscitative measures and be submitted to operation. The overall results of emergency operations for ruptured aneurysms of the descending thoracic aorta are poor (*Table I*).

The purpose of this paper is to present the successful surgical management of 2 cases of ruptured aneurysm of the descending thoracic aorta and a third in which rupture was imminent.

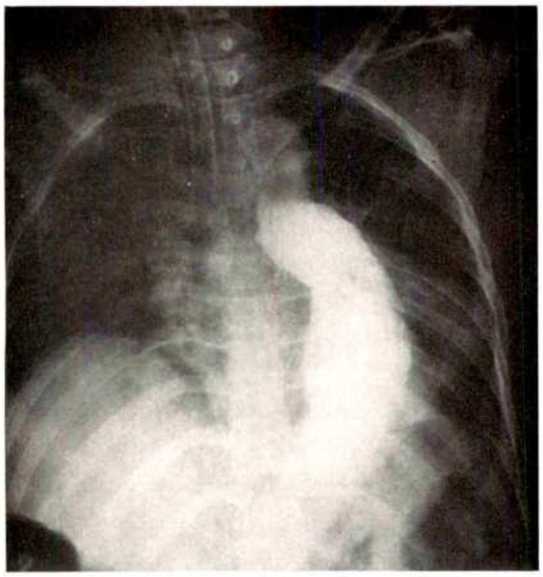

FIG. 1.—*Case* 1. Aortogram showing constrictions and dilatations of the descending thoracic aorta.

CASE REPORTS

Case 1.—A thoracic aortic aneurysm was diagnosed in a 35-year-old male Indian doctor in 1962. In childhood he had had severe hypertension, but following the removal of an ischaemic left kidney when he was 14 his blood-pressure had returned to normal. In May, 1958, at a routine medical examination he was symptomless and normotensive and an intravenous pyelogram had shown a reasonable caliceal pattern. In March, 1960, his blood-pressure was 180/110 mm. Hg. One year later it had risen to 190/120 mm. Hg and retinoscopy had revealed marked arteriolar narrowing. Blood-urea was 55 mg. per cent and the urine contained red and white cells, albumin, and casts. Increase in the aortic shadow was noted on a plain chest radiograph. He was effectively treated with Salupres (reserpine, hydrochlorothiazide, and potassium chloride). He had remained symptomless until October, 1962, when he had severe pain in his left chest and to the left of the thoracic spine accompanied by rigors, a temperature of 40° C., and an erythrocyte-sedimentation rate of 72 mm. per hour. There was a marked increase in the size of the aortic shadow compared with the film taken 18 months previously. A barium-swallow examination demonstrated compression and deviation of the oesophagus. He was referred to the Thoracic Unit at the Westminster Hospital. Aortography revealed an aneurysm of irregular calibre with dilatations and constrictions which extended from immediately distal to the left subclavian artery to the right renal artery—a picture typical of Sen's disease (*Fig.* 1). Function of the remaining kidney was poor as judged by intravenous pyelography and the blood-urea, which was 100 mg. per cent. He was considered unfit for surgery. He had further attacks of severe chest pain and the aneurysm increased in size. On 31 Dec. he had chest pain with haemoptysis, indicating rupture of the aneurysm into the left lung. As a doctor he realized the significance of this symptom and the ultimate outcome. Immediate surgery offered the only prospect of survival, and preparation was made for a left atriofemoral extracorporeal circulation.

The aorta was exposed via a thoraco-abdominal incision resecting the left fourth and ninth ribs. The aneurysm extended from immediately below the left subclavian artery to about 5 cm. above the aortic bifurcation and was a series of constrictions and dilatations, the major sacculation being just above the diaphragm where rupture had occurred into the left lung. The aorta below was uniformly stenosed.

The aorta distal to the left subclavian artery was mobilized and the pericardium was then opened and the left atrium cannulated after heparin had been given. The left femoral artery was similarly cannulated. By-pass was commenced but a large pelvic haematoma was noted with a dramatic fall in blood-pressure, and at this point cardiac arrest was imminent. Dissection of the pelvic vessels had occurred. By-pass was discontinued and the aorta above the aneurysm was clamped to improve cerebral and myocardial perfusion. During the 3 minutes of aortic cross-clamping the adherent portion of the left lung was rapidly stripped off the aneurysm and organized thrombus was removed. The lateral ruptured portion of the major sacculation was excised and several lateral clamps were applied to the longitudinal incision which had been made. The aortic clamp was then removed and the defect in the aneurysm, which was 10 cm. long, was repaired with Teflon buttressed sutures. The chest was closed with drainage.

The patient required 28 pints of blood and later surgical evacuation of a haemothorax which had resulted from generalized bleeding. Tracheostomy was necessary and he was ventilated for 1 week. In the second postoperative week he became icteric with the total bilirubin reaching 28 mg. per cent and the blood-urea rising to 300 mg. per cent. He survived without dialysis and was discharged 2 months after operation, with a bilirubin of 1·2 mg. per cent and blood-urea of 20 mg. per cent.

PATHOLOGY OF THE ANEURYSM WALL.—Microscopy showed the aortic media to be replaced by a thick layer of vascular collagen which had neither the lipid encroachment of atherosclerosis nor the round-cell infiltration of syphilis. The elastic tissue was greatly diminished and fragmented. The intima was replaced by organizing mural thrombus. Where the aneurysm abutted on the lung its wall contained clusters of multi-nucleated giant cells. These features are consistent with a diagnosis of middle aortic disease due to an arteritis.

SUBSEQUENT HISTORY.—Two months later a painful abdominal incisional hernia was repaired without complication and a chest film showed no increase in size of the aneurysm. The patient died 3 years later in another country during an operation for aortic excision and graft replacement.

Case 2.—In January, 1967, a 63-year-old white female presented with generalized chest pain of 1 year's duration and a 4-month history of palpitations and faintness precipitated by food. Her blood-pressure was 160/100 mm. Hg. Serological tests for syphilis were negative and an electrocardiogram suggested an old anteroseptal infarction. A plain chest film showed dilatation of the aorta and on barium-swallow examination the oesophagus was deviated to the left by a large uncalcified aneurysm of the descending thoracic aorta. A transfemoral aortogram revealed the entire descending thoracic aorta to be aneurysmal. She was advised to lose weight and to restrict physical activities. One year later her symptoms and chest radiograph were unaltered.

In May, 1968, she gave a 3-month history of left submammary pain which radiated into her left back. There was tenderness in the left epigastrium and the blood-pressure was 170/105 mm. Hg. Marked increase in size of the aneurysm was confirmed by a transfemoral arteriogram. Operation was indicated because of aggravation of symptoms and the recent increase in size of the aneurysm.

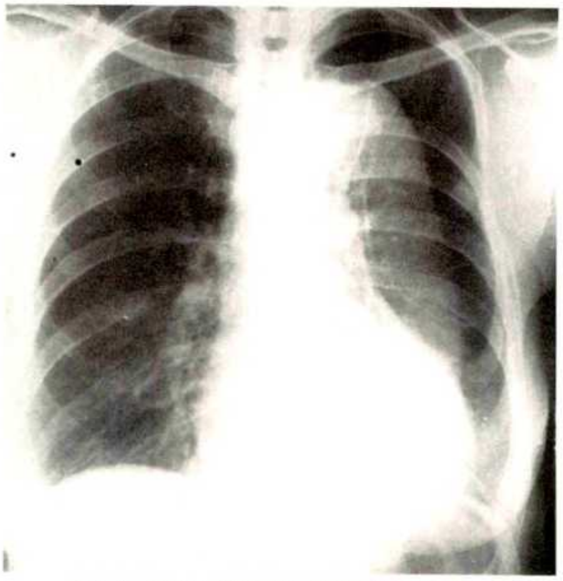

FIG. 2.—*Case* 2. Chest film 1 year after operation.

On 6 June thoracotomy with excision of the left fourth and ninth ribs exposed a fusiform aneurysm of the descending thoracic aorta which was adherent to the lung, oesophagus, and vertebral column. Rupture appeared to be imminent. The size and position of the aneurysm precluded left atrial cannulation. It was therefore decided to insert a Dacron graft end to side to the aorta below and above the aneurysm. The aorta was mobilized below the left subclavian artery and distally at the level of the diaphragm. Following the insertion of this shunt the entire descending thoracic aorta was resected. The aortic cuffs adjacent to the shunt were sutured and the shunt was left to function as the permanent graft. Following operation a left haemothorax developed which required evacuation and a Teflon patch was sutured over a leak in the upper anastomosis. Her course was then uneventful and she was discharged 1 month after operation.

PATHOLOGY OF THE ANEURYSM.—The specimen consisted of a boot-shaped vessel 14 cm. long and dilating in the middle to a diameter of 6 cm. with proximal and distal diameters of 2·5 and 3·5 cm. respectively. The interior was divided into three parts; proximally by an almost transverse diaphragm 3 cm. from the divided end from which the intimal layers had been stripped and folded up and the resulting bare area covered with thrombus. The wall in this region was very thick, white, and fibrous. In the middle third there was a fusiform aneurysm containing mural thrombus and bounded distally by a distinct ridge. Along this ridge the intima showed a slight spiral split 3 cm. long in the floor of which there was thrombus.

Microscopically, the aneurysm wall consisted of collagen interrupted with a network of lymphocytes with total destruction of muscle and almost complete disappearance of elastic tissue. The aneurysm was lined by amorphous thrombotic material undergoing peripheral organization. The picture is one of syphilis.

SUBSEQUENT HISTORY.—The graft is well shown in the chest film taken 1 year after operation (*Fig.* 2). An aortogram was performed in May, 1971 (*Fig.* 3). The patient remains well 5 years after operation and leads an active life. All the peripheral pulses are present apart from a right dorsalis pedis.

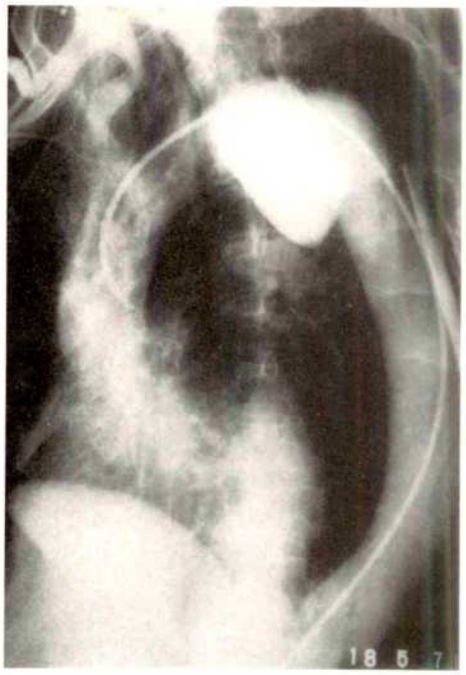

FIG. 3.—*Case* 2. Aortogram 3 years after operation.

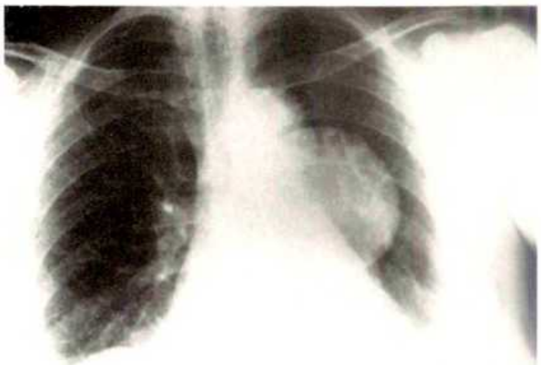

FIG. 4.—*Case* 3. Chest film demonstrating the aneurysm.

Case 3.—An aneurysm of the descending thoracic aorta was diagnosed in a 66-year-old, totally blind, obese white female by mass miniature radiography in February, 1970 (*Fig.* 4). She had congenital syphilis and since 1929 had been blind as a result of luetic keratitis. In 1963 her left eye had been enucleated because of a secondary glaucoma. For 2 weeks prior to radiographic diagnosis of the aortic aneurysm she had complained of a bruised sensation in her left breast and retrosternal pain on walking. Her blood-pressure was 130/90 mm. Hg and all the peripheral pulses were present. Because of her age, obesity, blindness, and lack of knowledge as to the age of the aneurysm surgery was not advised. On 27 Sept., 1970, she developed back pain which 3 days later was so severe that morphine was required and she was admitted as an emergency. She was severely shocked with a systolic blood-pressure of 50 mm. Hg, although both femoral pulses were present. There was a precordial systolic murmur and evidence of bilateral pleural effusions with tracheal deviation to the right (*Fig.* 5). Following blood transfusion she was submitted to operation.

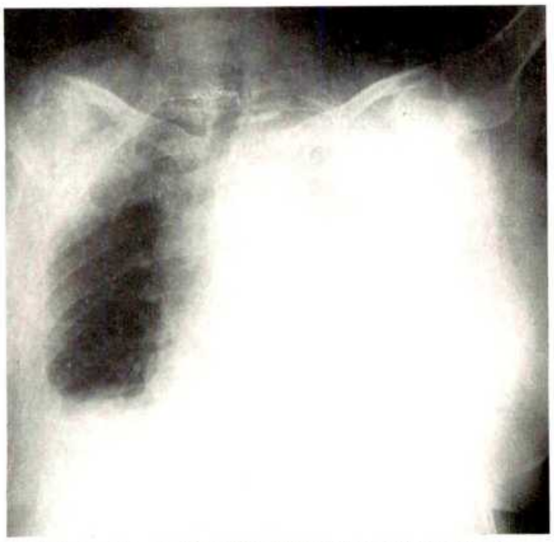

FIG. 5.—*Case* 3. Chest film after rupture of the aneurysm.

Left thoracotomy, excising the fourth and ninth ribs, revealed a large haemothorax but no attempt was made to inspect the aneurysm or the site of rupture. A massive haematoma in the mediastinum had probably limited further leakage. The aorta was mobilized just distal to the left subclavian artery so that any sudden additional haemorrhage could be controlled. The aorta at the level of the diaphragm was treated in a similar manner. A 22-mm.-wide Dacron graft was sutured end to side to the aorta and above the aneurysm, the superior anastomosis being just below the left subclavian artery and the inferior one just below the diaphragm. The aneurysm was then excised between clamps. All the intercostal vessels were thrombosed. The aneurysm was fusiform and atheromatous and on the medial aspect there was a 4-cm. rupture. Her recovery was uneventful and she was discharged home 6 weeks after operation.

PATHOLOGY OF THE ANEURYSM.—The specimen consisted of a retort-shaped aorta up to 7 cm. in diameter at its dilated proximal end, which was thin-walled, obliquely torn, and coated on its inner aspect by laminated mural thrombus. Elsewhere the thin wall appeared somewhat pearly white. The distal 6 cm. of the aneurysm measured less than 3 cm. in diameter and presented an atheromatous inner surface.

Microscopically the original aortic wall was represented by a layer of lipid mush of atheromatous type and a few strands of elastic tissue. Clusters of lymphocytes were seen in the adventitia. This picture is typical of an atherosclerotic aneurysm.

SUBSEQUENT HISTORY.—An aortogram was performed in May, 1971 (*Fig.* 6). The patient remains asymptomatic 2½ years later and leads an active social and domestic life. All the peripheral pulses are present.

OPERATIVE TECHNIQUE OF THE TEMPORARY TO PERMANENT SHUNT GRAFT

Because of its successful application in 2 cases it is perhaps of use to describe the operative details.

1. The patient is placed as for a standard left posterolateral thoracotomy. One long skin incision is made and with adequate retraction the fourth and ninth ribs are removed.

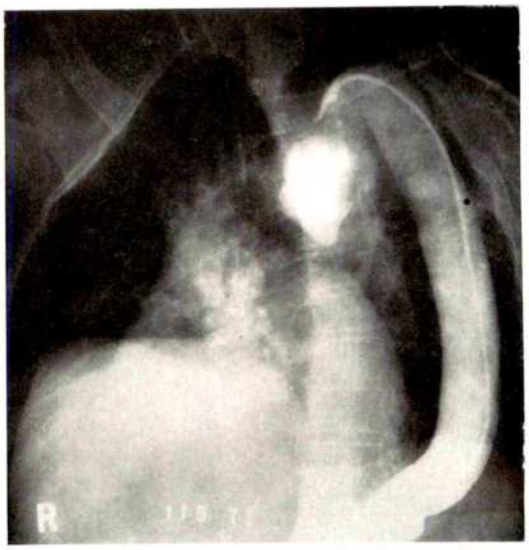

FIG. 6.—*Case* 3. Aortogram 8 months after operation.

2. The exposure is such that the subclavian artery and the aorta above the aneurysm may be mobilized and taped, as may the aorta below the aneurysm, usually at the level of the diaphragm. The aneurysm itself is undisturbed.

3. A Dacron graft of suitable dimension is then sutured end to side to the aorta distal to the aneurysm, employing a Satinsky clamp to occlude the aorta partially (*Fig.* 7). The clamp is then removed and blood is allowed to fill the graft to a convenient level where it is clamped.

4. The graft is then brought up lateral to the aneurysm and sutured to the aorta above the aneurysm in a manner similar to that in which the distal anastomosis was effected (*Fig.* 8).

5. The upper Satinsky clamp is removed and provided that haemostasis is adequate and the graft functioning well the aortic aneurysm, which has not yet been disturbed, is removed after the application of clamps at convenient levels. Each aortic cuff is then oversewn, inevitably producing a small cul-de-sac (*Figs.* 9, 10, 11).

6. The chest is closed in a routine manner after further checking haemostasis and graft function.

DISCUSSION

It is only within the past 20 years that the treatment of aortic aneurysms by resection and graft replacement has been made possible by advances in surgical and anaesthetic techniques and the development of surgical materials. It is not, however, always possible to resect the entire aneurysm, and partial aneurysmectomy in which a portion of the aneurysm wall is excised and aneurysmorrhaphy performed with sutures has been applied to an intact thoracic aortic aneurysm (Cooley and De Bakey, 1955). It appears that this technique has not been described in the treatment of ruptured aneurysms. This method was applied to the first case of the present series. The technique of temporary to permanent shunt successfully employed in *Cases* 2 and 3 could not be used in this instance because of gross constriction of the aorta at the level of the diaphragm and below. *Case* 1 suffered from Sen's disease or the middle aortic syndrome, which is due to a non-specific allergic panarteritis of a segmental nature involving the middle part of the aorta and characterized by irregular constrictions and dilatations (Sen, Kinare, Engineer, and Parulkar, 1963). During the 3-minute period of aortic cross-clamping the aneurysm was partially excised and side-clamps were placed over the defect. The aortic cross-clamp was then removed and the aneurysm was repaired with Teflon-buttressed sutures. This simple procedure undoubtedly saved the life of a patient who was a poor operative risk. A more extensive procedure would have caused his death, which occurred 3 years later during further aortic surgery.

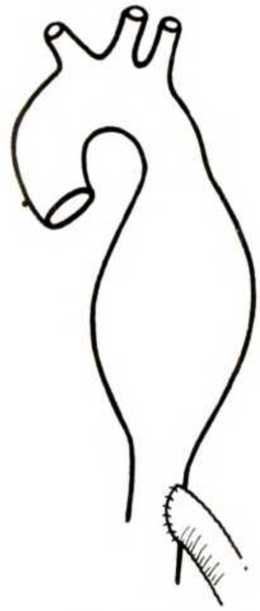

FIG. 7.—The graft is sutured to the aorta distal to the aneurysm.

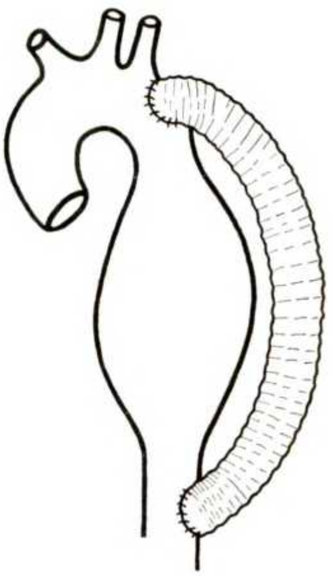

FIG. 8.—The graft in situ prior to excision of the aneurysm.

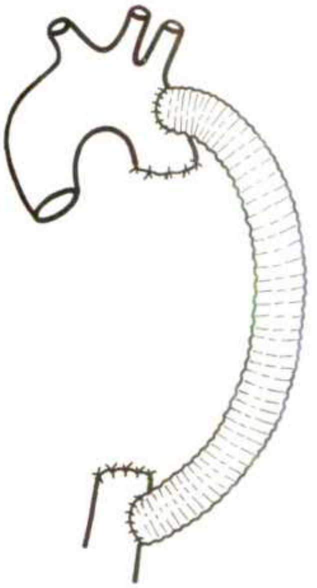

FIG. 9.—Graft with aortic cuffs which are oversewn.

The first successful removal of an aneurysm of the descending thoracic aorta and homograft replacement was performed by De Bakey in 1951 (De Bakey and Cooley, 1953). Natural materials do not form satisfactory grafts and of the many synthetic materials which have been used, the crimped Dacron tube has produced the least number of complications (De Bakey and others, 1958; Crawford, De Bakey, and Cooley, 1958; Nagel and Williams, 1966).

Prior to excision the aorta is cross-clamped above and below the aneurysm. The haemodynamic disturbances thus produced are the proximal deleterious effects on the heart and brain and distal ischaemia, especially of the spinal cord and kidneys (Adams and van Geertruyden, 1956). The effect of clamping or removal of the descending thoracic aorta on the viability of the spinal cord depends on anatomical pattern and segmental distribution of spinal arteries and the development of a collateral circulation following previous obstruction to intercostal vessels associated with disease (Cooley and De Bakey, 1955; Crawford, Fenstermacher, Richardson, and Sandiford, 1970). Attempts to reduce the effect of ischaemia led to the employment of general body hypothermia and local spinal cooling (Beattie, Adovasio, Keshishian, and Blades, 1953; Hardin, Reisman, and Dimond, 1954; Pontius, Brockman, Hardy, Cooley, and De Bakey, 1954; Cooley and De Bakey, 1955; Ellis, Kirklin, and Bruwer, 1958). These techniques were abandoned in favour of methods whereby blood is supplied to the aorta distal to the aneurysm by means of a shunt (De Bakey, Creech, and Morris, 1956). Intraluminal shunts have a limited application in the treatment of aneurysms of the descending thoracic aorta (Lam and Aram, 1951; Crawford, De Bakey, and Blaisdell, 1961; Keon and Trimble, 1968). External shunts detour the aneurysm and either depend on proximal blood-pressure or the assistance of a pump to deliver blood to the distal aorta. Pump-assisted shunts include subclavian-aortic, cardiopulmonary, and the more common left atriofemoral by-pass (De Bakey and others, 1958). The last method failed in *Case* 1 of this series and was technically impossible in *Cases* 2 and 3.

The use of a shunt from the left ventricle to the descending thoracic aorta (Molloy, 1970) is of value in traumatic rupture of the thoracic aorta as this injury usually occurs in a young patient with good ventricular function and a healthy aorta. The technique has a limited application in patients with arteriosclerosis and poor cardiac reserve and would not have been technically possible in the cases described here.

Other external shunts without mechanical assistance convey blood to the distal aorta from the proximal aorta (Chamberlain, Klopstock, Parnasa, Grant, and Cincotti. 1956) or the left subclavian artery (Nagel and Williams, 1966; Kahn, Vathayanon, and Sloan, 1968).

The shunt may be removed after the aneurysm has been excised and a graft then inserted, or it may be left in situ and thereafter function as the graft. Mahorner and Spencer (1954) employed this technique experimentally in 1952 when they by-passed the canine descending thoracic aorta with an homologous arterial shunt which served as the definitive graft after the by-passed segment of the aorta had been removed. There were no neurological complications despite a 50 per cent occlusion of the aortic lumen when the anastomoses were made. This method was first used successfully in 1952 in a patient who had an aneurysm which involved the innominate artery, the first part of the right subclavian artery, and the origin of the right common carotid artery. Because of dense adhesions the posterior surface of the aneurysm was not dissected. A frozen arterial graft was sutured end to side to the base of the innominate artery (below the aneurysm) and to the common carotid artery (above the aneurysm), using clamps to occlude the blood-flow partially during the formation of the anastomoses. The innominate and carotid ends of the aneurysm were then ligated and the shunt was left in situ to function as the permanent graft. About 7 months later re-exploration was indicated because of increasing size of the aneurysm. The pulsating graft had rotated anteriorly over the aneurysm which was then excised. It was observed that the graft was then too long, as it did not have to course across the surface of the aneurysm, although this redundancy caused no ill effects.

Satinsky, Neptune, and Alai (1955) experimentally replaced an aneurysm of the aortic arch with the aid of a homograft vessel shunt which later served as the graft. Bahnson (1956) utilized this technique when resecting an aneurysm of the aortic arch. He also commented on the redundant length of graft but noted that it caused no embarrassment to the patient. Ellison, Cope, and Moretz (1960) employed a shunt of Ivalon sponge which later served as the permanent graft following the resection of descending thoracic aortic aneurysms in 2 patients. They stressed the shorter operating time which is especially important in patients who have other serious organic disease. Bradham and Buxton (1963) used a Teflon shunt to convey blood from the aortic arch to the right common carotid artery when excising a syphilitic aneurysm involving the proximal aortic arch and proximal two-thirds of the innominate artery. The innominate artery was then implanted into a more proximal site in the arch and the Teflon shunt which was functioning well was left in situ.

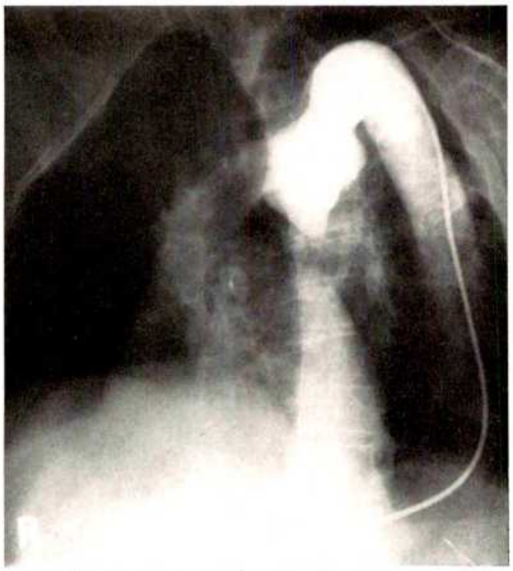

FIG. 10.—*Case* 3. Aortogram demonstrating the upper cul-de-sac.

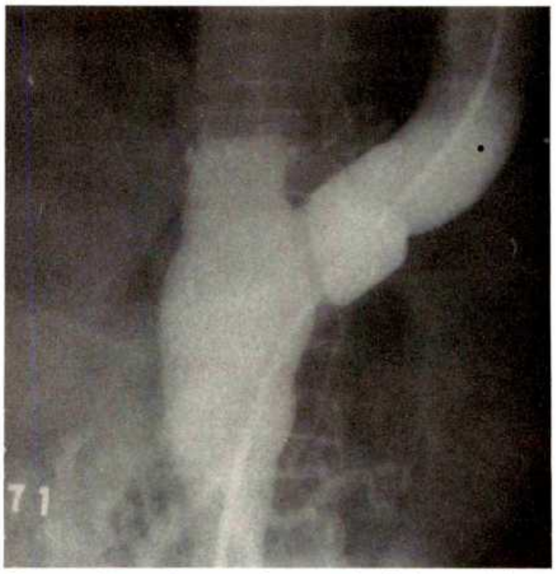

FIG. 11.—*Case* 3. Aortogram demonstrating the lower cul-de-sac.

The development of the crimped Dacron tube allowed this principle to be applied much more readily (De Bakey and others, 1958; De Bakey, 1959). The technique has the disadvantage of leaving an aortic cul-de-sac adjacent to each anastomosis (*Figs.* 9, 10, 11) and, as yet unrecorded, there is the possibility of cul-de-sac disruption, aneurysm formation, or the development of thrombus within a cul-de-sac. The redundant length of the graft appears to cause no inconvenience.

With ruptured aneurysms pump-assisted by-pass is not always possible as the aneurysm is large and prevents access to the left atrium. Crawford and others (1970) reported a series of cases of thoracic aortic resection and replacement with a graft in which a by-pass was not employed. An occluding aortic cross-clamp was placed above and below the aneurysm which was excised and a graft inserted. The series included 2 cases of ruptured aneurysm of the descending thoracic aorta. Although the aortic occlusion time was less than 30 minutes in 70 per cent of the cases it is significant that the occlusion times for the ruptured cases (46 and 64 minutes) were the longest of the series. These patients were already severely shocked prior to operation and any further reduction of the blood-flow to vital organs was therefore critical. Both cases died; one of cerebral insufficiency and the other with paraplegia and pulmonary emboli (*Table I*).

Encouraged by the success of partial aneurysmectomy and the use of a temporary to permanent shunt graft technique it is suggested that these simple procedures have a place in the management of ruptured aneurysms of the descending thoracic aorta. The techniques can be used adjunctively. If during the insertion of the by-pass graft further leakage occurs from the aneurysm, partial aneurysmectomy or merely the application of lateral clamps may be carried out before the insertion of the graft. The methods that we have used have the advantages of simplicity, speed, the avoidance of anticoagulants, and the minimal interference with aortic flow.

1. *Simplicity*: The technique does not involve the use of complicated equipment or the highly trained personnel required for extracorporeal perfusion methods which are available in a thoracic surgical centre. Provided that the surgeon is competent in thoracic and vascular techniques the procedure may be performed in most hospitals.
2. *Speed*: Because of its simplicity the technique results in a reduced operating time.
3. *The avoidance of anticoagulants*: In a patient who has already suffered a severe haemorrhage the avoidance of anticoagulation, which is necessary when a pump is used, considerably reduces haemorrhage at operation.
4. *Minimal interference with aortic flow*: The aorta above and below the aneurysm is only partially occluded during the formation of the graft–aorta anastomoses. The aneurysm is undisturbed until the graft is in place.

Acknowledgements.—Our thanks are due to Professor A. D. Morgan for reporting on the pathological specimens, Dr. B. Strickland for radiological investigations, the Department of Medical Photography and Illustration, Westminster Medical School, for the illustrations, and to Mrs. Goodwynn for secretarial assistance.

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ABO BLOOD GROUPS IN OCCLUSIVE AND ECTATIC ARTERIAL DISEASE

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SUMMARY

A study of 864 patients with occlusive disease and 246 with ectatic disease was made with reference to their ABO blood groups. The results confirmed the findings of other workers that occlusive disease and myocardial infarction occur more commonly in group-A individuals and that blood group O seems to confer some immunity to occlusive disease. There was also a probable correlation between group A and ectatic disease, but belonging to group O did not seem to confer any protection in this disease. It was also found that the incidence of myocardial infarction was much lower in ectatic disease than in occlusive disease. It is suggested that ectatic disease and occlusive disease are two distinct entities.

THE incidence of the ABO blood groups in many different diseases has been studied for some years and there seems to be a relationship between certain diseases and particular blood groups. For instance, gastric cancer and pernicious anaemia are associated with blood group A, and duodenal ulcer with group O. More recent work suggests that blood groups may also have some influence on arterial diseases. Kingsbury (1971) found a convincing preponderance of blood group A over O in a large number of patients with occlusive arteriosclerosis, and Marcus (1969), in a review of the ABO system, mentioned that myocardial infarction is reported to be more common in group-A subjects. Because of this we decided to study the blood groups in patients with occlusive arterial disease and ectatic disease.

Ectatic disease is characterized by aneurysmal dilatation of arteries and in its extreme form results in localized aneurysms, particularly in the abdominal aorta and the popliteal arteries. These patients rarely have arterial occlusions unless an aneurysm has thrombosed or thrown off emboli.

MATERIAL AND METHODS

The case notes of 1110 non-diabetic white patients treated at Hammersmith and Chelmsford Hospitals since 1958 were reviewed. There were 864 males with occlusive arteriosclerosis, and 246 patients with ectatic disease, of whom 218 were male and 28 female. The patients with ectatic disease had an abdominal aortic aneurysm, a popliteal aneurysm, or both, without arteriosclerotic stenosis of any lower limb vessel; 208 patients had abdominal aortic aneurysm, with or without popliteal aneurysms, and 38 had popliteal aneurysms. Patients with iliac or femoral aneurysms alone were not included in this study, for these aneurysms commonly occur in occlusive disease and we believe that they are often post-stenotic dilatations. For the same reason patients who had an aortic aneurysm together with atherosclerotic stricture were excluded. There were 20 patients with popliteal aneurysms whose blood group had not been recorded and these were also excluded.

The blood group in each case was noted together with any history of myocardial infarction proved by investigation in hospital. The results for the ectatic and occlusive groups were compared with each other and the normal population, using the χ^2 test.

RESULTS

Table I shows the relative frequency of the ABO blood groups among 864 patients with occlusive atherosclerosis and 246 patients with ectatic disease, together with the incidence in the general population. Of the patients with occlusive disease, 47·1 per cent were group A, a higher incidence than would be expected to occur by chance ($\chi^2 = 13{\cdot}313$, $P < 0{\cdot}001$, 1 d.f.), and 37·2 per cent were group O, which is a lower incidence than would be expected to occur by chance ($\chi^2 = 33{\cdot}56$, $P < 0{\cdot}001$, 1 d.f.). Of the patients with ectatic disease, 48·6 per cent were group A and this high incidence is significant ($\chi^2 = 4{\cdot}938$, $0{\cdot}05 > P > 0{\cdot}01$), while the incidence of group O was lower than that in the general population but not significantly so ($\chi^2 = 2{\cdot}204$).

Table II shows the incidence of myocardial infarction related to blood group of 246 patients with ectatic disease and 864 with occlusive disease. There was a large proportion of patients with myocardial infarction among those with occlusive disease compared with those with ectatic disease and this difference was highly significant ($\chi^2 = 88{\cdot}4$, $P < 0{\cdot}001$). The number of patients with myocardial infarction in each blood group was proportional to the total number of patients in that group and the proportions did not differ statistically between one group and another.

DISCUSSION

There are similarities between occlusive and ectatic arterial disease but there are also some differences. The first similarity is the fact that atheromatous plaques, although perhaps not as common in ectatic disease as in occlusive disease, do occur in both. One encounters large calcified plaques in aneurysms, particularly in the aorta and iliac arteries. The second similarity is that aneurysms occur in conjunction with occlusive disease, most commonly in the common femoral artery and the aorto-iliac segment. However, these aneurysms are probably post-stenotic dilatations, for they are always localized, occur distal to a stricture, and can be treated satisfactorily by relieving the stricture, reducing the aneurysm to a normal calibre, and suturing the vessel (Hardy and

Eadie, 1972). The aortic ones are small and do not usually rupture (Bouhoutsos, 1972).

The known differences between occlusive and ectatic disease are more striking than the similarities. First, in ectatic disease all the arteries are of wide bore even when there is no obvious aneurysm, whereas in occlusive disease the vessels are narrow and any aneurysm is very localized. Secondly, unless an aneurysm has thrombosed or thrown off emboli patients with ectatic disease have good pulses and do not usually claudicate. Thirdly, at operation the wide-bore arteries in ectatic disease feel soft and although their walls are quite thick they seem structureless and sutures cut out very easily, compared with normal or even rebored atheromatous arteries. They must be considerably weaker than the arteries in occlusive disease, for the latter can be rebored to leave only a tissue-paper-thick wall without becoming aneurysmal. Fourthly, we have shown (Morris and Bouhoutsos, 1973) in our series of patients that those with ectatic disease are more commonly Rhesus negative than the general population and patients with occlusive disease are more commonly Rhesus positive.

Table I.—INCIDENCE AND PERCENTAGE FREQUENCY OF THE ABO BLOOD GROUPS AMONG 864 CASES OF OCCLUSIVE DISEASE AND 246 CASES OF ECTATIC DISEASE COMPARED WITH THE PERCENTAGE INCIDENCE IN THE GENERAL POPULATION

BLOOD GROUP	GENERAL POPULATION (per cent)	OCCLUSIVE DISEASE		ECTATIC DISEASE	
		No.	Per cent	No.	Per cent
A	41	407	47·1	118	48·6
O	47	321	37·2	104	43·3
B	9	96	11·1	20	6·7
AB	3	40	4·6	4	1·4

Because of these differences between occlusive and ectatic disease we undertook this study to see if they differed in relation to ABO blood groups and myocardial infarction. Our results confirm the findings of Kingsbury (1971) that blood group A tends to predispose to occlusive arterial disease whereas group O seems to confer some degree of immunity to it. We found a probable relationship between group A and ectatic disease, but this was not definite and the incidence of group O among the patients with ectatic disease did not differ significantly from the incidence of group O in the general population. Kingsbury (1971) also found no change in the A : O ratio in patients with aneurysms. These findings, together with the highly significant difference in the incidence of myocardial infarction between the groups with occlusive and ectatic disease, are further evidence in favour of the hypothesis that these are two different disease entities which share some characteristics rather than two manifestations of a single disease.

Table II.—INCIDENCE OF MYOCARDIAL INFARCTION AMONG 246 CASES OF ECTATIC DISEASE AND 864 CASES OF OCCLUSIVE DISEASE RELATED TO ABO BLOOD GROUPS

BLOOD GROUP	ECTATIC DISEASE			OCCLUSIVE DISEASE		
	Total No.	*Myocardial Infarction*		*Total No.*	*Myocardial Infarction*	
		No.	Per cent		No.	Per cent
A	118	12	10	407	71	17·5
O	104	7	6·6	321	56	17·5
B	20	2	10	96	23	24
AB	4	0	0	40	7	1·8
Total	246	21	8·6	864	157	18·1

Acknowledgements.—We are grateful to Mr. P. Martin for allowing us to study his patients and to Mr. P. Martin, Mr. C. Jamieson, and Professor R. B. Welbourn for reading and criticizing this paper.

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A REVIEW OF 174 PATIENTS WITH ARTERIAL EMBOLISM*

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SUMMARY

Experience of 174 patients suffering from arterial embolism is recorded. One hundred and fifty cases occurred in the lower limb and 24 in the upper limb. Embolectomy was performed in 119 patients. The overall limb salvage rate was 62 per cent and the hospital mortality was 27 per cent. Amputation was performed in 13 per cent of the patients in this series. Operative techniques and management are discussed. Delay in diagnosis and effective surgical treatment appears to be a major factor influencing the end-result.

PRESENT SERIES

Between 1959 and 1972, 174 patients were admitted to the Surgical Professorial Unit of St. Laurence's Hospital, Dublin, with arterial embolism. The age range was 32–88 years, most patients being aged between 60 and 70 years. The male : female ratio was 2 : 1. The upper limb was affected in 24 patients and the lower limb in 150. Two patients sustained a second femoral embolus after an interval of 2–3 years. Both of these patients had been on oral anticoagulant therapy after the first operation, but this had been discontinued by a physician some 2 weeks prior to readmission. A second embolectomy was successfully performed and both patients were re-established on oral anticoagulant therapy.

DIAGNOSIS

In a known cardiac patient, particularly with atrial fibrillation, a sudden vascular incident in a limb or limbs is suggestive of peripheral arterial embolism. Pratt's points (Pratt, 1949) are still useful guides to diagnosis: the 'pistol-shot' onset of pain, pallor, paraesthesia or anaesthesia, paralysis, and pulselessness in a limb 'perished' with cold are still simple pointers to the diagnosis of this common condition. Acute thrombosis in a diseased vessel can be confused with an acute embolism and sometimes arteriography may be necessary to determine the diagnosis. With peripheral embolism there is a sharp 'cut-off' and a concave defect in the contrast caused by the embolus. Collateral circulation is poor or absent. In acute thrombosis these features are usually absent and a collateral circulation is evident (*Figs.* 1, 2).

Arteriography.—Arteriography is only used as an aid to diagnosis; for instance, when there is difficulty in distinguishing thrombosis from embolism. It may also be used for investigating the source of the embolism such as an aneurysm. However, it is very useful as an intra-operative investigation and is used routinely for this purpose in this unit (*see below*).

ORIGIN OF THE EMBOLUS

The origin of the embolus (*Table I*) was determined by chest radiography, arteriography, operative findings, and autopsy findings where appropriate in 59 of the 174 patients. The commonest site of origin was an atheromatous aorta or aneurysm of the aorta or its main branches. Thrombus in the left atrium associated with mitral valve disease was considered to be responsible for peripheral embolism in 17 patients. Mural thrombus associated with infarction of the left ventricle was found in 10 patients. In 2 patients the embolus originated from a subclavian aneurysm associated with a cervical rib. In 115 patients the cause was undetermined but in 107 patients (two-thirds) atrial fibrillation was present.

SITE OF EMBOLISM

Although in most instances there were multiple emboli in one or both limbs, the primary site of occlusion appeared to be, in the case of the lower limb (*Table II*), the aorta in 8, iliac artery 4, femoral artery 102, and popliteal artery 36. The femoral artery, therefore, appears to be the commonest impaction site for embolism in the lower limb but there was often a further smaller embolus impacted in the popliteal artery as well. This was not an uncommon combination. In the case of the upper limb (*Table III*) the subclavian artery was the site of impaction in 2 patients, the axillary artery 3, the brachial artery 17, and the radial artery 2. In this series the brachial artery, therefore, appeared to be the commonest site of impaction for an embolus in the upper limb.

TREATMENT

The treatment will depend mainly on the age and general condition of the patient, the state of the limb (whether it is salvageable or irreversibly damaged), and the time interval between the onset of symptoms and admission to a vascular unit. In general, operative treatment is preferred. The patient must be generally fit for surgical treatment and the limb must be salvageable, otherwise there is no definite time limit. If there are irreversible changes in the limbs such as skin staining, rigidity of the muscles, or obvious gangrene then it is best to proceed with amputation. The treatment of choice, however, is embolectomy performed with the aid of a balloon catheter (Fogarty, Cranley, Krause, Strasser, and Hafner, 1963). This has made the operation a simple procedure which can be performed if necessary under a local anaesthetic. Heparin, 12,000 units intravenously, is given immediately the condition is diagnosed to prevent propagation of thrombus (proximal and distal to the embolus) and deterioration in the limb prior to surgical treatment. Heparin is also used intra-operatively in saline (5000 I.U. per 500 ml.) to flush the vessels. It is occasionally used as an intravenous infusion postoperatively in a patient prone to further clotting incidents, particularly when a late embolectomy has been performed. After a late embolectomy the vessels are often still roughened by adherent mural thrombus and re-thrombosis is a common complication. Heparin therapy in the early postoperative period may be of value under these circumstances in reducing postoperative re-thrombosis, although haemorrhage from the operative wound is a hazard. Closed-wound drainage is mandatory when anticoagulation is used. All patients are established on oral anticoagulant therapy after operation and this is continued on a permanent basis unless the causative lesion is corrected; if not there is a definite danger of further embolism.

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* Based on a paper read at the Annual Meeting of the Vascular Surgical Society of Great Britain and Ireland in Dundee, October, 1972.

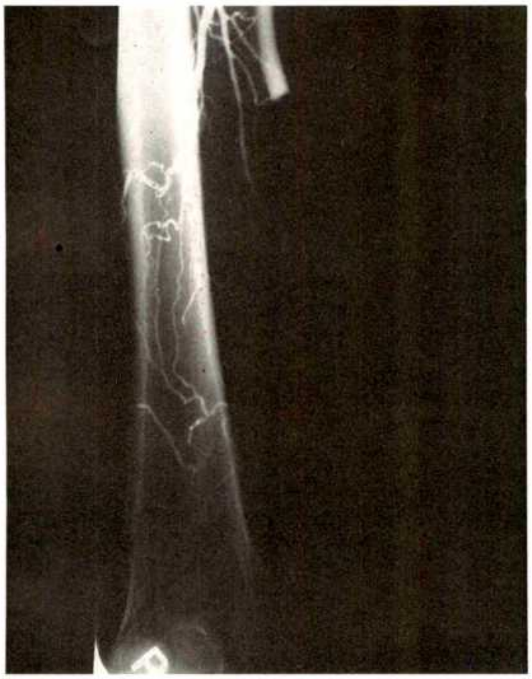

FIG. 1.—Arteriogram showing the typical 'cut-off' appearance of a femoral artery embolus.

Table I.—ORIGIN OF EMBOLUS IN 174 PATIENTS

Origin of Embolus	*No. of Cases*
Atheromatous aorta or aneurysm	32
Left atrium	17
Left ventricle	10
Undetermined	115
Atrial fibrillation	107

Table II.—SITE OF THE EMBOLUS IN 150 CASES OF LOWER-LIMB EMBOLISM

Site of Embolus	*No. of Cases*
Aorta	8
Iliac artery	4
Femoral artery	102
Popliteal artery	36

Operative Technique.—The procedure is performed preferably under a general anaesthetic, although occasionally with a local anaesthetic. In the lower limb the approach is usually made through the common femoral artery. Both arteries should be exposed if an iliac or aortic embolism is suspected because clot can be pushed up by the catheter and then find its way down the contralateral limb so that operative removal is required. To prevent distal embolization to the contralateral limb it is a wise precaution to occlude the opposite femoral artery temporarily before passage of the catheter.

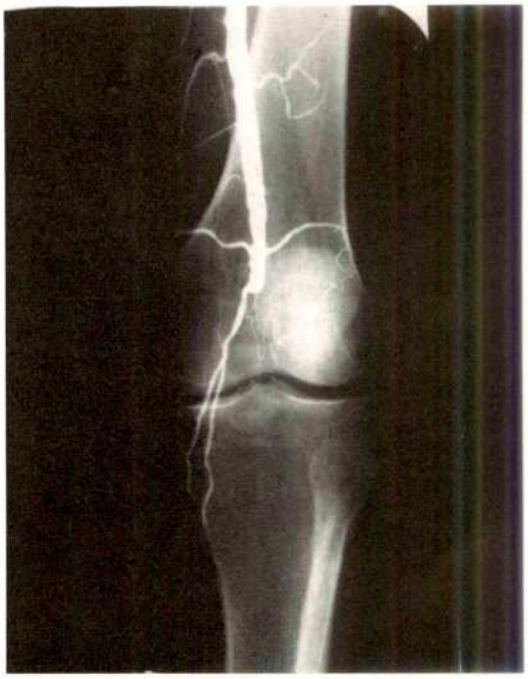

FIG. 2.—Arteriogram showing an acute occlusion of the popliteal artery caused by atherosclerosis. Note the tapered appearance of the vessel and the irregularity of its wall. A collateral circulation is evident.

Table III.—SITE OF THE EMBOLUS IN 24 CASES OF UPPER-LIMB EMBOLISM

Site of Embolus	*No. of Cases*
Subclavian artery	2
Axillary artery	3
Brachial artery	17
Radial artery	2

In the upper limb embolectomy is usually performed through a small transverse incision in the brachial artery. Occasionally the more difficult exposure of the subclavian or axillary vessels may be necessary. A Fogarty catheter (available sizes 3–7F) is passed gently upwards, avoiding trauma to the intima. The correct inflation pressure advised by the manufacturer should be used and over-distension avoided. During withdrawal if resistance is met the balloon should be deflated, the object being to have a snug fit between balloon and vessel wall. A Foley urinary catheter (size 18F) can be a very useful instrument for removal of iliac and aortic emboli (MacGowan, 1965). The catheter's position above the embolus is apparent when blood gushes from the central lumen of the Foley catheter. The catheter is clamped, inflated, and withdrawn. It is less rigid than the Fogarty catheter and thus damage to the iliac artery and aorta may be avoided. If the proximal obstruction cannot be cleared or the catheter fails to pass, then an intra-operative angiogram is called for and will demonstrate the causative lesion, e.g., an acute thrombosis in a stenosed vessel. Under these circumstances the vessel is exposed and an appropriate reconstruction performed. The proximal obstruction must, therefore, be cleared first and a good flow restored. The vessel is then secured on the proximal side of the arteriotomy and attention is now paid to the distal arterial tree. A Fogarty catheter of smaller

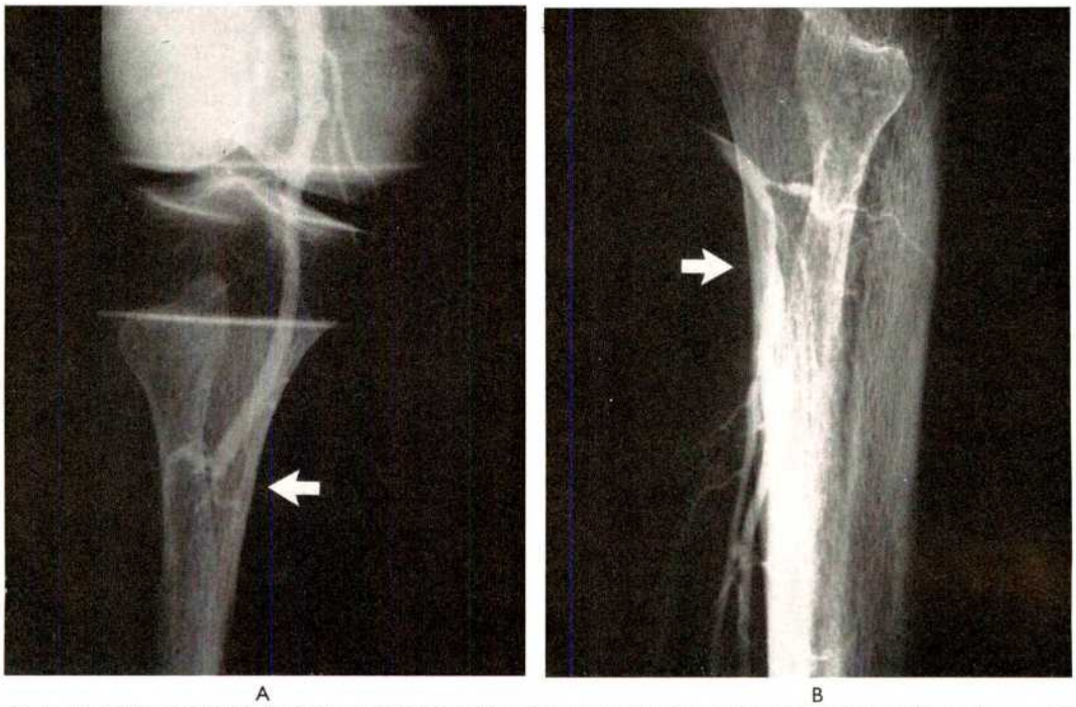
A B

FIG. 3.—A, Anteroposterior intra-operative arteriogram performed by direct injection of contrast into the open femoral artery. Note residual clot occluding the posterior tibial artery (arrowed). Passage of a small Fogarty catheter (size 3F) cleared this obstruction as arrowed in the lateral radiograph (B).

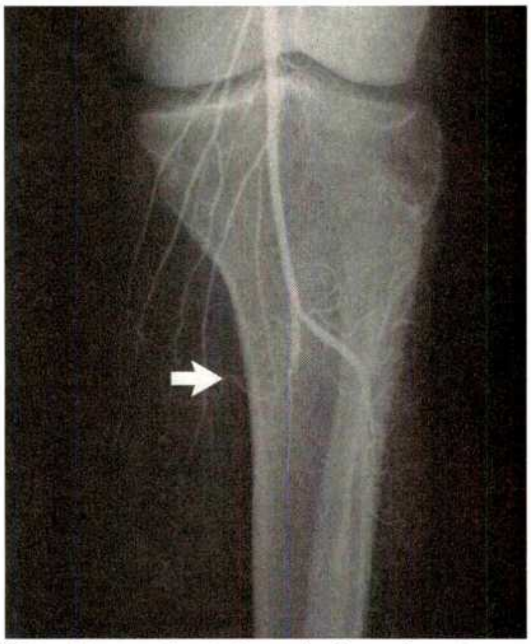
FIG. 4.—Intra-operative arteriogram showing persistent obstruction of the posterior tibial artery by residual clot.

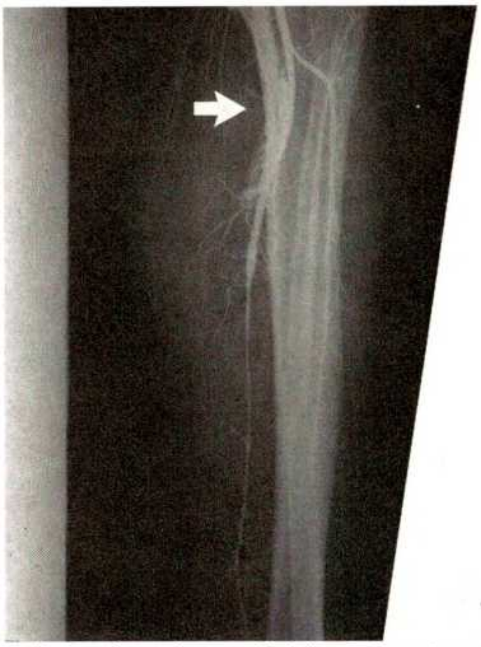
FIG. 5.—Over-zealous use of a balloon catheter clears the clot at the expense of the artery. Over-distension of the balloon has ruptured the vessel and contrast has escaped into the tissues. This vessel must now be repaired.

size is passed distally again with care to avoid intimal damage and vessel penetration. Retrograde flushing (Olwin, Dye, and Julian, 1953) through the anterior tibial or radial artery combined with 'milking' of the limb are useful procedures to augment the balloon-catheter extraction. Intra-operative arteriograms are now performed on the open femoral or brachial vessel by a single injection of contrast through a cannula or catheter. Before closing the arteriotomy the operator should be satisfied that the distal arterial tree has been cleared of clot as far as is possible. It is imperative to remove the distal clot and this applies particularly to the popliteal artery and its three main branches. If necessary the popliteal artery is exposed and the clot removed at arteriotomy. Reliance on backflow is unsatisfactory and unless the distal vessels can be cleared the chances of saving the limb are considerably reduced (*Figs.* 3). Intra-operative arteriography may also demonstrate unsuspected damage to the vessels by the balloon catheter (*Figs.* 4, 5) (Mavor, Walker, and Dahl, 1972; Mavor, Walker, Dahl, and Pegg, 1972). Closed drainage of the wound is usually employed to avoid haematoma formation.

Conservative Treatment.—Conservative treatment consists of the continuous intravenous infusion of heparin followed by oral anticoagulants. It is usually reserved for the elderly or infirm who are unfit for operation, or for a limb which is obviously improving after the initial embolus. Such treatment may prevent deterioration by further thrombosis or embolism. Amputation is reserved for the limb which is irretrievably damaged and frank gangrene. It is thus required when embolectomy fails to salvage a limb.

Table IV.—COMPARISON OF CONSERVATIVE AND SURGICAL TREATMENT

TREATMENT	UPPER LIMB		LOWER LIMB	
	No. of Cases	No. of Limbs salvaged	No. of Cases	No. of Limbs salvaged
Embolectomy	20	20	99	78
Conservative	4	4	51	7

RESULTS OF TREATMENT

On comparing conservative and operative treatment (*Table IV*) for the upper limb all the limbs were salvaged. The risk to the limb in the case of the upper limb is less than with the leg. Nevertheless loss of upper limbs can occur and is a catastrophe compared with the excellent prostheses now available to replace the amputated lower limb. Twenty embolectomies were performed for upper-limb emboli which we believe would, if treated conservatively, have led to loss of a limb or at least a severely damaged one. Embolectomy of the upper limb-vessels is usually necessary, particularly if the limb remains cold and discoloured some hours after the onset of the embolism. Conservative management is justifiable for the poor-risk elderly patient whose limb is obviously improving.

In the lower limb conservative treatment yields poor results and operative treatment is necessary in the vast majority of patients if the limb is to be salvaged (*Table IV*).

The overall results are reviewed in *Table V* and it is to be noticed that the number of admissions has increased over the years of the survey. The number of patients having operative treatment has also increased, while the hospital mortality has been reduced from somewhere in the region of 50 per cent in the period 1959–65 to 7 per cent in 1972. This is because of better selection, anaesthetic care, and medical care, and the speed and effectiveness with which the operation can now be performed using the Fogarty catheter. The amputation rate is 13 per cent overall and the overall limb salvage rate is 62 per cent, which again has improved over the years from 53 per cent in 1959–65 to 82 per cent in 1972. The number of hospital deaths (*Table VI*) was 48 and most of those were caused by cardiac failure or pneumonia. Many of the so-called 'pneumonic' deaths were probably unsuspected pulmonary infarction which is so common after peripheral embolism. The high mortality is indicative of the serious cardiovascular and respiratory disease from which these patients suffer. Embolism is an incident in these diseases; an incident, however, which can have fatal consequences for many patients.

Table V.—SUMMARY OF THE RESULTS OF TREATMENT IN 174 PATIENTS WITH PERIPHERAL ARTERIAL EMBOLISM, 1959–72

YEAR	NO. OF CASES	OPERATION	HOSPITAL MORTALITY		AMPUTATION	LIMBS SALVAGED	
			No.	Per cent		No.	Per cent
1959–65	32	22	16	50	3	17	53
1966	16	7	6	37	2	8	50
1967	4	2	1	25	2	2	50
1968	18	9	5	27	2	11	61
1969	27	18	8	29	4	15	55
1970	35	25	8	22	4	23	65
1971	14	11	2	14	2	10	71
1972 (Jan.–Aug.)	28	25	2	7	5	23	82
Total	174	119 (68 per cent)	48	27	24 (13 per cent)	109	62

Table VI.—CAUSE OF HOSPITAL DEATHS

Cause of Death	*No. of Cases*
Cardiac failure	18
Pneumonia	11
Myocardial infarction	9
Pulmonary embolism	4
Uraemia	3
Cerebrovascular accident	3

Table VII.—TIME BETWEEN ONSET OF SYMPTOMS AND EFFECTIVE TREATMENT IN LOWER-LIMB EMBOLISM

DELAY	NO. OF CASES	PER CENT	EMBOLECTOMY	NO. SALVAGED	FAILURE RATE (per cent)
0–12 hr.	18	12	18	17	5·5
12–24 hr.	38	25	38	35	8
1–2 d.	60	40	49	39	35
2–4 d.	29	19	10	5	82
4–8 d.	19	12	3	1	94
Over 8 d.	10	6	1	1	90

Analysing the delay before effective treatment was instituted (*Table VII*) the average time interval between the occurrence of the embolism and treatment in the upper limb was 12–72 hours, with one exception of 4 days. Obviously the patients presented earlier in the case of the upper limb because the effects are manifested earlier to the patient, relatives, and medical practitioner. In the lower limb (*Table VII*) only 12 per cent of our patients arrived within the first 12 hours of the onset of the embolism, presuming that this coincided with the onset of symptoms. The success rate of embolectomy in this group of patients was 94·5 per cent. The vast majority of patients, however, appeared to arrive in hospital some days after the onset of embolism and it can be clearly seen that the failure rate of embolectomy increases as the delay before effective treatment increases. This is shown graphically in *Fig.* 6; the percentage failure for embolectomy increases to its maximum of nearly 100 per cent following a delay of over 8 days before effective treatment is instituted. Nevertheless, surprisingly, many limbs are salvaged after a considerable delay.

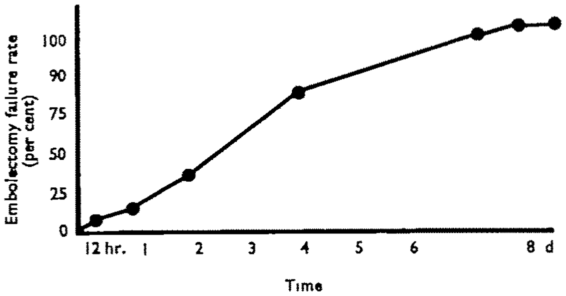

FIG. 6.—Embolectomy failure rate related to the delay before operation.

DISCUSSION

A large series of patients with peripheral arterial emboli, comprising 174 consecutive patients seen over a period of 13 years, has been reviewed. One hundred and nineteen embolectomies were performed and this compares with series of 260 patients reported by Darling, Austen, and Linton (1967) and 80 patients by Martin, King, and Stephenson (1969). In the present series there was commonly a delay of 1–8 days after the onset of symptoms before the patients were admitted for effective treatment. Only 12 per cent of the patients were admitted within 12 hours of the onset of symptoms. This compares with 76 per cent in Darling's series and 41 per cent in Martin's series. It is probable that both of these hospitals were dealing with a local metropolitan area whereas the catchment area of St. Laurence's Hospital is countrywide. Many of the patients were referred from long distances and hence the delay. The overall salvage rate was 62 per cent, but over the past 3 years this has risen to between 70 and 80 per cent. In Darling's series the salvage rate was 91 per cent and in Martin's series 84 per cent. The overall amputation rate in the present series was 13 per cent, in Darling's series it was 9 per cent and in Martin's series 11 per cent. As the delay before effective treatment increases, the amputation rate also increases. The results of embolectomy in this series are, therefore, somewhat less favourable when compared with other published series. This is explained by the late admission for effective surgical treatment caused by the delay in diagnosis and the distances to be travelled to the appropriate specialist hospital. Most of the patients arrived at least 12 hours after the onset of symptoms, the clot having become adherent and propagated thrombosis having caused deterioration in the collateral circulation. The longer the clot is present, the greater is the extent of the thrombosis, the more adherent it becomes, and the more difficult it becomes to remove it, and the less effective its removal (Thompson, Sigler, Raut, Austin, and Patman, 1970; Hamer, 1972).

The overall hospital mortality in our series was 27 per cent but in 1971 it had reduced to 14 per cent and now in 1972 to 7 per cent. In Darling's series it was 29 per cent and in Martin's series 21 per cent.

CONCLUSIONS

On review of this series of 174 patients with arterial embolism the following conclusions were reached:—

1. The diagnosis of peripheral embolism is still made too late. Earlier diagnosis can be made by clinical awareness in susceptible patients and will lead to a higher limb salvage rate.
2. Intravenous heparin should be given immediately diagnosis is made to prevent spreading of thrombosis and further deterioration in the limb.
3. The vast majority of patients will need embolectomy if the limb, either upper or lower, is to be saved.
4. Intra-operative arteriography is mandatory if consistently good results are to be achieved.
5. The balloon-catheter extraction technique has considerably improved operative results and mortality.
6. Long-term anticoagulants are necessary to prevent recurrence unless it is possible to remove the source of the emboli.

Acknowledgements.—I wish to acknowledge the assistance of my colleagues Mr. Gearoid Lynch and Mr. Hyacinth Browne. I am also indebted to Mr. James Mulvanny, A.I.I.P. (Med.), for the radiographs.

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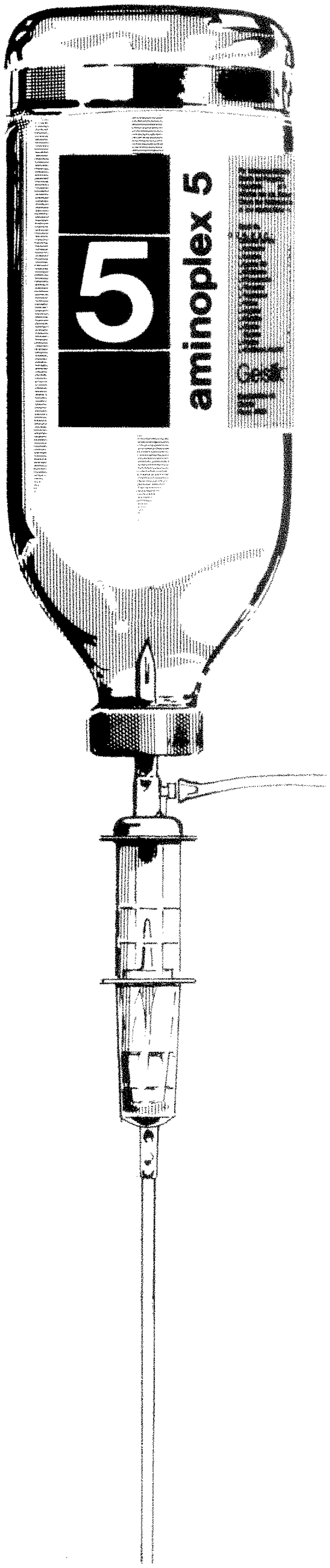

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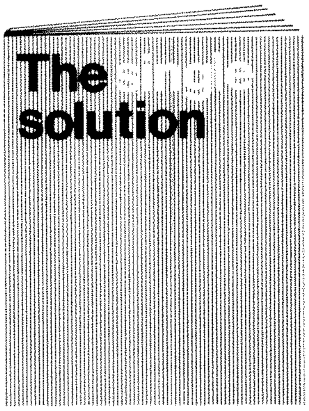

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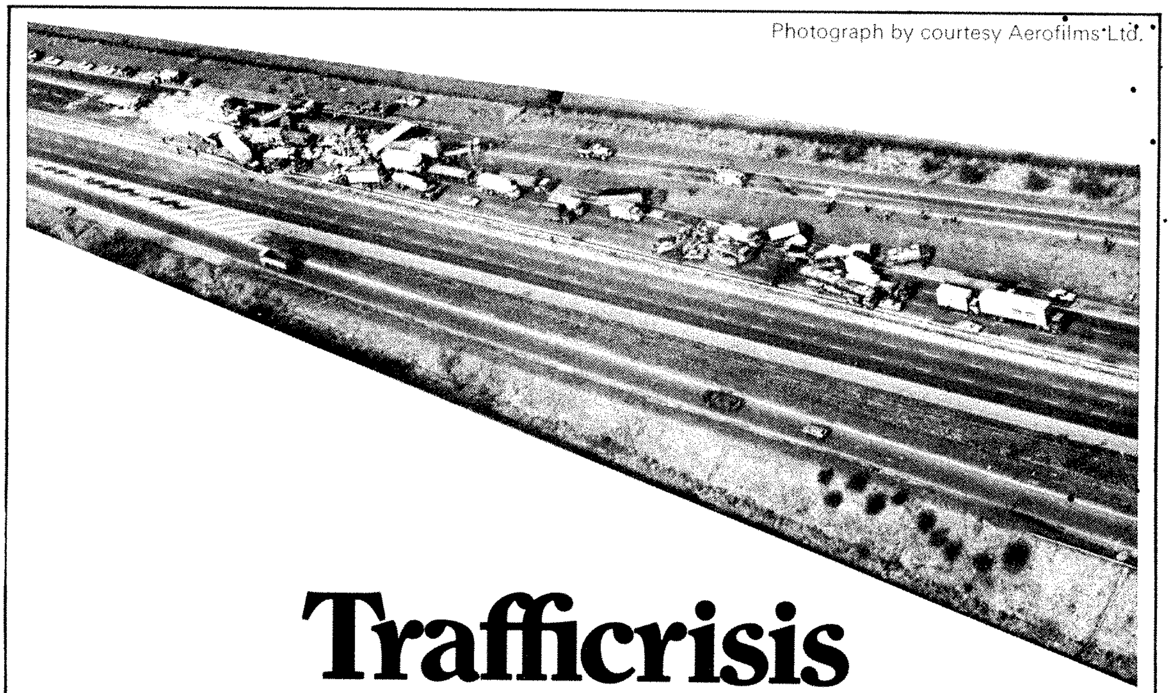

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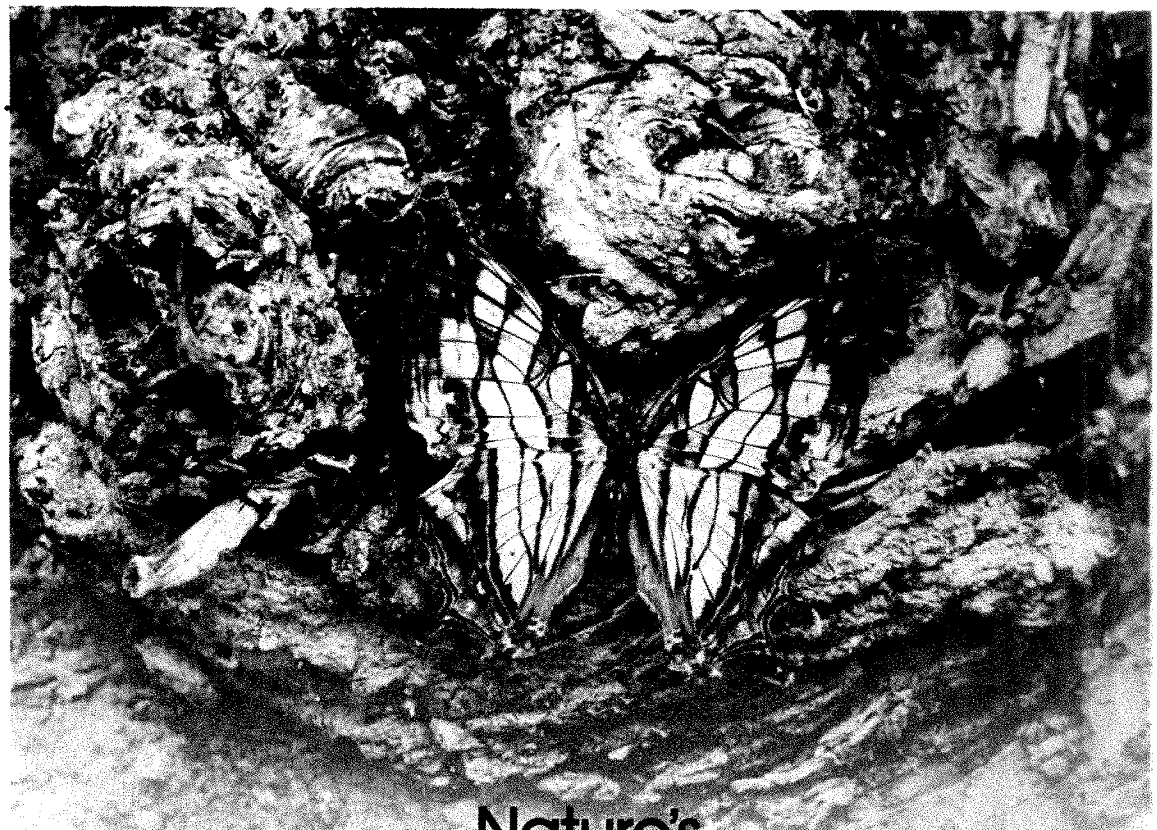

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1. Vinnicombe, J. and Shuttleworth, K.E.D. (1966). Lancet. **1**, 230.
2. Sack, E. et al. (1962). New Engl. J. Med. **266**, 19.
3. Ladehoff, A. and Otte, E. (1963). Scand. J. Clin. Lab. Invest. **15**, 239.
4. Andersson, L. (1964). Acta Chir. Scand. **127**, 552.

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SURGICAL RESEARCH SOCIETY

A meeting of the Surgical Research Society was held in the University of Bristol on 6 and 7 July, 1973, with Professor L. P. Le Quesne (President of the Surgical Research Society) in the Chair. The following papers were presented:—

1. Arterial Damage by Trackless Lesions in the Spinal Cord made by Focused Ultrasound: H. B. Griffith, B. Brownell, J. B. Bowes, M. Halliwell, and P. N. Wells, Departments of Surgery and Neurosurgery, University of Bristol.

Ultrasound brought to a focus can produce uniform trackless lesions in the nervous system. In the brain white matter is more vulnerable than grey, but the converse has been found in the spinal cord (Lele, 1967). In an experimental study in pigs, mounted to test the practicability of ultrasonic commissurotomy for pelvic pain in man, a series of uniform lesions were made, using a power output of 2 W. for 4 seconds at a frequency of 2 MHz.

It was found that the grey matter is spared selectively and that when the midline branches of the anterior spinal artery are involved in the ultrasonic lesion an obliterative arteritis results. It was also noted that even in the presence of this vascular change, the motor neurons of the anterior horns, which are especially liable to ischaemic or mechanical damage, may not show pathological changes.

It is likely that focused ultrasound at this frequency produces its effects by thermal release, and the rates of blood-flow through grey and white matter may be crucial in determining whether a lesion is produced. The hitherto undescribed arteritis may partly explain why grey-matter damage has been previously seen. There is a good prospect of making a safe selective therapeutic lesion in man.

Lele, P. P. (1967), *Ultrasonics*, **6**, 105.

2. Antidiuretic Hormone Response in Patients undergoing Surgery on High and Conservative Fluid Régimes: C. S. Sinnatamby, M. H. Irving, C. R. W. Edwards, and M. Kitau, Departments of Surgery and Chemical Pathology, St. Bartholomew's Hospital, London.

The view that postoperative water loads should be restricted because of an obligatory antidiuretic hormone (ADH) response is challenged by the intravenous administration of sufficient fluid to compensate for reductions in blood-volume and effective extracellular fluid, both of which act as stimuli to ADH production.

ADH production was studied in two groups of 4 patients by radio-immunoassay of arginine vasopressin production in 24-hour urine samples from the day prior to operation through to the end of the second postoperative day.

Fluid intake was identical in both groups on the day prior to operation. On the day of operation patients in the high fluid-load group received replacement of the estimated blood-loss plus 15 ml. per kg. per hr. of Hartmann's solution. At the end of the operation the patients commenced on a régime of dextrose, 5 per cent, and normal saline at a rate of 4 litres per 24 hours. The second group, on the conservative régime, received replacement of all blood-loss plus 5 ml. per kg. per hr. during the operation and 1·5 litres of fluid per 24 hours from the end of the operation.

Operation caused a marked increase in the arginine vasopressin content of the urine in both groups, the level being unaffected by the fluid load. Patients on a high fluid load excreted significantly more urine on the first and second postoperative days (3851 ± 762; 3269 ± 592) than did patients on the conservative régime (1351 ± 271; 1695 ± 224). The high fluid-load group had lower urine and plasma osmolalities.

It is concluded that although urine output in the immediate postoperative period can be increased by a high fluid intake this is not the result of suppression of the ADH response.

3. The Effect of Cholecystectomy on the Composition of Bile in Gall-stone Patients: D. C. Smith, R. A. McAllister, and C. Mackay, University Department of Surgery, Western Infirmary, Glasgow.

Eleven patients, each with a functioning gall-bladder, admitted for elective cholecystectomy for gall-stones were studied. At operation bile was aspirated from the gall-bladder and the common duct and the stones were retained for analysis. Six months to 2 years later further samples of bile were obtained by duodenal intubation. The concentrations of bile-salt, cholesterol, and phospholipid were estimated and the relative composition of each sample was calculated (Admirand and Small, 1968). Individual bile-salts were estimated using thin-layer chromatography.

Eight patients had cholesterol gall-stones (mean cholesterol content 92 per cent) and 3 had pigment stones (mean cholesterol content 6·8 per cent). The relative composition of the common bile-duct bile at operation in 5 of the 8 patients with cholesterol stones lay outwith the zone of cholesterol solubility. However, on follow-up the relative composition lay within the zone of cholesterol solubility on both occasions. Cholecystectomy produced no significant changes in the individual bile-salts.

Cholecystectomy alters the relative composition of bile in such a way as to render further stone formation less likely.

Admirand, W. H., and Small, D. M. (1968), *J. clin. Invest.*, **47**, 1043.

4. Macrophage Phagocytic Activity in Patients with Breast Cancer: M. Baum, D. Sumner, M. H. Edwards, and P. Smythe, Department of Surgery, King's College Hospital, London.

The monocyte/macrophage system of cells plays a critical role in the host response to cancer (Baum and Fisher, 1972). An indirect method of monitoring the activity of these cells by measuring the clearance of radioactive micro-aggregated albumin by the sinusoidal macrophages of the liver and spleen was first described to the Society by Mackay et al. (1968).

Using this technique the macrophage phagocytic activity (K value) of 47 women with breast cancer was estimated prior to any treatment. The patients were subdivided according to whether the disease was localized to the breast and underlying muscle (T1–4, N0, M0), or whether the cancer had disseminated to the regional nodes or beyond (T1–4, N1 and/or M1). Included in the latter group were patients with occult bone metastases detected by skeletal scintigraphy.

The mean K value of the patients with localized disease was 63, whilst for those with dissemination it was 52. This difference is significant ($\chi^2 = 4{\cdot}584$, $P = 0{\cdot}05$). There appeared to be a linear correlation between tumour size and K value when the disease was localized ($r = 0{\cdot}47$, $P < 0{\cdot}05 > 0{\cdot}02$), but this relationship was lost in patients with dissemination.

These results suggest that as long as the macrophage response of the host to cancer remains intact the disease may remain localized.

BAUM, M., and FISHER, B. (1972), *Cancer Res.*, **32**, 2813.
MACKAY, W. D., BAUM, M., MAGAREY, C. J., VERNON-ROBERTS, B., and QUANTOCK, D. S. (1968), *Br. J. Surg.*, **54**, 229.

5. A Comparison of Methods of Immunological Reconstitution of Immunologically Unresponsive Mice: D. N. H. HAMILTON, C. E. REID, D. G. GILMOUR, and P. R. F. BELL, University Department of Surgery, Western Infirmary, Glasgow.

In human malignancy the establishment and growth of the tumour may be the result of an absent or ineffectual immunological response. Immunotherapy designed to stimulate (Mathé, 1972) or to restore with lymphocytes (Yonemoto and Terasaki, 1972) this possible deficiency in cell-mediated immunity has met with some success.

To study methods of reconstitution CBA mice were rendered unresponsive to 'A' strain grafts by two methods:—

1. *Specific Tolerance*: Induced by neonatal injection of F^1 CBA/A cells.

2. *Non-specific Anergy*: Obtained by adult thymectomy, lethal irradiation, and bone-marrow reconstitution ('B' mice).

The ability of various immunological therapies to reject the graft was studied and showed first, using infusion of lymphocytes, that while 10^7 sensitized cells were required to restore the tolerant mice only 10^5 sensitized cells were required for the 'B' mice; 10^6 normal lymphocytes could restore the 'B' mice but the maximum dose of normal lymphocytes given (10^7) failed to affect the tolerant mice. Young thymus grafts placed under the kidney capsule restored the 'B' mice but did not reconstitute the tolerant animals.

Thus specific tolerance presents a much greater barrier to reconstitution than anergy by a factor of 100, and suggests that the clinical success of immunotherapy may be related to the type of deficiency present.

MATHÉ, G. (1972), *Prog. Immunology*, **1**, 958.
YONEMOTO, R. H., and TERASAKI, P. I. (1972), *Cancer, N.Y.*, **30**, 1438.

6. An Assessment of a Simple Test for Gram-negative Endotoxaemia: D. P. FOSSARD and V. V. KAKKAR, Department of Surgery, King's College Hospital Medical School, London.

The diagnosis of endotoxic shock in surgical patients usually depends on obtaining a positive blood-culture, which may take several days. The value of a simple and rapid test which can be used to detect the presence of circulating Gram-negative endotoxins has been assessed. The test is based on the ability of Gram-negative endotoxins to coagulate a protein moiety obtained from the horseshoe crab.

The study was done in two parts. In the first part using 20 experimental animals blood samples were obtained from the portal and systemic circulations before and after bowel resection. It was possible to detect endotoxin in concentrations as low as 10^{-8} μg. per ml. In the second part of the study 12 patients with acute inflammatory abdominal conditions were investigated. Frequent blood samples were withdrawn for blood-culture and endotoxin assay. The endotoxin assay was positive in all except 1 patient. Once the infection was controlled the assay became negative. In 3 patients who had positive blood-cultures the assay also detected the presence of endotoxin.

It is concluded that the endotoxin assay is a simple, rapid, and sensitive method of detecting endotoxaemia and observing the patient's response to treatment. It may also be useful as a screening test for detecting patients who have minor degrees of endotoxaemia prior to surgery.

7. Gall-stone Dissolution *in vitro:* K. E. FARRELL, D. C. SMITH, and C. MACKAY, University Department of Surgery, Western Infirmary, Glasgow.

Retained stones after choledocholithotomy present a surgical problem and their dissolution by means of solutions introduced through an indwelling T-tube is an attractive goal. Cholesterol, the major constituent of gall-stones, is readily dissolved in lipid solvents but these are unphysiological. We have therefore measured the rate of dissolution of gall-stones in physiological solvents.

Gall-stones weighing 40–50 mg. and containing more than 95 per cent cholesterol were placed in 5 per cent bile-salt solutions with and without lecithin. The bile-salts studied were glycine and taurine conjugates of cholic, chenodeoxycholic, and deoxycholic acids. The solutions were sterilized by Millipore filtration, sealed in sterile tubes, and gently agitated in a water-bath at 37° C. The stones were weighed regularly using an aseptic technique.

Stones lost weight rapidly over the first 7 days and more gradually thereafter. To standardize interpretation the dissolution rate for each solvent was expressed as the time required to reduce the stone to half its original weight ($T_{\frac{1}{2}}$) at the dissolution rate occurring during the first 7 days of study. The $T_{\frac{1}{2}}$ was lowest for the glycodeoxycholate and lecithin solution (4 days) and greatest for the taurocholate solution (20 days). Glycine-conjugated dihydroxy bile-salts were the best solvents and all the solvents were improved by the addition of lecithin.

Thus, cholesterol gall-stones comparable in size to common-duct stones can be dissolved *in vitro* at a rate which would be useful in clinical practice.

8. Cervical Lymphovenous Shunt in Intractable Ascites—A Clinical Study: M. M. SEIN (R. Shields), Departments of Surgery, Institute of Medicine, Rangoon, Burma, and University of Liverpool.

Hitherto the surgical treatment of ascites which does not respond to conventional medical treatment has been unsatisfactory. In 8 patients with intractable ascites and advanced hepatic cirrhosis cervical lymphovenous shunt was performed—the thoracic duct in the neck was divided and anastomosed to the lower end of the internal jugular vein.

In 7 patients there was a marked reduction in ascites as demonstrated by a significant fall in the body-weight (mean fall, 13·7 kg.; $P < 0·001$) and decrease in abdominal girth (mean decrease, 41·85 cm.; $P < 0·001$) by the seventh to fourteenth postoperative days.

Immediately after operation the central venous pressure was increased and remained elevated (mean increase 5·4 cm. water; $P < 0·001$) for 7–8 hours to return eventually to preoperative levels. After an initial oliguria there was a massive diuresis with return of serum sodium and blood-urea to normal concentrations. By the fourteenth postoperative day there was a significant increase ($P < 0·001$) in the total serum protein and albumin to return their concentrations to within the normal range.

The mechanisms underlying the reduction of the ascites are of physiological and pathological interest. It is suggested that cervical lymphovenous shunt has a place in the surgical treatment of intractable ascites.

9. Arrival Time of Bromsulphophthalein (BSP) in the Duodenum—A Method for Assessing Function of the Biliary Sphincter after Sphincterotomy: A. L. G. PEEL (H. D. Ritchie), Surgical Unit, The London Hospital, London.

In an attempt to gain more information about the long-term effects of biliary sphincterotomy the arrival time of injected BSP in duodenal aspirate and the effect of morphine on this was measured.

In 26 patients with a functioning gall-bladder the mean arrival time was $17\cdot4 \pm 6\cdot6$ minutes. Where the gall-bladder did not function (15 patients) or had been removed (30 patients) the mean arrival times were $11\cdot3 \pm 1\cdot9$ and $11\cdot6 \pm 2\cdot2$ minutes respectively ($P < 0\cdot01$). However, in 8 anicteric patients with non-functioning gall-bladders and stones in the duct it was $19\cdot4 \pm 1\cdot2$ minutes.

In 47 of 49 patients who had had cholecystectomy and sphincterotomy 1–12 years previously the time of arrival fell within the above range for cholecystectomized patients, suggesting that bile-flow was not impeded. This was in accordance with clinical, laboratory, and hypotonic duodenography findings. However, in 2 patients with normal liver-function tests it was 19 and 36 minutes respectively which suggests some degree of obstruction to bile-flow.

Morphine prolonged the arrival time by 3–9 minutes in control patients with an intact sphincter and also after sphincterotomy, suggesting that the operation had not completely abolished muscular activity in the sphincter region.

10. The Composition of Bile in Patients with Disease of the Terminal Ileum:

D. C. Smith, R. A. McAllister, and C. Mackay, University Department of Surgery, Western Infirmary, Glasgow.

There is an increased incidence of gall-stones in patients who have undergone resection of the terminal ileum (Heaton and Read, 1969). Fourteen patients with disorders of the terminal ileum were studied; 5 had previously undergone resection and 9 had radiological evidence of Crohn's disease.

Bile was obtained by duodenal intubation and cholecystokinin administration. The concentrations of bile-salt, cholesterol, and phospholipid were estimated and the relative composition of each sample was calculated by the method of Admirand and Small (1968).

In all 5 patients who had undergone resection of the terminal ileum the relative composition of bile lay without the zone of cholesterol solubility. In the remaining 9 patients who each had an intact but diseased terminal ileum the relative composition lay within the zone of cholesterol solubility.

These findings suggest that patients who have undergone resection of the terminal ileum may develop gall-stones because they secrete bile which is supersaturated with cholesterol relative to bile-salt and phospholipid, probably owing to a lack of bile-salt as a result of impaired absorption.

Admirand, W. H., and Small, D. M. (1968), *J. clin. Invest.*, **47**, 1043.

Heaton, K. W., and Read, A. E. (1969), *Br. med. J.*, **2**, 494.

11. Experimental Hepatic Coma and Lethal Barbiturate Intoxication Response to Total-body Asanguineous Hypothermic Perfusion in Dogs:

K. B. Absolon, A. W. Carroll, J. C. Agostini, L. R. Goldbaum, and M. E. Applebaum, Departments of Surgery of the Washington Hospital Center, the George Washington University, and the Hyman Research Foundation, Department of Toxicology, Armed Forces Institute of Pathology, Washington, D.C.

Removal of the total circulating blood-volume and temporary replacement with an asanguineous perfusate under hypothermic conditions was investigated as a method of treatment for acute hepatic insufficiency and lethal barbiturate poisoning.

Biochemical (liver profile, electrolytes, complete blood-count, blood-urea nitrogen, blood-sugar) and physiological (central venous pressure, blood-pressure, electrocardiogram, core body temperature) parameters were studied in two groups of dogs. Ten dogs underwent end-to-side portacaval shunt followed 24 hours later by hepatic artery ligation, while 6 dogs underwent total body asanguineous hypothermic perfusion (T.B.A.P.) in addition within an average of 6 hours following hepatic artery ligation (Rappaport et al., 1953).

In the first group there was a progressive onset of coma and an average rise in blood-ammonia by 3·07 mg. per cent (5·27 mg. per cent initial to 8·34 mg. per cent over the 7 hours preceding death; in the control series blood-ammonia levels averaged 5·37 mg. per cent). The second group presented an average rise of blood-ammonia of 2·92 mg. per cent (9·41 mg. per cent initial to 13·33 mg. per cent) in the 6 hours prior to T.B.A.P., with post-T.B.A.P. ammonia levels decreasing to an average of 7·90 mg. per cent. Following T.B.A.P. all the animals died within 12 to 24 hours, a prolongation of survival by 100–400 per cent.

A series of 10 dogs received toxic doses of phenobarbital intravenously (50–100 mg. per kg. of body-weight) followed by T.B.A.P. after allowing adequate distribution. It was calculated that an average of 25 per cent of the phenobarbital was removed by T.B.A.P.

Rappaport, A., MacDonald, M., and Borowy, Z. (1953), *Surgery Gynec. Obstet.*, **97**, 748.

12. A New Model for Acute Hepatic Failure:

C. D. Derry and M. Slapak, Sears Surgical Laboratory, Harvard Medical School, Massachusetts, U.S.A.

There is a pressing need for a model of acute hepatic failure which is cheap and reproducible and in which only the liver is damaged. A preparation is described in the rat in which periods of hepatic ischaemia can be produced without the need for portal decompression.

Six groups of rats were used. Each received Keflin intramuscularly and dextrose subcutaneously. Using Penthrane inhalation anaesthesia and making use of the rat's segmental hepatic anatomy, an occluding clamp was placed on the blood-supply to 70 per cent of the liver, leaving 30 per cent normally revascularized, thus decompressing the portal circulation. After 20 (group A), 40 (group B), or 60 (groups C, D, and E) minutes of ischaemia the occluding clamp was removed. In groups A, B, and C the 30 per cent erstwhile vascular segment was immediately resected. In group D it was left for 24 hours and then resected. In group E it was left permanently.

All the animals were conscious and ambulant 4 hours after the operation. Animals died with a high SGOT level, abnormal prothrombin times, and a histological picture of acute pericortical necrosis. The mortality in groups A (12 rats), B (16 rats), C (8 rats), D (12 rats), and E (14 rats) was 27, 87, 83, 38, and 14 per cent respectively.

A cheap reproducible model for hepatic necrosis has been described. A 30 per cent vascularized fragment of liver present for only 24 hours exerts a very significant effect on the mortality consequent to prolonged hepatic ischaemia.

13. The Effect of Colectomy on Survival of Rats after 90 Minutes' Hepatic Ischaemia:

K. Chatamara and M. Slapak, Department of Surgery, University of Cambridge.

Non-absorbable oral Kanamycin reduces the mortality of a 90-minute period of hepatic ischaemia in the rat from 94 per cent in control animals to 21 per cent (Slapak et al., 1973). This reduction was probably related to the presence of bacteria in the bowel. The effect of colectomy on the same model has now been investigated. Male Wistar rats were used in three groups, A, B, and C. All the animals received intramuscular cephalin and dextrose-saline subcutaneously. In group A (10 rats) laparotomy was followed by occlusion of a 70 per cent segment of the liver for 90 minutes. The remaining 30 per cent segment served to decompress the portal circulation. During the 90-minute interval total colectomy with ileorectal anastomosis was performed. At 90 minutes the occluding clamp on the blood-supply to the liver was removed and the vascularized 30 per cent segment was resected, leaving the erstwhile ischaemic lobe in place. In group C (10 rats) the 90-minute occlusion was not performed but total colectomy and resection of the 30 per cent segment were carried out. In group B (17 rats) 90 per cent occlusion was performed, the 30 per cent segment being resected.

All the animals regained consciousness and were fully ambulant within 3 hours. In groups A, B, and C 7 (70 per cent), 1 (5 per cent), and 9 (90 per cent) rats survived for over 2 months.

Colectomy lowered a 95 per cent mortality to 33 per cent. This finding supports a major role of intestinal organisms as a factor in acute liver failure.

SLAPAK, M., DERRY, C. D., JONES, E. A., and CUEVAS, O. (1973), *Nature, Lond.*, in the press.

14. Haematological and Pulmonary Disturbances in Septic Shock: G. F. MILLIGAN, J. A. E. MACDONALD, A. MELLON, and I. MCA. LEDINGHAM, University Department of Surgery, Western Infirmary, Glasgow.

The relationship between the haematological and pulmonary disturbances in septic shock has not been defined.

Twenty-one consecutive patients suffering from septic shock were studied prospectively. Thrombocytopenia of less than 150,000 per c.mm. was found in 18 patients and of less than 50,000 per c.mm. in 12 patients. Prolongation of the prothrombin time and of the partial thromboplastin time was noted. Two patients died of haemorrhage. The fibrinogen degradation products were elevated in 18 patients. The bulk of the haematological changes had occurred within the first 12 hours and persisted for 6 days.

An increase in the alveolar arterial oxygen $(A\text{–}a)O_2$ gradient exceeding 100 mm. Hg occurred in 19 patients and was most marked within the first 24 hours. Radiographic evidence of pulmonary oedema was found in 17 patients and was most marked on the third day. There was an almost immediate improvement in the $(A\text{–}a)O_2$ gradient with intermittent positive-pressure ventilation while the radiographic appearances resolved more slowly.

The nature of the coagulation abnormalities indicated a multifactorial deficiency which resolved spontaneously. The pulmonary disturbances were independent of fluid replacement and infection. An explanation for the mechanism of the pulmonary lesion in these patients is that of disseminated intravascular coagulation.

15. Ventricular Function in Canine Haemorrhagic Shock: J. A. E. MACDONALD, G. F. MILLIGAN, A. MELLON, and I. MCA. LEDINGHAM, University Department of Surgery, Western Infirmary, Glasgow.

A cardiac mechanism has been postulated as a factor in refractory shock (Crowell and Guyton, 1962). Shock was induced in three groups of 6 spontaneously breathing greyhounds by bleeding into a reservoir until the mean arterial pressure was 40 mm. Hg. In group I the shed blood was reinfused immediately; in group II hypovolaemia was sustained for 2 hours, while the arterial pressure rose spontaneously to $105 \pm 2{\cdot}4$ mm. Hg (mean ± S.E.); in group III the arterial pressure was maintained at 40 mm. Hg for 2 hours by further exsanguination. Ventricular function was tested before and after shock by rapid infusion of 300 ml. of blood.

After resuscitation groups I and II showed a return to pre-shock haemodynamic values. Group III showed a significant reduction in arterial pressure (33 per cent), left ventricular stroke work (57 per cent), and myocardial contractility (dP/dt_{max} 34 per cent); left ventricular end-diastolic pressure was significantly raised (36 per cent).

Ventricular function curves were constructed for each animal. In groups I and II the curves were comparable before and after shock. In group III the curves were hypo-effective after shock.

Impairment of ventricular function after sustained hypovolaemic hypotension may contribute to the phenomenon of refractory shock.

CROWELL, J. W., and GUYTON, A. C. (1962), *Am. J. Physiol.*, **203**, 248.

16. The Metabolic Response to Abdominal Surgery in a Tropical Environment:* E. A. ELEBUTE (I. D. A. Johnston), Lagos University Teaching Hospital, Lagos, Nigeria.

Nitrogen balance studies were conducted in 17 adult male Nigerian patients who had vagotomy and a drainage operation for chronic duodenal ulceration. In 9 patients intravenous isotonic dextrose and dextrose-saline were given after operation; the remaining 8 patients had intravenous supplements of nitrogen and calories as amino-acids and 50 per cent dextrose. Accurate records of ward temperature and humidity were obtained during the studies. There was an increased amount of urinary nitrogen which showed no correlation with either nitrogen or calorie intake. This indicated an increased catabolism of endogenous protein after surgery. The resulting negative nitrogen balance was abolished by an increased intake of nitrogen and calories. The level of intake required is much higher in the early than in the late postoperative period. A significant negative correlation of maximum air temperature with deviations of nitrogen balance from the nitrogen-balance/nitrogen-intake regression line indicates that higher environmental temperatures may increase the catabolic response.

Comparison of these results with those obtained by Spivey and Johnston (1972) shows that in permanent inhabitants of the tropics surgery of moderate severity produces a metabolic response of similar magnitude to that observed in temperate climates.

SPIVEY, J., and JOHNSTON, I. D. A. (1972), *Br. J. Surg.*, **59**, 93.

17. The Effect of Surgical Operations of Varying Severity on the Secretion of Growth Hormone: P. D. WRIGHT and I. D. A. JOHNSTON, Department of Surgery, University of Newcastle upon Tyne.

Raised levels of serum growth hormone have been recorded after injury (Glick et al., 1965). A study was planned to examine the growth-hormone response to operations of differing degrees of severity.

Three groups each containing 6 patients were studied after inguinal herniorrhaphy (group I), vagotomy and pyloroplasty (group II), and aortofemoral by-pass (group III). Serum growth-hormone levels were measured under fasting conditions and during a 25-g. intravenous glucose-tolerance test. Tests were performed before, during, and at intervals up to 8 days after operation.

There was no increase in serum growth hormone in response to glucose in any group before operation. Fasting growth-hormone levels only rose significantly on the eighth day in group III. There was a significantly increased secretion of growth hormone in response to glucose during surgery which was greatest in group III ($P < 0{\cdot}0025$). The growth-hormone response to glucose remained elevated after surgery. The response in group III was significantly greater than in groups I and II on the third, fifth, and eighth postoperative days.

The secretion of growth hormone is related to the degree of severity of trauma. Changes in growth-hormone secretion correlated with changes in glucose utilization after injury.

GLICK, S. M., ROTH, J., YALOW, R. S., and BESON, S. A. (1965), *Rec. Prog. Hormone Res.*, **21**, 241.

18. Changes in Thyroid Status after Experimental Femur Fracture in the Rat: J. R. RICHARDS (L. H. Blumgart), Departments of Surgery and Physiology, University of Glasgow.

The role of the thyroid gland in the post-injury situation is controversial, largely owing to failure to appreciate potential sources of experimental error. Rats used in this study were kept singly within a sound-proof, temperature-controlled chamber. Behavioural studies were used to select the least stressful methods of estimating thyroxine turnover. A high-protein, low-residue, ultra-low-iodide diet was found necessary to achieve consistent pre-injury results. Using a double-isotope technique (Harland et al., 1972) fracture of the femur resulted in a 35 per cent increase in the thyroxine degradation rate from 0·88 μg. T_4 per 100 g. body-weight per day prior to injury, rising to 1·13 μg. T_4 per 100 g. body-weight after injury. This increase was of short duration, lasting from 0 to 30 hours after fracture, and was found in only 66 per cent of the injury rats, closely associated with a biphasic urinary nitrogen excretion pattern after injury.

In a separate study, using a modification of Oppenheimer's method (Sterling and Brenner, 1966), femur fracture was found to cause a rise in the serum 'free thyroxine' from 1·3 ± 0·3 ng. per 100 ml. before injury to 3·4 ± 0·6 ng. per 100 ml. after injury. Here there was an initial peak at 6 hours, but the maximum values occurred between 36 and 48 hours and had returned to the pre-injury values by 72 hours.

HARLAND, W. A., ORR, J. S., and RICHARDS, J. R. (1972), *Scott. med. J.*, **17**, 92.
STERLING, K., and BRENNER, M. A. (1966), *J. clin. Invest.*, **45**, 153.

19. The Measurement of Extracellular Fluid Volume with Radiobromide Simultaneous Plasma and Lymph Disappearance in Man: J. R. W. GUMPERT and R. M. ZOLLINGER, jun. (A. G. Riddell), Department of Surgery, Bristol Royal Infirmary, Bristol, and The Peter Brent Brigham Hospital, Boston, Massachusetts, U.S.A.

Most work with tracer-dilution techniques in body-fluid distribution has been concerned with information obtained after the achievement of equilibrium (tracer statics). There is increasing interest in the study of decreasing tracer concentration during the process of equilibration (tracer kinetics). The unusual opportunity of simultaneously studying the kinetics of radiobromide in plasma and lymph, unhampered by urine loss, in the human presented itself.

Five fasting nephrectomized patients maintained on haemodialysis with thoracic duct fistulae (T.D.F.) received 30 μc. of $Na^{82}Br$ intravenously. Arterial blood and T.D.F. lymph were sampled simultaneously 25 times each over 5 hours.

After correction for the delay in lymph-flow up to the T.D.F., equilibrium between plasma and lymph occurs between 7 and 11 minutes. Thereafter lymph and plasma behave as one compartment.

Lymph and plasma disappearance was compared by graphic analysis and serial exponential subtraction. It is concluded that the first rate constant in radiobromide equilibration is a summation of mixing within the plasma and that part of extracellular fluid exemplified by thoracic duct lymph. Despite the absence of urinary loss, there are two further rates of transfer, possibly representing penetration further into the extracellular space and into the cells respectively.

20. Factors Determining Marker Concentration during Continuous Blood-volume Measurement during Haemorrhage and Infusion: J. M. T. GRIFFITHS (A. N. Smith), Department of Clinical Surgery, University of Edinburgh and Edinburgh Northern Hospital Group.

A method is described of monitoring bleeding from a concealed source by the changing plasma concentration of ^{125}I human serum albumin (H.S.A.) with a measured infusion.

The principal physiological parameters affecting single-dose marker concentration under conditions of haemorrhage and fluid replacement were examined in the baboon as follows:—

1. In 6 animals time/concentration curves for simultaneously injected ^{51}Cr-labelled red cells and ^{125}I H.S.A. were obtained. During the 10-minute equilibration period ^{125}I (blood) activity decreased 22·5 ± 2·9 per cent relative to ^{51}Cr activity. Over the next 3 hours ^{51}C activity fell 0·5 ± 0·2 per cent and ^{125}I, 9·6 ± 1·1 per cent.

2. Transcapillary refilling of the circulation was measured following acute haemorrhages of 10–30 per cent of the blood-volume in 12 experiments. The mean results of three simultaneous methods (^{51}Cr R.B.C. concentrations, ^{125}I H.S.A., microhaematocrit) suggested a two-component curve with almost immediate replacement of 10–15 per cent of the loss.

3. In 9 experiments the net loss of fluid from the circulation was measured during sequential small haemorrhages replaced by Dextran 70. Between 9·5 and 54 per cent of the infused fluid volume had disappeared after 3 hours.

It is concluded that the methodology is valid and that it demonstrates early and substantial fluid transfer across the capillary wall during haemorrhage and infusion.

21. Early Results of Jejuno-ileostomy for Massive Obesity: R. M. BADDELEY, General Hospital, Birmingham.

Because of failure to respond to conventional dietary régimes 60 consecutive massively obese patients were submitted to jejuno-ileostomy. There were 51 women and 9 men who were 75–150 per cent above standard body-weight. Endocrine causes were excluded and routine haematology, serum iron, folic acid and vitamin-B_{12} estimations, serum electrolytes, liver-function tests, and serum cholesterol, calcium, and magnesium levels were measured.

Jejuno-ileostomy was performed after the method of Payne and Dewind (1969), in which the proximal part of the jejunum, measuring 35 cm., was anastomosed to the terminal ileum 10 cm. from the ileocaecal valve. The duration of follow-up was 3–42 months.

There was 1 death (1·7 per cent). At 3 months the average weight-loss was 20·7 kg., at 6 months 31·0 kg., and at 1 year 44·0 kg. There were 4 cases of acute fatty liver, 1 of which was fatal. Transient difficulties were experienced with diarrhoea and vomiting during the first 3 months. The only significant biochemical abnormalities were folic-acid deficiency in 19 patients, low serum iron in 27 patients, elevation of SGOT in 13 patients, low magnesium in 6 patients, and low calcium in 2 patients. These abnormalities were corrected. The results are regarded as satisfactory and further trial of the operation seems justified.

PAYNE, J. H., and DEWIND, L. T. (1969), *Am. J. Surg.*, **118**, 141.

22. Preliminary Comparison of Results following the Intramural Inoculation of Crohn's Disease and Normal Ileal Homogenates in Rabbit Bowel:

D. R. CAVE, S. KANE, and D. N. MITCHELL (B. N. Brooke), Surgical Unit, St. George's Hospital Medical School, London.

Human Crohn's disease and normal ileal tissues were obtained from comparable sites at elective surgery. Homogenates were prepared in normal saline from each frozen tissue. Identical volumes of these homogenates were injected at comparable sites into the wall of the terminal ileum in each of three groups of New Zealand white rabbits. The following observations were made at 3-monthly intervals: (*a*) changes in weight; (*b*) changes in the macroscopic appearances of the terminal ileum and related mesentery; (*c*) histological changes were assessed 'blind' by two independent observers from a full-thickness biopsy of the terminal ileum.

Granulomatous changes with the presence of focal epithelioid and giant-cell granulomas were observed to evolve in the submucosa and other tissues of the bowel wall and in the draining mesenteric nodes of a proportion of rabbits receiving Crohn's disease tissue but *not* in those receiving normal ileal homogenate.

The results of these studies are compatible with the evidence for a transmissible agent from Crohn's disease tissues (Mitchell and Rees, 1970).

MITCHELL, D. N., and REES, R. J. W. (1970) *Lancet*, **I**, 168.

23. Jejuno-ileal Colonic Interposition (J.I.C.I.) following Massive Small-bowel Resection (S.B.R.) in Rats:

D. A. LLOYD (J. Terblanche), Department of Surgery, Groote Schuur Hospital and University of Cape Town, South Africa.

Massive S.B.R. in man results in serious malabsorption. This study in rats assesses the value of colonic interposition between the jejunal and ileal remnants at the time of resection. Eighty-two rats were grouped according to the length of the remaining small bowel (group I, 100 per cent, 75–100 cm.; group II, 20 per cent; group III, 10 per cent) and the surgical procedure performed (S.B.R. alone, with iso- or antiperistaltic J.I.C.I., or with a reversed segment of terminal ileum).

Weight-gain following S.B.R. was increased by isoperistaltic J.I.C.I. and impaired by antiperistaltic J.I.C.I. Transit times of barium from the stomach to the caecum assessed radiologically were 110 minutes in group I and 45 minutes in group II with or without isoperistaltic J.I.C.I. In group III the transit time of 20 minutes was doubled by iso- or antiperistaltic J.I.C.I. ($P > 0\cdot05$).

After S.B.R. radio-isotopic studies showed normal sodium-iodide absorption and impaired absorption of human albumin, triolein, and vitamin B_{12}. Isoperistaltic J.I.C.I. increased the absorption of all the test substances. Antiperistaltic J.I.C.I. increased albumin (large dose only) and triolein absorption but further impaired vitamin-B_{12} absorption.

Compensatory morphological changes occurred in the residual small bowel in all groups after S.B.R. Features suggestive of intestinal obstruction were present proximal to reversed segments of colon and ileum.

These results indicate that isoperistaltic J.I.C.I. improves intestinal absorption following massive S.B.R. in rats and may be a useful procedure in man.

24. The Role of Humoral Factors and Diamine Oxidase Activity in Shock after Intestinal Ischaemia in Rabbits:

J. KUSCHE, H. RICHTER, R. HESTERBERG, and W. LORENZ, Division of Experimental Surgery and Pathological Biochemistry, University Surgery Clinic, Marburg/Lahn, Germany.

The revascularization after superior mesenteric artery occlusion (S.M.A.O.) produces shock due to the release of vasoactive substances. Diamine oxidase (DAO) may protect against such substances, and therefore the influence of a simple perfusion of the ischaemic gut and of the inhibition of DAO on the survival time of rabbits was investigated. The DAO activity was measured using ^{14}C-putrescine as substrate (Okuyama and Kobayashi, 1961).

The small intestine of rabbits contained a high activity of DAO ($2\cdot2 \pm 1\cdot0$ mU. per g. of tissue, $n = 10$). The injection of the specific DAO inhibitor, aminoguanidine (25 mg. per kg. i.v.), into rabbits (anaesthetized with 10–20 mg. per kg. pentobarbitone) 1 hour before S.M.A.O. reduced the survival time from 187 ± 104 minutes in the control group ($n = 10$) to 55 ± 27 minutes after a S.M.A.O. of 90 minutes ($n = 10$, $P < 0\cdot005$). This decrease was dependent on the dose of aminoguanidine. In 30 rabbits under the same conditions the survival time was 153 ± 59 minutes after saline injection, but 134 ± 57, 64 ± 17, 49 ± 22, and 37 ± 15 minutes following 10, 30, 50, and 100 mg. of aminoguanidine per kg. The perfusion of the ischaemic gut by Ringer's solution (37° C., 120 ml. per kg.) and the elimination of the perfusate through a catheter in the portal vein prolonged the survival time from 15 ± 4 to 114 ± 7 minutes ($P < 0\cdot005$, $n = 20$).

OKUYAMA, T., and KOBAYASHI, Y. (1961), *Archs Biochem. Biophys.*, **95**, 242.

25. Myoelectrical Activity in the Recto-sigmoid in Man:

I. TAYLOR, H. L. DUTHIE, B. H. BROWN, and R. SMALLWOOD, University Departments of Surgery and Medical Physics, Royal Infirmary, Sheffield.

By means of intraluminal suction electrodes the myoelectrical activity and associated pressure changes in the rectum and sigmoid have been studied in 60 subjects at rest. The electrical activity in this area possesses two distinctive characteristics which have not so far been observed in recordings from other areas of the gastro-intestinal tract.

1. The slow wave activity is not present all the time. In the lower rectum it is regularly present for an average of 67 per cent of the recording time (range, 36–100 per cent). In the more proximal areas of the bowel it is present for an average of 25 per cent of the recording time (range, 10–52 per cent).
2. There are two rhythms. The most commonly observed one has a frequency between 6 and 9 cycles per minute and an amplitude ranging between 0·25 and 1 mV. The other rhythm has a slower frequency (3–4 cycles per minute) but a higher amplitude (0·6–2·5 mV.).

26. Use of the Leucocyte-migration Test to demonstrate Specific Cellular Immunity in Lymph-nodes draining Colorectal Cancer:

P. J. GUILLOU and G. R. GILES, University Department of Surgery, Leeds (St. James's) University Hospital, Leeds.

A two-stage technique for the demonstration of specific cellular immunity to tumour-associated antigen in lymph-node lymphocytes by the technique of leucocyte-migration inhibition has been developed. A simple one-stage procedure has been used to study sensitization of peripheral blood lymphocytes.

In 5 patients undergoing laparotomy for benign gastro-intestinal disease no inhibition of migration has been observed in response to either normal colonic mucosal (N.C.M.E.) or colonic carcinoma extract (C.C.E.) whether cultured in autologous or homologous AB serum. Of 6 patients with colorectal carcinoma studied so far, 5 showed significant sensitization of peripheral blood lymphocytes to C.C.E. when cultured in AB serum, but only 2 of these showed sensitization in autologous serum. No inhibition of migration was observed in response to N.C.M.E.

Sensitization to N.C.M.E. was not demonstrated in control lymph-nodes or in mesenteric nodes from patients with cancer. However, in the patients with cancer 5 of the 6 nodes from the root of the mesentery exhibited sensitization to C.C.E. but only 3 of the 6 nodes directly draining the tumours were sensitized to the tumour extract.

It is concluded that although lymphocytes are readily sensitized to colonic carcinoma antigen the immune responses of the cells residing in the lymph-nodes in close proximity to the tumour may be impaired by the neoplasm itself.

27. Can a Heterotopically Placed Segmental Liver Graft be Fully Life-supporting? An Affirmative Finding: T. Maki and M. Slapak, Sears Surgical Laboratory, Harvard Medical School, Massachusetts, U.S.A.

Auxiliary liver transplantation for temporary hepatic support would provide optimal liver function for extended periods of time. The use of an auxiliary graft fed by renal, rather than portal, vein blood as the only means of support was studied. In order to examine these questions unhindered by the variables imposed by rejection a new technique of autotransplantation was devised.

Ten 18–22-kg. dogs were used. In group A (5 dogs) two lobes of the liver comprising 40 per cent of the total liver mass were autotransplanted followed by a portacaval shunt and resection of the remaining liver. In group B the left central and left lateral lobes were also transplanted heterotopically but the right lateral and caudate lobes (30 per cent of the liver) were left intact. A portacaval shunt was not performed.

In group A all 5 dogs survived longer than 6 days. One animal died on the sixth day and the other animals were killed on days 63, 84, 113, and 114 respectively whilst in excellent health. At sacrifice a mean increase of 67 per cent had occurred in the graft.

In group B, 5 out of 7 dogs survived for more than 2 months. Of these, 3 were sacrificed on days 91, 74, and 41 respectively. The other 2 animals had resection of the orthotopically placed lobes and a portacaval shunt on days 104 and 18 respectively. Both are alive and healthy.

Renal vein blood instead of portal vein blood can be used in a temporary life-supporting auxiliary liver transplant, and a 40 per cent graft is adequate to maintain healthy life in such circumstances.

28. Phosphate Compounds as Bone-scanning Agents: S. P. F. Hughes, K. Jeyasingh, P. Lavender, and J. I. Burn, Departments of Surgery, Medical Physics, and Radiodiagnosis, Hammersmith Hospital, London.

Both strontium 87^{m} and fluorine 18, the two agents conventionally used for skeletal scintigraphy, have their disadvantages. Recently, phosphate compounds labelled with the readily available isotope technetium 99^{m} have been introduced as possible bone-scanning agents. The comparative merits of the compounds currently available, (1) pyrophosphate, (2) tripolyphosphate, and (3) ethylhydroxydiphosphonate (EHDP), have been investigated by studying these substances in rabbits and dogs and in patients with malignant disease.

The mean blood-levels in rabbits 4 hours after intravenous injection were as follows: tripolyphosphate, 25 per cent; pyrophosphate, 8 per cent; EHDP, less than 2·4 per cent. EHDP gave the best bone : blood ratio of radioactivity at 4 hours, with an impressively high mean value of 47·60. The ratio for pyrophosphate was 39·80 and that for tripolyphosphate was 5·99.

The skeletal scintiscans obtained with EHDP were of superior quality, with good delineation of normal bone in dogs and clearly defined deposits in patients with metastatic disease.

29. Anti-tumour Effects of *Corynebacterium parvum*: J. E. Castro, Division of Surgical Science (Transplantation Biology Section), Clinical Research Centre, Northwick Park, Harrow.

Corynebacterium parvum has inhibitory effects on some mouse tumours (Woodruff and Boak, 1966) and it has been suggested as a therapeutic agent for human tumours.

The effect of *C. parvum* on a syngeneic, transplantable, methylcholanthrene-induced sarcoma of Balb/C mice has been investigated. Intraperitoneal *C. parvum* significantly increased survival when given before or 1 week after intraperitoneal tumour challenge, and there was a good dose–response curve. The anti-tumour effect of *C. parvum* was maintained for 50 days after injection, and prior thymectomy or antilymphocyte serum did not abrogate the anti-tumour effect, suggesting a mechanism of action independent of cell-mediated immunity.

After giving *C. parvum* there was decreased cell-mediated immunity as shown by prolonged allograft survival, decreased graft-versus-host disease, thymus atrophy, and a decrease of θ-positive cells. In contrast, there was increased macrophage activity associated with splenomegaly and hepatomegaly, but prior splenectomy had no effects on the tumour protection afforded by *C. parvum*.

It is concluded that *C. parvum* has powerful anti-tumour effects mediated through increased macrophage function.

Woodruff, M. F. A., and Boak, J. L. (1966), *Br. J. Cancer*, **20**, 345.

30. Cellular Immunity to Malignant Melanoma: R. M. Grant, A. J. Cochran, C. E. Thomas, R. M. Mackie, D. E. Cameron-Mowat, and W. G. S. Spilg (J. N. Norman), University Departments of Pathology and Dermatology, the Western Infirmary, Glasgow.

The usefulness of the leucocyte-migration inhibition test in the measurement of cell-mediated immune responses was assessed in patients with malignant disease.

The effect of tumour extracts on the migration of peripheral blood leucocytes from 55 patients with malignant melanoma and 63 control donors was examined. The leucocytes from the majority of tumour-bearing patients (60 per cent) were inhibited on contact with extracts of histogenetically similar tumours but only occasionally by extracts of dissimilar tumours and normal tissues (8 per cent). Leucocytes from control donors were rarely inhibited by any of the tissue extracts (14 per cent). A striking decline in the frequency of tumour-extract-mediated inhibition of leucocyte migration was associated with advanced disease.

Cell-mediated immunity to tumour-associated antigens was measured in 22 patients in the early postoperative period, 16 of these cases having also been studied prior to surgery. Twelve of these 16 cases tested preoperatively showed significant inhibition of migration on contact with extracts of histogenetically similar tumours. Of the 22 cases studied in the early postoperative period, only 1 had significant inhibition of leucocyte migration. Significant inhibition of leucocyte migration returned in most patients within 5–22 days of operation.

31. Effects of Hyperthermia in Advanced Malignancy: C. M. Ludgate, R. T. Pettigrew, J. M. Galt, D. B. Horn, and A. N. Smith, Hyperthermia Unit and Departments of Anaesthetics and Clinical Chemistry, Western General Hospital and University of Edinburgh.

Human total-body hyperthermia to 42° C. has been produced in attempts to cause tumour necrosis. Energy is introduced at the rate of 3000–5000 cal. per minute during immersion in molten wax and ventilation under deep narcosis with a helium/oxygen mixture at 80° C. (Henderson and Pettigrew, 1971). Twelve patients had intensive physiological studies. There was an initial and sustained increase in the heart-rate, but an initial rise in the blood and central venous pressures was not maintained. Fluid and electrolyte losses were high but could be replaced using a standard intravenous régime. The serum bilirubin rose by an average of 0·13 mg. per 100 ml., but not above 0·6 mg. per 100 ml. if the temperature did not exceed 41·8° C. with no change in the serum-enzyme levels. Above this temperature the latter (SGOT, SGPT, and LDH) rose by 50 per cent and the serum bilirubin to 1·3 mg. per 100 ml. The tumours which responded most favourably to thermotherapy were sarcomas, and relief of pain was common.

HENDERSON, M. A., and PETTIGREW, R. T. (1971), *Lancet*, **1**, 1275.

32. Cutaneous Delayed Hypersensitivity Responses to 2-4-Dinitrochlorobenzine—A Prognostic Guide in Malignant Disease: G. BONE, D. R. APPLETON, and C. W. VENABLES, Department of Surgery, University of Newcastle upon Tyne.

An accurate assessment of the prognosis in individual patients with cancer would be valuable in planning treatment. It is possible that cellular immunity may have a role in restricting the progress of malignant disease (Burnet, 1970).

A study was set up to investigate the relationship of cellular immunity in 70 patients suffering from gastro-intestinal tract cancer and their survival. Cellular immunity was assessed by measuring the patient's ability to produce a cutaneous delayed hypersensitivity response to four different strengths of 2-4-dinitrochlorobenzine after initial sensitization with this chemical (Eilber and Morton, 1970).

Over a 6-month follow-up there was a highly significant ($P < 0{\cdot}001$) relationship between good cellular immune responses and a favourable prognosis.

It is suggested that this test will prove of value in the surgical management of patients with gastro-intestinal malignancies, in that radical surgery would not appear to be justified in patients with a greatly diminished cellular immune response.

BURNET, F. M. (1970), *Immunological Surveillance*. Oxford: Pergamon Press.
EILBER, F. R., and MORTON, D. L. (1970), *Cancer*, **25**, 362.

33. The Influence of Transplantable Tumours on the Healing of Colonic Anastomoses in the Rat: R. J. STEWART and J. I. MACNAUGHTON (H. Ellis), Westminster Hospital, London.

The early healing of colonic anastomoses in Sprague-Dawley rats bearing a Walker carcinoma, a Novikoff hepatoma, or a Yoshida sarcoma has been investigated.

In 200 animals, randomly divided into groups of 10, anastomoses were constructed in the proximal colon using a standard technique. Rats bearing between 10^4 and 10^8 tumour cells, as estimated at the time of anastomosis, were compared with control animals. The tumour cells were implanted either at the site of anastomosis (local) or in the dorsal subcutis (distant).

Healing was assessed on the seventh postoperative day by histology, hydroxyproline estimations (Woessner, 1961), and bursting strength measurements (Nelsen and Anders, 1966). The serum total protein, urea, electrolytes, and haemoglobin were also estimated.

Significant impairment of healing was noted when at least 10^5 Walker cells, 10^6 Novikoff cells, or 10^7 Yoshida cells were present locally at the time of anastomosis. However, 10^7 Walker cells or more than 10^8 Yoshida cells were required to cause similar impairment when distant from the wound. In all the groups bursting strength fell linearly with total serum protein.

NELSEN, T. S., and ANDERS, C. J. (1966), *Archs Surg., Chicago*, **93**, 309.
WOESSNER, J. F. (1961), *Archs Biochem. Biophys.*, **93**, 440.

34. A Method of Evaluation of Renal Preservation Techniques: G. A. MCLOUGHLIN, R. A. SELLS, and I. M. TYRRELL, Department of Surgery, University of Liverpool.

Successful renal preservation depends upon the maintenance of cell-volume homeostasis. Change in the intracellular water during preservation provides an estimate of cell-volume change and an index of preservation efficacy at the cellular level.

Canine kidneys subjected to 30 minutes' warm ischaemia were preserved either by an ice-flush technique (Collins C_4) or continuous perfusion at 9° C. with one of several different perfusates (either cryoprecipitated plasma or purified protein fraction (P.P.F.) with or without additives). Cortical biopsies were taken during 36 hours' cold ischaemia, and by estimation of the total tissue water and extracellular fluid (inulin) space (Flear et al., 1960) the intracellular water was derived.

No significant difference was found in the mean increase in intracellular water between ice-flush and cryoprecipitate perfusion for cold ischaemic periods of up to 12 hours ($P > 0{\cdot}4$). For longer cold ischaemic periods cryoprecipitate perfusion was significantly more effective in arresting cell swelling than the ice-flush technique ($P < 0{\cdot}001$). P.P.F. perfusion was significantly better than all other methods for all periods of cold ischaemia ($P < 0{\cdot}001$). The addition of glucose, hydrocortisone, insulin, and magnesium to either cryoprecipitated plasma or P.P.F. made no significant difference ($P > 0{\cdot}4$ and $P > 0{\cdot}2$ respectively). Only the addition of 15 mEq./l. of potassium to P.P.F. significantly reduced the mean increase in intracellular water for all cold ischaemic periods ($P < 0{\cdot}001$).

FLEAR, C. T. G., CRAMPTON, R. F., and MATHEWS, D. M. (1960), *Clin. Sci.*, **19**, 483.

35. Renal Preservation by Hypothermic Perfusion—The Importance of Pressure Control: C. J. GREEN and D. E. PEGG, Animal Division and Division of Cryobiology, Clinical Research Centre, Harrow, Middlesex.

The best combination of physical variants in a perfusion system designed for renal graft preservation is uncertain. Experiments were designed to study systematically the influence of different perfusion parameters in order to decide whether perfusion should be by constant pressure or constant flow.

Experiments were performed on isolated rabbit kidneys which were preserved for 24 hours and then autografted into the donor animal with immediate contralateral nephrectomy. A defined perfusate (Pegg and Green, 1972) designed to mimic rabbit plasma was used and the temperature was controlled at 5° C. throughout the 24-hour period. A direct comparison was made between 10 kidneys perfused at a constant pressure of 40 mm. Hg and 10 kidneys perfused at a constant flow of 13 ml. per minute. Vascular resistance and organ weight were recorded continuously and changes in perfusion composition were monitored. Subsequent function was assessed by ability to support life, by measurement of urea and creatinine levels at 2-day intervals, and finally by histological appearance at autopsy.

The kidneys in the constant-pressure group scored significantly better on all counts but particularly in their blood-urea-handling capacity. It is concluded that constant-pressure is preferable to constant-flow perfusion.

PEGG, D. E., and GREEN, C. J. (1972), *Cryobiology*, **9**, 420.

36. The Effect of Allopurinol in sparing ATP, ADP, and AMP in Anoxic Kidneys:

T. V. KEAVENY, S. K. CUNNINGHAM, and P. FITZGERALD, Department of Surgery, University College, Dublin.

Vasko et al. (1972) postulated that the protective effect of allopurinol in renal ischaemia was through preservation of the nucleotide pool. The effect of allopurinol on the levels of ATP, ADP, and AMP in rat kidneys made anoxic by clamping was studied.

The normal total of ATP, ADP, and AMP was 4·42 ± 0·482 μmol per g. wet weight. Total levels in the kidneys of rats which had received 20 mg. of allopurinol 20 minutes before vascular clamping of 30 minutes' duration (group 3) were significantly greater than the total levels in kidneys of rats similarly treated but with no allopurinol (group 2) (2·169 ± 0·200 and 1·791 ± 0·164 μmol per g. wet weight respectively, $P < 0·0025$). In groups 4 and 5 the kidneys were revascularized for 30 minutes after 30 minutes' clamping. Levels where rats were pre-treated with allopurinol (group 5) were significantly greater than in the untreated group (group 4) (2·541 ± 0·064 and 2·151 ± 0·228 μmol per g. wet weight respectively, $P < 0·01$). Groups 6 and 7 and groups 8 and 9 were similar to groups 2 and 3 and groups 4 and 5 respectively, except that the period of anoxia was extended to 60 minutes. Levels in the allopurinol pre-treatment groups were significantly higher than in the untreated groups (1·694 ± 0·098 compared with 1·257 ± 0·194, $P < 0·0005$; 2·410 ± 0·381 compared with 1·828 ± 0·321, $P < 0·005$, respectively).

The results indicate that allopurinol pre-treatment maintains a higher level of the adenine nucleotide pool in anoxic kidneys.

VASKO, K. A., DE WALL, R. A., and RILEY, A. M. (1972), *Surgery, St Louis*, **71**, 787.

37. Implantation of Pancreatic Islets into the Portal Vein of Diabetic Rats:

C. B. KEMP, M. J. KNIGHT, D. W. SCHARP, P. E. LACY, and W. F. BALLINGER (B. N. Brooke), Departments of Surgery and Pathology, Washington University School of Medicine, St. Louis, Missouri, U.S.A.

Intraperitoneal implantation of isolated pancreatic islets ameliorates the effects of streptozotocin-induced diabetes in the rat (Ballinger and Lacy, 1972), but normal values for blood-glucose and urine volumes are rarely achieved. As insulin is normally secreted into the portal venous system the effects of intraportal and intraperitoneal siting of implanted islets in diabetic rats has been compared.

Streptozotocin diabetes was induced in 20 inbred Lewis rats. Ten of these rats acting as controls passed between 82 and 186 ml. of urine containing 8·1–15·6 g. of glucose daily, with blood-sugars fluctuating between 320 and 760 mg. per cent. Pancreatic islets isolated by the collagenase-digestion method (Lacy and Kostianovsky, 1967) were implanted intraperitoneally into 5 diabetic rats and directly into the portal vein of 5 other diabetic rats. Urine volume and glucose content as well as blood-sugar levels were monitored regularly.

Rats receiving intraperitoneal islets showed an amelioration of the diabetic state in that urine volumes stabilized between 50-[illegible]50 ml. containing 4–5 g. of glucose daily with blood-sugar levels of 200–410 mg. per cent. Portal vein implantation resulted in normoglycaemia and normal urine volumes without glycosuria which are being maintained 6 weeks later.

These results suggest that the portal system may be the site of maximal effectiveness for transplanted pancreatic islets.

BALLINGER, W. F., and LACY, P. E. (1972), *Surgery, St Louis*, **72**, 175.
LACY, P. E., and KOSTIANOVSKY, M. (1967), *Diabetes*, **16**, 35.

38. The Survival of Transplanted Isolated Pancreatic Islets in the Omentum and Testis:

J. FERGUSON and R. J. SCOTHORNE (I. D. A. Johnston), Department of Anatomy, University of Newcastle upon Tyne.

Isolated pancreatic islets transplanted as allografts into the testis in guinea-pigs may survive for periods of up to 11 weeks—some five to six times longer than orthotopic skin allografts (Ferguson and Scothorne, 1972). The factors thought to be responsible for extended survival were the graft dosage, the special properties of the grafted tissue, or special properties of the testis as a graft site.

A study was planned to assess the relative importance of these factors by three groups of experiments. Skin allografts of varying size were implanted into the testis. Large-dose grafts showed a 28 per cent survival at 21 days and small-dose grafts showed a 100 per cent survival at 28 days. Skin allografts in large and small dosage were implanted into the omentum, which is technically a favourable site and not usually regarded as 'privileged'. Large-dose grafts showed a 33 per cent survival at 21 days and small-dose grafts showed a 100 per cent survival at 28 days. Isolated pancreatic islets were implanted into the omentum. Intra-omental islet-cell allografts were all alive when recovered at intervals from 10 days to 11 weeks.

The results support the view that the extended survival of islet-cell allografts in the testis is probably due to a combination of factors such as the privileged nature of the testis and the fact that islet tissue may be less antigenic than skin or that the survival period is related to 'dose' of tissue grafted.

FERGUSON, J., and SCOTHORNE, R. J. (1972), *Br. J. Surg.*, **59**, 316.

39. Passive Enhancement of Heterotopic Rat Heart Transplants:

P. R. F. BELL and N. L. TILNEY, University Department of Surgery, Western Infirmary, Glasgow.

French and Batchelor (1969) demonstrated an increased survival of renal allografts in rats by passive transfer of specific allo-antiserum. The aim of this study was to define more fully the effects of enhancement using the heterotopic cardiac transplant model in similar inbred rat strains.

AS rats were immunized by 5 weekly intraperitoneal injections of $1–2 \times 10^7$ spleen or lymph-node cells from August donors. Serum was pooled and stored at −20° C. The antibody titre measured by a standard cytotoxic method was consistently 1 : 256.

Hearts from (AU × AS) F_1 donors were transplanted heterotopically to AS recipients. Allografts were rejected by control animals in 8 ± 1 days. Allo-antiserum was administered to test animals using the régime of French and Batchelor (1969). One ml. was given intravenously on completion of the transplant, 1 ml. intraperitoneally at 24 hours, and 0·5 ml. intraperitoneally at 48, 72, and 96 hours postoperatively. Cardiac allografts in these animals have survived with good function for over 100 days.

Serum was collected from enhanced recipients with grafts functioning for at least 50 days and transferred adoptively to a second group of heart-graft recipients using a similar dosage schedule. These hearts continue to beat normally for over 50 days. These observations show that enhancing antibody can successfully prolong heart-allograft survival. In addition, enhanced recipients actively produce their own auto-enhancing antibody.

FRENCH, M. E., and BATCHELOR, J. R. (1969), *Lancet*, **2**, 1103.

40. The Influence of Calcium on Graft Rejection and Immunity to Malignancy:

G. W. ODLING-SMEE (H. W. Rodgers), Department of Surgery, Queen's University, Belfast.

Immunity to all grafts and immunity to malignancy is mediated by lymphocytes. These are cytotoxic for the foreign cells of the graft or the 'non-self' cells of a malignant tumour. Whitfield et al. (1971) have shown that *in vitro* lymphocytes will transform at a lesser rate with a lowered calcium concentration in the media and vice versa. Since cell-mediated immunity is carried out by lymphocytes and since lymphocyte transformation is an accurate *in vitro* correlate of cell-mediated immunity it is suggested that low calcium concentrations depress cell-mediated immunity and, conversely, high concentrations stimulate it.

Experiments were set up to test this hypothesis. Rats had their serum calcium depressed by parathyroidectomy and a calcium-free diet for 15 days. Fifteen out of 20 rats were then able to accept allogeneic skin-grafts. When rats with chemically induced tumours were depleted of calcium in the same way 8 tumours disappeared and 17 tumours regressed out of a total of 27 animals with tumours. The results with the skin-grafts confirm the hypothesis, but the results with malignant tumours suggest that the effect may be due to a direct action of calcium on cell division.

WHITFIELD, J. R., MACMANUS, J. P., YOUDALE, T., and FRANKS, D. J. (1971), *J. cell. Physiol.*, **78**, 855.

41. A New Bedside Radio-isotope Test for the Detection of Deep Venous Thrombosis in the Legs:

D. A. D'AURIA, G. J. DUFFY, T. G. BRIEN, D. ORMOND, and J. A. MEHIGAN, Department of Surgery, University College, Dublin, and Radio-isotope Department, St. Vincent's Hospital, Dublin.

Macro-aggregates of albumin (^{131}I MMA) have been shown by Webber et al. (1969) to have an affinity for blood-clot. The possibility of detecting venous thrombosis using ^{131}I MMA and a simple portable scintillation detector system (Pitman Isotope Localizing Monitor) which would allow the procedure to be carried out at the bedside has been investigated.

Following the production of acute femoral venous thrombosis in 10 dogs by electrocautery, 20–30 μc. of ^{131}I MMA was injected intravenously distal to the thrombus. The count-rate over the clot area and over the corresponding area on the opposite leg was measured at 5-minute intervals for 20 minutes. There was an increase in radioactivity over the clot area of 20–100 times when compared with the control area. This increase persisted throughout the period of observation.

Fifty-four patients with clinical evidence of deep venous thrombosis were investigated using ^{131}I MMA and the portable scintillation detection system. Approximately 100 μc. of ^{131}I MMA were injected into the deep venous system using tourniquets. Count-rates were obtained at 5-minute intervals for 20 minutes at seven points along the injected leg and at corresponding points on the opposite leg. There was retention of radioactivity in 30 out of 34 limbs (88 per cent) shown by phlebography to contain thrombi. There was rapid clearance of radioactivity in 17 of 20 limbs (85 per cent) for which the phlebograms were normal. There was an 87 per cent agreement between phlebography and the ^{131}I MMA venous clearance test.

WEBBER, M. M., BENNETT, L. R., and CRAGIN, M. (1969), *Radiology*, **92**, 620.

42. Evaluation of Elastic Stockings in Venous Insufficiency:

J. J. F. SOMERVILLE and P. J. BYRNE (W. G. Fegan), Clinical Research Department, Sir Patrick Dun's Hospital, Dublin.

This evaluation was carried out on full-length two-way-stretch elastic stockings. Two groups were studied: (1) 10 normal volunteers and (2) 12 patients with venous insufficiency. Group 1 was studied once and group 2 on four occasions, each separated by 30 days. Stockings were worn continuously for the first 60 days and not worn for the last 30 days. At each visit assessments were made of the severity of symptoms, the venous ambulatory pressures monitored from a superficial foot vein, and the pressure exerted by the stockings.

While walking group 1 reduced their mean superficial venous pressure from 84 to 18 mm. Hg. In group 2 before treatment with stockings the superficial venous pressure fell from 91 to 48 mm. Hg on walking, whereas after wearing stockings for 60 days the patients in this group could reduce their pressure from 91 to 29 mm. Hg on walking. After a further 30 days without stockings they could reduce their pressure to 36 mm. Hg. The improvement with treatment was significant ($P < 0\cdot005$).

There was a highly significant improvement in symptoms ($P < 0\cdot001$) after 60 days' treatment with stockings, and the severity of symptoms correlated closely with venous ambulatory pressures.

Pressures exerted by the stockings showed a decrease from the ankle to the thigh which was maintained between visits.

43. The Organization of Pulmonary Thrombi in relation to Their Site and Time of Origin:

M. T. MORRELL and M. S. DUNNILL, Nuffield Department of Surgery and Gibson Laboratories, Radcliffe Infirmary, Oxford.

The autopsy finding of multiple pulmonary emboli in various stages of organization has been held to indicate recurrent embolism in spite of the lack of corroborative clinical episodes. Secondly, adherent organizing lesions are believed by some to be locally formed thrombi and not emboli.

Experimental evidence for these beliefs was sought in dogs. Thrombi were induced in flowing blood by the thrombogenic action of lead in the inferior vena cava and lobar pulmonary arteries; emboli were released from the former. Twelve dogs had pulmonary emboli, 20 had pulmonary thrombi formed in situ, and 8 had both emboli and thrombi. The dogs were killed at intervals of up to 40 days and the expanded lungs were fixed and then sliced.

The histologist (unaware of the experimental procedure) could not distinguish between locally formed and embolic thrombi at any stage of organization. Although older thrombi tended to show greater organization the more remarkable finding was the wide variation in organization relative to the age of the lesion.

It is concluded that the presence at autopsy of pulmonary emboli with varying degrees of organization may be the result of one embolic episode, and that there is no histological difference between locally formed and embolic pulmonary artery thrombi.

44. Reversal of Lethal Carbon-monoxide Intoxication by Total-body Asanguineous Hypothermic Perfusion:

K. B. ABSOLON, J. C. AGOSTINI, A. P. BASU, S. N. ALBERT, and L. R. GOLDBAUM, Departments of Surgery of the Washington Hospital Center, the George Washington University and the Hyman Research Foundation, Department of Toxicology, Armed Forces Institute of Pathology, Washington, D.C., U.S.A.

The role of total-body asanguineous hypothermic perfusion following the administration of lethal doses of carbon monoxide was investigated (Klebanoff et al., 1972).

Three groups of 5 dogs each were studied. The first group received a 10 per cent mixture of carbon monoxide and room air through an endotracheal tube for 3 minutes (Smith, 1965). The second group underwent total-body asanguineous hypothermic perfusion (T.B.A.P.) only. The third group was similarly intoxicated and treated with T.B.A.P. after signs of irreversible carbon-monoxide intoxication were evident.

The first group of dogs suffered cardiorespiratory arrest within 1 hour of exposure to the gas, averaging carboxyhaemoglobin concentrations of 80 per cent (70–100 per cent) prior to death. The group treated by T.B.A.P. alone showed only evidence of haemodilution and all survived. The third group was subjected to carbon monoxide, and their carboxyhaemoglobin concentrations averaged 72·8 per cent (52–86 per cent); as soon as signs of anoxia appeared they underwent T.B.A.P. Following T.B.A.P. their carboxyhaemoglobin concentrations dropped to an average of 8·12 per cent (1–15 per cent) and all the animals survived. The average time to T.B.A.P. was 19·8 minutes (14–30 minutes).

This study shows that the severe systemic hypoxia resulting from carbon-monoxide intoxication can be completely reversed by the rapid removal of the circulating carboxyhaemoglobin by T.B.A.P. with no sequelae.

Klebanoff, G., Armstrong, R., Cline, R., Powell, J., and Bedingfield, J. (1972), *J. surg. Res.*, **13**, 159.

Smith, G. (1965), *Ann. N.Y. Acad. Sci.*, **117**, 684.

45. Gastrin Release in Response to Oral Glucose in Patients before and after Gastric Operations: R. C. G. Russell, J. P. S. Thomson, S. R. Bloom, and M. Hobsley, Department of Surgical Studies, The Middlesex Hospital, London.

Evidence for the effect of oral glucose on gastrin release before and after gastric operations is inconclusive. Accordingly, 19 preoperative patients and 74 postoperative (truncal vagotomy, 26; selective vagotomy, 29; partial gastrectomy, 19) duodenal ulcer patients were studied. Fasting and serial blood samples after oral glucose (200 ml., 50 per cent solution) were taken and the plasma-gastrin concentration was measured by radioimmunoassay.

The mean basal plasma-gastrin concentration was 19·3 pg. per ml. in the preoperative patients, 12·7 pg. per ml. in those after partial gastrectomy, and 42·6 pg. per ml. in those after vagotomy, this latter value being significantly higher ($P < 0·01$) than the preoperative mean. In these three groups the plasma-gastrin concentration increased after glucose ingestion. There was no difference in this increase between truncal vagotomy and selective vagotomy and between those with and without dumping symptoms. In the vagotomy group only a significant ($P < 0·01$) 'rebound' fall in plasma gastrin below the fasting level was observed at 120 minutes, at which time the plasma gastrin was insignificantly different from the preoperative group.

These results indicated that gastrin is released following a pure carbohydrate meal, that the gastrin release is greatest in patients having had vagotomy in whom there is a significant but unexplained fall below the fasting level at 120 minutes, and that gastrin is not related to the dumping syndrome.

46. The Effect of Transit through the Gastric Fundus on Circulating Gastrin: J. C. W. Evans, D. D. Reeder, and J. C. Thompson (J. H. Peacock), Department of Surgery, University of Texas Medical Branch, Galveston, Texas, U.S.A.

The organs responsible for the rapid catabolism of gastrin have yet to be accurately identified. The effect on circulating levels of endogenous gastrin of transit through the gastric fundus has been studied during basal conditions and conditions of stimulated gastrin release in 14 anaesthetized dogs. Gastrin release was stimulated by antral perfusion with acetylcholine.

During basal conditions transit through the gastric fundus resulted in no significant loss of gastrin, being 108 ± 15 pg. per ml. in the arterial serum and 99 ± 10 pg. per ml. in the venous serum. During antral stimulation gastrin levels rose in both arterial and venous samples, but concentrations were significantly lower in all of the venous samples compared with the arterial samples. The average arterial concentration of gastrin during this period was 278 ± 11 pg. per ml. while the average venous concentration was 208 ± 13 pg. per ml. ($P < 0·05$).

The subsequent introduction of acid into the antrum caused both arterial and venous levels to fall to almost basal levels and abolished the significant difference between arterial and venous levels.

It is concluded that the gastric fundus is an important site for the inactivation of elevated levels of circulating gastrin.

47. Serum-gastrin Levels following Pylorus-preserving Gastrectomy: T. Hennessy (W. G. Fegan), Department of Surgery, University College, Cork.

The technique of pylorus-preserving gastrectomy requires the retention of a 2-cm. cuff of antrum proximal to the pylorus. The effect of retaining this antral cuff was studied.

Ten patients with chronic duodenal ulcer had serum-gastrin levels estimated in the fasting state and after stimulation with a standard protein meal. Six weeks after pylorus-preserving gastrectomy the estimations were repeated.

The mean fasting level of gastrin fell from a preoperative figure of 35 ± 5·2 pg. to 16 ± 8 pg. after operation ($P = 0·005$).

The mean peak stimulated level was reduced from 118 ± 31·4 pg. to 21 ± 6·6 pg. after operation ($P = 0·0005$).

It was concluded that gastrin secretion from the retained antral cuff was unlikely to be a factor in precipitating recurrent ulceration after pylorus-preserving gastrectomy.

48. Operative Measurements of Cerebral Blood-flow (C.B.F.) and Internal Carotid Artery (I.C.A.) Pressure during Carotid Ligation: P. J. Leech, W. Fitch, J. Barker, and J. D. Miller, Medical Research Council Cerebral Circulation Research Group, Institute of Neurological Sciences, Glasgow.

Eighteen normotensive patients with intracranial aneurysms underwent temporary clamping of the internal and then the common carotid arteries while C.B.F. and I.C.A. pressure measurements were made to assess the probability of ischaemic complications following ligation.

C.B.F. reduction of more than 25 per cent may be associated with immediate or delayed hemiparesis (Jennett et al., 1966). Using this criterion in the past a low incidence of ischaemia has been achieved, but since the cost was the rejection of 39 per cent of patients for permanent ligation a review of the method was undertaken.

In this series a correlation between C.B.F. reduction and I.C.A. pressure reduction was observed ($P < 0·001$) but the scatter was too wide to predict C.B.F. reduction accurately from the I.C.A. pressure reduction.

Ligation was safe during temporary clamping when the C.B.F. exceeded 40 ml. per 100 g. per minute or when the I.C.A. pressure exceeded 60 mm. Hg, but was always unsafe with a C.B.F. of less than 20 ml. per 100 g. per minute. In the C.B.F. range 20–40 ml. per 100 g. per minute, using I.C.A. pressure with C.B.F. reduction, enabled a higher proportion of patients to be successfully ligated than was possible using C.B.F. alone. By utilizing this revised method 15 patients were ligated in this series and none suffered a permanent neurological deficit.

Jennett, W. B., Harper, A. M., and Gillespie, F. C. (1966), *Lancet*, **2**, 1162.

49. Human and Computer-aided Diagnosis of 'Dyspepsia': J. C. Horrocks and F. T. de Dombal, Department of Surgery, University of Leeds.

This paper reports an evaluation of and comparison between various modes of diagnosis and their ability to discriminate between diseases such as duodenal ulcer, gastric ulcer, cholecystitis, and gastric cancer. A prospective unselected series of 168 patients with upper abdominal pain was studied. For each patient we recorded the initial diagnosis in the out-patients department, the final preoperative diagnosis after full investigation, the computer's diagnostic prediction based solely upon the house-surgeon's *interview* (excluding findings on examination), and the final operative diagnosis.

Overall the initial (out-patient) diagnosis was 52·8 per cent accurate, the computer's diagnostic prediction was 86·8 per cent accurate, and the final preoperative diagnosis was substantiated at operation in about 91 per cent of cases. These results suggest that a computer-aided system may have something to offer the unaided clinician, that it offers no diagnostic advantage over radiography although it is much quicker and cheaper, and that the *history* is crucial in dyspepsia, and may form a basis for future studies in which the case history might be elicited by a 'physician's assistant'.

50. The Feasibility of Scaling up the Space for Implantable Prosthetic Lungs: J. L. Wosornu and D. G. Melrose, Hammersmith Hospital, London.

Previous experiments in rats showed that a reproducible technique could create an artificial gas cavity (a skin-lined hemithorax) which the rats could ventilate (Wosornu and Melrose, 1971). The validity of these conclusions has been tested in larger animals. The aim was to provide space inside the chest cavity which could safely house implantable prosthetic lungs.

Autogenous skin capsules were grafted into the pleural spaces of 6 pigs of mean weight 16·0 ± 1·6 kg. They all survived ($P < 0{\cdot}016$). Their mean weight was 32·4 ± 2·6 kg. 3 weeks after intrapleural skin-grafting. The skin capsule enlarged to occupy the left hemithorax, closely reproducing its contour.

The skin-lined hemithorax was opened to the exterior 5 weeks later to create an artificial gas cavity. Among the variables monitored were arterial pressure (M.A.P.), electrocardiogram, arterial *p*H, Po$_2$, and Pco$_2$, and ventilation. Paired data were obtained in 4 pigs, before (A) and 2 hours after (B) creation of the stoma in the chest wall.

	M.A.P. (mm. Hg)	Heart-rate (per min.)	Arterial		
			*p*H	Po$_2$	Pco$_2$
A	70 ± 4	150 ± 7	7·346 ± 0 009	78·2 ± 6·4	45·7 ± 1·8
B	73 ± 5	158 ± 5	7·316 ± 0 023	57·4 ± 2·8	45·3 ± 3·3
P(d.f. = 3)	0·39	0·05*	0·38†	0 014*	0·92†

* Significant.
† Not significant.

Ventilation in the normal hemithorax was 85 ± 10 ml. per kg. per minute compared with 40 ml. per kg. per minute in the skin-lined hemithorax ($P < 0{\cdot}001$).

It is thus feasible to scale up the space for implantable prosthetic lungs, and the conclusions drawn from the rat are valid for larger animals.

Wosornu, J. L., and Melrose, D. G. (1971), *Br. J. Surg.*, **58**, 865.

51. Amine Levels in the Cerebrospinal Fluid after Subarachnoid Haemorrhage: B. H. Cummins and D. Lothian (J. H. Peacock), Frenchay Hospital, Bristol, and Department of Surgery, Bristol Royal Infirmary.

Spasm of the cerebral arteries complicates about one-third of cases of subarachnoid haemorrhage. This paper reports the levels of noradrenaline, adrenaline, and 5-hydroxyindole acetic acid (5HIAA) found in the cerebrospinal fluid (C.S.F.) after subarachnoid haemorrhage using a modified spectrofluorimetric technique.

Information on normal levels of catechol amines in human C.S.F. is sparse. C.S.F. from 9 cases of minor neurological disorders was studied. The mean value of noradrenaline was 0·181 ± 0·075 μg. per litre and of adrenaline was 0·041 ± 0·044 μg. per litre, in agreement with Klensch and Gott (1970).

C.S.F. and plasma levels of 35 cases of subarachnoid haemorrhage were studied concurrently with carotid angiography. No spasm was present in 22 cases, and in these cases the catechol amines were within normal limits (noradrenaline 0·154 ± 0·069 μg. per litre, adrenaline 0·045 ± 0·070 μg. per litre). In 7 cases where spasm was present but localized to the aneurysm site the noradrenaline level was raised (0·341 ± 0·185 μg. per litre). Six cases showed intense spasm. In these cases the C.S.F. noradrenaline content was 0·764 ± 0·355 μg. per litre which is very significantly above normal values ($P < 0{\cdot}001$).

The C.S.F. level of noradrenaline was not dependent upon the plasma level. Neither the adrenaline nor the 5HIAA levels were significantly raised in these 35 cases.

It is considered that the presence of excess noradrenaline in the C.S.F. may contribute to cerebral arterial spasm.

Klensch, H., and Gott, U. (1970), *Klin. Wschr.*, **14**, 853.

52. Controlled Trial of Wound Spraying with Poly-antibiotic or Povidone Iodine Aerosols: O. J. A. Gilmore (R. B. Welbourn), Royal Berkshire Hospital, Reading.

Four hundred and fifty consecutive appendicectomies through grid-iron incisions done in a district general hospital were included in a controlled trial of wound spraying as a prophylactic measure against postoperative wound infection. The infection rate was reduced by about one-half ($P < 0{\cdot}02$).

Patients were allocated randomly to one of three groups: (1) no spray (control), (2) sprayed with a poly-antibiotic aerosol (Dispray containing neomycin sulphate, zinc bacitracin, and polymixin B sulphate), (3) sprayed with a povidone iodine aerosol (Disadine D.P. giving 5 per cent available iodine). The surgeon was informed of the spraying procedure after he had removed the appendix and closed the peritoneum. Bacteriological swabs were taken from the appendix and from the wound before spraying. The wounds were inspected on the sixth post-operative day and after 1 month by observers who were unaware of the spraying procedure used.

When there were organisms on the appendix wall, wound contamination occurred seven times more frequently than when there was none. Contaminated wounds which were not sprayed became infected ten times more frequently than non-contaminated wounds.

Spraying with either spray reduced infection in all age-groups and in enlarged, drained, contaminated, and non-contaminated wounds.

GROUP	TOTAL No.	INFECTED		SIGNIFICANCE
		No.	Per cent	
Control	151	24	16·0	—
Poly-antibiotic aerosol	150	14	9·3	$P < 0\ 06$
Povidone iodine aerosol	149	12	8·0	$P < 0\cdot 25$

53. **Abnormal Reactions to Suture Materials and Wound Infection:** M. G. LORD (H. B. Torrance), Manchester Royal Infirmary, Manchester.

Various authors have demonstrated abnormally severe reactions to various suture materials. This paper demonstrates that in patients with this abnormal reaction there is a statistically significant incidence of wound infection and dehiscence.

Two hundred patients undergoing clean elective abdominal surgery had each of three materials (thread, chromic catgut, and nylon) inserted into the skin of the lower abdominal wall. The erythema around the materials was measured with dividers in two diameters at right-angles on days 1–5 postoperatively. The abdominal wound was sutured with the same materials.

Two groups of patients emerged. One group had minimal reaction around the sutures. All 15 patients in this group had terminal carcinoma and died within 14 days of operation. Another group had severe reactions of over 16 mm.

Of the 200 patients, 21 had infected wounds and dehiscence; 16 of these had severe reactions to one of the trial sutures. Eleven patients had severe reactions in the non-infected wound group ($P < 0\cdot 001$).

The conclusions drawn from these observations are that in certain cases severe reaction to suture materials contributes to wound infection and dehiscence. This reaction may be a delayed-type hypersensitivity reaction, explaining why no antibodies to suture materials are found in animals sensitized to them.

54. **What is the Optimal Dose of Insulin for Use in the Hollander Test?:** S. DAVIES, P. J. LYNDON, and D. JOHNSTON, University Department of Surgery, General Infirmary, Leeds.

It is important to choose the correct dose of insulin because side-effects such as cardiac irregularities, epileptiform convulsions, and coma sometimes occur and may occasionally be fatal. Careful dose–response studies by Baron (1969) and Isenberg et al. (1969) suggested that the optimal dose of insulin was 0·2 U. per kg. However, in many subjects maximal peak 30-minute acid output (P.A.O.^{I}) is elicited by 0·1 U. per kg.

In this study each subject underwent two insulin tests on separate days. In one test the dose was always 0·2 U. per kg. In the other it was either 0·1 or 0·125 U. per kg. Tests were done in random order. Insulin was given by rapid intravenous injection. Subjects were normal volunteers, patients with duodenal ulcer, and patients more than 1 year after vagotomy. Blood-glucose levels were measured serially and any side-effects were noted.

The dose of 0·1 U. per kg. proved inferior to 0·2 U. per kg. because in 7 paired tests the P.A.O.^{I} was much less in 3 tests and equal in 4. However, the dose of 0·125 U. per kg. proved as effective as 0·2 U. per kg. in stimulating acid output and in lowering blood-glucose. In paired tests in 10 subjects with intact vagi the smaller dose of insulin elicited P.A.O.^{I} of $24\cdot 28 \pm 3\cdot 48$ mEq. per hour and the larger dose $24\cdot 85 \pm 2\cdot 84$ mEq. per hour ($P < 0\cdot 02$). In paired tests in 10 patients after vagotomy P.A.O.^{I} was $2\cdot 79 \pm 0\cdot 92$ mEq. per hour (0·125 U. per kg.) and $2\cdot 87 \pm 0\cdot 85$ mEq. per hour (0·2 U. per kg., $P < 0\cdot 02$). One subject was Hollander 'negative' with the smaller dose, but 'positive' with the larger dose.

These results suggest that a dose of insulin of 0·125 U. per kg. may be 'optimal'.

BARON, J. H. (1969), *Br. J. Surg.*, **56**, 383.
ISENBERG, J. I., STENING, G. F., WARD, S., and GROSSMAN, M. I. (1969), *Gastroenterology*, **57**, 395.

55. **Reproducibility of Pepsin Output and Plasma Gastrin Concentration after Insulin in Peptic Ulcer Patients:** D. I. WALKER, J. B. ELDER, P. C. GANGULI, and I. E. GILLESPIE, University Department of Surgery, Manchester Royal Infirmary.

Little is known of the reproducibility of gastric pepsin output or of the plasma-gastrin concentration response following insulin-induced hypoglycaemic cholinergic stimulation.

In 12 peptic ulcer patients gastric juice obtained by nasogastric tube after a 12-hour fast was collected for four 15-minute intervals before and at eight 15-minute periods after the injection of soluble insulin, 0·2 U. per kg., and assayed for peptic activity by the method of Piper (1960); samples of venous blood were withdrawn at similar time intervals for measurement of plasma-gastrin concentration by the radio-immunoassay method of Ganguli and Hunter (1972). A repeat test was performed on each subject within 1 month.

Significant correlations between tests 1 and 2 were obtained for the mean 15-minute basal pepsin outputs before insulin ($r = 0\cdot 86$, $P < 0\cdot 005$) and for pepsin outputs in the first and second hours after insulin ($r = 0\cdot 87$, $P < 0\cdot 005$ and $r = 0\cdot 74$, $P < 0\cdot 05$ respectively). The best correlation between paired samples for pepsin output was obtained at 75 minutes after insulin injection ($r = 0\cdot 89$, $P < 0\cdot 001$).

Paired plasma-gastrin concentrations showed significant correlations for the mean 15-minute basal samples ($r = 0\cdot 51$, $P < 0\cdot 025$), but following insulin injection no significant correlations were found for paired 15-minute values.

These results suggest that the gastric pepsin response to insulin hypoglycaemia is more consistent for successive tests than is the plasma-gastrin concentration response, and that insulin may not be an adequate stimulus for the production of endogenous gastrin secretion.

GANGULI, P. C., and HUNTER, W. M. (1972), *J. Physiol., Lond.*, **220**, 499.
PIPER, D. W. (1960), *Gastroenterology*, **38**, 616.

56. **The Evaluation of Gastric Pepsin Output to Insulin in Patients with Recurrent Ulcer:** J. B. ELDER, D. I. WALKER, and I. E. GILLESPIE, University Department of Surgery, Royal Infirmary, Manchester.

Venables (1970) suggested that gastric pepsin output may be used as a discriminant in patients with recurrent ulceration. This hypothesis has been re-examined in 35 preoperative duodenal ulcer (D.U.) patients, 20 patients with proven recurrent ulcers (R.U.), and 14 patients who were symptom-free (S.F.) at 6–12 months after truncal vagotomy and drainage, all the groups being matched for age and weight. Each patient had an insulin test (0·2 U. per kg. i.v.) with measurement of the acid output on samples collected at 15-minute intervals by titration to *p*H 7, and of total proteolytic activity at *p*H 2 (Piper, 1960).

Patients with recurrent ulcers produced significantly more pepsin in the basal hour secretion (115 ± 30 mg.) than the symptom-free group (51 ± 10 mg., $P < 0\cdot 05$).

In the preoperative D.U. group the mean peak 30-minute output after insulin (499 ± 58 mg.) was significantly greater than that observed in the R.U. group (226 ± 54 mg.) and than that in the S.F. group (121 ± 50 mg., $P < 0\ 0005$).

Analysis using the ratios of peptic activity in stimulated : basal secretion gave the following results: D.U., $20·3 \pm 2·9$; R.U., $13·3 \pm 2·8$; S.F., $8·9 \pm 2·6$.

The use of absolute values resulted in better discrimination between the groups than did the use of ratios, and significant differences in peptic activity between groups of patients were noted.

PIPER, D. W. (1960), *Gastroenterology*, **38**, 616.
VENABLES, C. W. (1970), *Br. J. Surg.*, **57**, 757.

57. Inhibition of Human Gastric Secretion by Orally or Intravenously Administered Prostaglandin 16, 16 Dimethyl-E_2 Methyl Ester: D. C. CARTER, S. M. M. KARIM, D. BHANA, and P. A. GANESAN (A. P. M. Forrest), Departments of Surgery and Pharmacology, Edinburgh, and Makerere University, Kampala, Uganda.

Inhibition of human acid secretion by orally administered prostaglandin analogues has been reported (Carter et al., 1973) but to date no effective inhibition of gastric secretion has been reported following bolus i.v. injection of prostaglandins.

The synthetic compound prostaglandin 16, 16 dimethyl-E_2 methyl ester was given orally in the dose range 25–200 μg. to 23 healthy male volunteers and by bolus i.v. injection in the dose range 3·125–50 μg. in 16 subjects. When compared with control tests in the same subjects a highly significant mean reduction in the basal acid output of 92 per cent ($P < 0·001$) followed the oral administration of 200 μg. of prostaglandin analogue and a mean reduction of 77 per cent followed the i.v. injection of 50 μg. ($P < 0·001$).

When 200 μg. of the analogue were given orally in association with pentagastrin (6 μg. per kg. i.m.) the mean M.A.O. in response to pentagastrin alone was reduced by 66 per cent in 7 subjects ($P < 0·01$). Similarly, i.v. injection of 25 or 50 μg. of the analogue in 12 subjects brought about a mean reduction of 54 and 83 per cent ($P < 0·001$) respectively in the mean M.A.O. to pentagastrin alone.

It is concluded that this compound is a potent inhibitor of basal and pentagastrin-induced acid secretion when given orally or intravenously to male volunteers.

CARTER, D. C., KARIM, S. M. M., BHANA, D., and GANESAN, P. A. (1973), *Br. J. Surg.*, **60**, 828.

58. The Failure of Intra-arterial Vasopressin to break the Canine Gastric Mucosal Barrier: N. J. DORRICOTT and W. SILEN (G. Slaney), Departments of Surgery, Beth Israel Hospital, Boston, U.S.A., and Queen Elizabeth Hospital, Birmingham.

Ischaemia can break the gastric mucosal barrier to H^+ ions and may contribute to gastric ulceration (Skillman et al., 1970). Selective intra-arterial infusion of vasopressin is used in the treatment of gastro-intestinal haemorrhage (Nusbaum et al., 1969). Experiments to investigate the effect of intra-arterial vasopressin on the gastric mucosal barrier of the standing awake dog have been carried out.

The arteries of Heidenhain pouches in 5 antrectomized dogs were selectively catheterized in 9 experiments. Net 30-minute fluxes of H^+ and Na^+ were measured when the pouches were perfused with 100 m*M* HCl before, during, and after vasopressin was infused via the arterial catheter at 12 U. per hour for 3 hours. Gastric mucosal blood-flow was measured by aminopyrine clearances.

Vasopressin infusion decreased secretion of H^+ and Na^+ from control values of 24 ± 22 and 117 ± 17 Eq. per 30 minutes respectively to produce back-diffusion of H^+ to -28 ± 20 Eq. per 30 minutes associated with a secretion of Na^+ of 52 Eq. per 30 minutes after 3 hours. However, net fluxes of H^+ were not significantly different from control values or associated with an increase in Na^+ secretion to indicate breaking of the gastric mucosal barrier. Ischaemia of the gastric mucosa during vasopressin infusion was confirmed by a fall in the mucosal blood-flow from a mean control of $1·6 \pm 0·92$ ml. per minute to $0·25 \pm 0·12$ ml. per minute.

It is concluded that intra-arterial vasopressin at 12 U. per hour does not break the canine gastric mucosal barrier after 3 hours.

NUSBAUM, M., BAUM, S., and BLAKEMORE, W. S. (1969), *Ann. Surg.*, **170**, 506.
SKILLMAN, J. J., GOULD, S. A., CHUNG, R. S. K., and SILEN, W. (1970), *Ann. Surg.*, **172**, 564.

59. Increased Faecal Excretion of Bile-acids in Post-vagotomy Diarrhoea: V. P. GERSKOWITCH, J. G. ALLAN, and R. I. RUSSELL (L. H. Blumgart), Departments of Gastroenterology and Surgery, Royal Infirmary, Glasgow.

The pathogenesis of severe post-vagotomy diarrhoea is uncertain. Excessive amounts of dihydroxy bile-acids in the colon stimulate water and electrolyte secretion and cause diarrhoea (Mekhjian et al., 1971).

The role of bile-acids in post-vagotomy diarrhoea has been evaluated by measuring their faecal excretion in patients with severe symptoms, in patients after vagotomy and drainage operations but with no diarrhoea, and in normal control subjects.

Seven subjects with post-vagotomy diarrhoea were studied; all had undergone operation 1–8 years prior to the study and had continuous watery diarrhoea. Three patients had increased daily faecal fat excretion but all had normal jejunal mucosal histology.

The mean total faecal bile-acid excretion measured over 5 days in patients with post-vagotomy diarrhoea by gas–liquid chromatography was 2538 ± 632 mg. per day (range, 1044–5222 mg.). These results are significantly higher than those in the normal control subjects (mean, 671 ± 128 mg. per day; range, 311–1059 mg.; $P < 0·02$). Individual bile-acids in the post-vagotomy diarrhoea group and the normal control subjects were as follows: cholic acid, 232 and 26 mg.; deoxycholic acid, 1290 and 377 mg.; chenodeoxycholic acid, 438 and 83 mg.; lithocholic acid, 705 and 185 mg. respectively. Statistically significant increases were found in the excretion of deoxycholic ($P < 0·05$) and chenodeoxycholic acid ($P < 0·001$).

Excessive amounts of bile-acids in the colon (notably dihydroxy acids) may be a factor in the pathogenesis of post-vagotomy diarrhoea.

MEKHJIAN, H. S., PHILIPS, S. F., and HOFMANN, A. (1971), *J. clin. Invest.*, **50**, 1569.

60. The Duodenal Brake—Hormonal or Vagal?: M. SHAHIDULLAH, T. L. KENNEDY, and T. G. PARKS, Royal Victoria Hospital and The Queen's University, Belfast.

The loading effect of acid, sugar, and fat on the rate of gastric emptying in man has been reviewed by Hunt and Knox (1966).

To investigate the mechanisms involved, dogs were prepared with gastric and duodenal fistulae. Gastric emptying was measured by the dye-dilution method of George (1968). HCl, dextrose, and fat left the stomach significantly slower than water ($P < 0·001$).

Another dog model was prepared by dividing the duodenum immediately beyond the intact pylorus, which was implanted 50 cm. below the duodenal stump. A 600-ml. water meal left the stomach in 52 minutes. When water, acid, dextrose, or fat was placed in the stomach each meal emptied at the same rate. However, when acid, dextrose, or fat was added to the duodenal loop, emptying of water from the stomach was 75, 133, and 181 minutes respectively ($P < 0·001$). Following truncal or extragastric selective vagotomy the braking mechanism remained intact.

When 500 ml. of blood taken from a dog 30 minutes after the introduction of fat into the duodenum were transfused into a fasting animal a twofold increase in the emptying time of a water meal resulted ($P < 0·001$). The braking mechanism may be hormonally rather than vagally mediated.

GEORGE, D. (1968), *Gut*, **9**, 237.
HUNT, J. N., and KNOX, M. T. (1966), *Handbook of Physiology*, section 6, vol. IV, p. 1917. Baltimore: Waverley Press.

61. The Effects of varying the Extent of Vagotomy on the Canine Gastric and Duodenal Myoelectrical Activity: C. J. STODDARD, B. H. BROWN, and H. L. DUTHIE, University Surgical Unit, Sheffield Royal Infirmary, and Sheffield Regional Medical Physics Department.

Transthoracic vagotomy in dogs is followed by a temporary disorganization of the gastric myoelectrical activity (Kelly and Code, 1969) and in humans this disorganization is related to the extent of the vagal denervation (Stoddard et al., 1973). The aim of this study was to assess the changes in the canine gastric and duodenal myoelectrical activity after graded abdominal vagal denervation.

Six Ag–AgCl electrodes were attached to the serosa of the stomach and duodenum in 4 dogs and exteriorized via a metal cannula. Recordings of 5 hours' duration were made after an 18-hour fast and, on separate occasions, the characteristics of the electrical activity were observed following a meat meal. All the dogs had a pyloroplasty performed prior to vagotomy. One dog received a truncal vagotomy (T.V.) alone and the other 3 had a highly selective vagotomy (H.S.V.) which was converted to a T.V. 6 weeks later.

Pyloroplasty had no effect on the myoelectrical activity. T.V. alone produced a permanent disorganization of the gastric pace-setter potential (P.S.P.). Following H.S.V. there was a temporary decrease in frequency of the gastric P.S.P. and a persistent diminution of its amplitude but no disorganized activity. The succeeding T.V. only produced transient disorganization of the P.S.P. Following T.V. and H.S.V. the normal myoelectrical responses to feeding were impaired. Changes in the canine gastric myoelectrical activity are thus dependent on the extent of the vagotomy.

KELLY, M. A., and CODE, C. F. (1969), *Gastroenterology*, **57**, 51.
STODDARD, C. J., WATERFALL, W. E., BROWN, B. H., and DUTHIE, H. L. (1973), in the press.

62. Effect of Vagotomy on Co-ordination of the Interdigestive Myoelectrical Complex of the Antrum and Duodenum: I. H. KHAN and B. S. BEDI, University Department of Surgery, Western Infirmary, Glasgow.

The electrical activity can be used as an index of motility of the gastro-intestinal tract (Daniel and Chapman, 1963). This activity has a regular pattern in the small intestine and is controlled by the extrinsic nerves (Carlson et al., 1972). The purpose of the present study was to investigate the effect of vagotomy on the pattern and the co-ordination of electrical activity of the stomach and duodenum.

Three mongrel dogs were prepared with chronically implanted Ag–AgCl electrodes on the serosal surface of the stomach and duodenum. The electrical activity was detected in healthy, fasted, and conscious dogs.

Prolonged recordings of the myoelectrical activity showed periods when no action potentials (phase I) were present and this was followed by periods (phases II, III, and IV) with varying numbers and amplitudes of action potentials. Each cycle (phases I–IV), lasting for 105 minutes, started in the stomach and propagated into the duodenum. Each phase of the cycle in the stomach and duodenum was well co-ordinated across the gastroduodenal junction. Pyloroplasty had no effect on this co-ordination. Total vagotomy with previous pyloroplasty caused disruption of the phases and loss of co-ordination between the complexes of the stomach and duodenum.

These experiments show that the vagus nerves control the co-ordination of the interdigestive myoelectrical complex across the gastroduodenal junction.

CARLSON, G. M., BEDI, B. S., and CODE, C. F. (1972), *Am. J. Physiol.*, **222**, 1027.
DANIEL, E. E., and CHAPMAN, K. M. (1963), *Am. J. digest. Dis.*, **8**, 54.

63. Objective Assessment of Electrical Treatment of Stress Incontinence: C. D. COLLINS (J. H. Peacock), Department of Surgery, Bristol Royal Infirmary.

Urethral pressure profiles were measured in 18 normal subjects and 32 stress-incontinent patients under three conditions: at rest, during voluntary contraction of the pelvic floor muscles, and during the Valsalva manœuvre. Comparison of urethral length and maximal pressure-profile measurements revealed a significantly ($P < 0·05$) shorter length and lower pressure under each of the three test conditions in the stress-incontinent group. This indicated that urethral pressure-profile measurements might show a change in patients treated successfully by electrical stimulation.

Fifteen stress-incontinent female patients had been treated with intermittent electrical stimulation and physiotherapy (Collins, 1972) over 1 year previously, of whom 8 were symptomatically cured and 5 were improved. In the cured group only the urethral length measurement during the Valsalva manœuvre showed a significant increase ($P < 0·05$) over pre-treatment levels.

These results suggest that successful treatment acts by improving pelvic floor muscle function. This reduces the degree of shortening of the urethra which occurs in the stress-incontinent patient when intra-abdominal pressure is increased.

COLLINS, C. D. (1972), *Proc. R. Soc. Med.*, **65**, 832.

64. Non-invasive Measurement of the Slope of the Arterial Pressure Curve in the Lower Extremities of Patients with Arterial Occlusion: K. W. JOHNSTON and V. V. KAKKAR, Departments of Surgery, University of Toronto, Canada, and King's College Hospital Medical School, London.

There is no ideal non-invasive method to assess patients with peripheral arterial occlusion. This paper describes a non-invasive technique from which the systolic pressure slope (S.P.S.) in the leg can be calculated and it may be applied to the assessment of arterial occlusion.

The R wave of an E.C.G. was used to signal the onset of a cardiac cycle, and the arrival of a pulse wave was recorded in the foot by an electrical impedance plethysmograph. A blood-pressure cuff at the ankle was inflated and as the pressure in the cuff increased above diastolic pressure the onset of the pulse wave was delayed in reference to the onset of the cardiac cycle (R wave). From the cuff pressure change and the recorded delay of arrival of the pressure wave the S.P.S. was calculated.

The S.P.S. was measured in 41 limbs of 30 patients and the extent of their arterial disease was classified by arteriography and clinical examination. The results were as follows: normal subjects (11 limbs), 645 ± 128 mm. Hg per second; patients with stenosis but no symptoms (8 limbs), 428 ± 123 mm. Hg per second; patients with occlusion (22 limbs), 133 ± 89 mm. Hg per second.

Non-invasive measurement of the S.P.S. distinguishes between normal limbs, those with symptomatic stenosis, and those with arterial occlusion ($P > 0\cdot001$), and is of potential value in the haemodynamic assessment of patients with peripheral vascular disease.

65. The Relationship between Doppler Ultrasound Assessment and Angiography in Occlusive Arterial Disease of the Lower Limbs:

P. L. Harris, L. A. Taylor, F. D. Cave, P. C. Williams, G. P. Naylor, and D. Charlesworth, Departments of Surgery and Physics, University Hospital of South Manchester.

Audiofrequency analysis of Doppler-shifted ultrasound was used to determine the pulse-wave velocity (P.W.V.), the pulsatility index (P.I.), and the damping factor (D.F.) in 45 patients and 30 asymptomatic volunteers. All the patients had an aortogram prior to reconstructive arterial surgery. Each arterial segment was graded according to the severity of the disease as seen on the arteriogram. The common femoral P.I. was related to angiographic grading in the aorto-iliac segment; there were significant differences between all the grades ($P < 0\cdot001$). In the femoropopliteal segment there was a significant difference in the popliteal P.I. between each grade ($P < 0\cdot001$). The tibial P.I. was not closely related to angiographic appearance but the difference between patients and normal volunteers was highly significant ($P < 0\cdot001$).

The D.F. in occluded femoropopliteal segments was significantly higher than in normal subjects ($P < 0\cdot001$) but in the popliteal to pedal segment the D.F. was not related to angiographic appearance. P.W.V. was not closely related to angiographic grading at any site.

The P.I. may be related to angiographic appearances and where there are differences they may reflect the limitations of aortography.

66. Lysozymuria following Aortic Surgery:

S. J. A. Powis, G. Slaney, and J. D. Blainey, Department of Surgery, Queen Elizabeth Hospital, Birmingham.

Lysozyme is a low molecular weight protein (M.W., 15,000) derived predominantly from leucocytes. It normally passes into the glomerular filtrate and undergoes almost complete reabsorption in the proximal tubules. Acute tubular necrosis which occasionally complicates major surgery is associated with lysozymuria. The frequency of renal tubular damage as judged by urinary lysozyme estimations in patients undergoing aortic surgery was investigated.

Twenty-one patients were studied for the first 10 days postoperatively. Twelve patients were operated on electively for abdominal aortic aneurysms or severe obliterative aorto-iliac disease. Nine patients had emergency operations for leaking abdominal aortic aneurysms.

Of the 12 patients having elective operations, 9 showed elevation of the urinary lysozyme level. This was short-lived (mean, 2·5 days) and only 4 patients had levels above 5 μg. per ml. (normal < 1·2 μg. per ml.). There was no clinical evidence of significant renal failure in any patient.

All of the patients having emergency operations had elevated urinary lysozyme levels, the duration being longer than in the elective group (mean, 4·5 days), and 6 of the 9 patients had levels in excess of 5 μg. per ml. All 9 patients had elevated blood-urea levels, and urine volume was abnormal in 3 patients.

Some degree of renal tubular damage which is related to the severity of the operation commonly follows major aortic surgery. However, this is not always clinically manifested.

67. Significance of Raised Plasma Fibrinogen in 95 Patients with Intermittent Claudication:

J. A. Dormandy, T. L. Dormandy, and D. Arrowsmith, Department of Surgery, Royal Free Hospital, and Department of Chemical Pathology, Whittington Group, London.

Ninety-five patients with intermittent claudication have been studied for up to 3 years (65 for over 1 year). In addition to full clinical assessment the calf blood-flow has been measured before and after a standard exercise at 2-monthly intervals. Whole-blood viscosity, plasma fibrinogen, and all lipid parameters were determined on blood taken simultaneously.

The commonest biochemical abnormality was a raised plasma fibrinogen; 57 (60 per cent) of the patients had a fibrinogen above 400 mg. per cent (2 standard deviations above the normal mean). The mean plasma fibrinogen of the patients was 428 ± 122 mg. per cent.

The initial fibrinogen level of individual patients correlated well with the severity and progress of the disease, as assessed by claudication distance ($R = 0\cdot44$, $P < 0\cdot01$). The mechanism of this effect may be related to changes in blood viscosity as there was also a positive correlation between plasma fibrinogen and whole-blood viscosity measured at 230 sec.$^{-1}$ ($r = 0\cdot39$, $P < 0\cdot005$).

These results suggest that the most important biochemical abnormality in intermittent claudication may be a raised plasma fibrinogen and that this may be related to the state and progress of the disease by its influence on blood viscosity.

68. The Evaluation of an Intravenous Fat-tolerance Test in assessing Fat Turnover in Surgical Patients:

J. G. W. Feggetter, H. A. Davidson, D. Appleton, and I. D. A. Johnston, Department of Surgery, University of Newcastle upon Tyne.

An intravenous fat-tolerance test has been used to measure the removal rate of fat in patients with hypertriglyceridaemia (Boberg et al., 1969). A study was planned to investigate fat turnover in patients before and after surgery.

Thirty-five patients admitted for elective surgery were studied. A bolus injection of a commercial fat emulsion (Intralipid 20 per cent) was administered intravenously in a dose of 150 mg. per kg. body-weight. Serial blood samples were taken and the serum-clearance rate was measured nephelometrically (Lewis et al., 1972). Elimination is by first-order kinetics (a constant fraction of plasma triglyceride is removed per unit time) so that a semi-logarithmic plot gives a straight line from which the slope K_2 may be calculated. The value K_2 per cent per minute represents the patient's rate of removal of fat (triglyceride) which may be related to utilization.

The mean K_2 value in preoperative patients was found to be 4·23 per cent per minute (range, 1·60–6·86 per cent per minute). The hyperbolic relationship between the K_2 value and the fasting triglyceride previously noted (Boberg et al., 1969) was confirmed and found to be significant at the 5 per cent level. Forty-eight hours after surgery the serum triglyceride had fallen by a mean 59·8 mg. per 100 ml. ($P < 0\cdot05$) and the mean K_2 value had increased by 2·51 per cent per minute ($P < 0\cdot001$).

The increased clearance of fat emulsion may be due to utilization which is increased for several days after surgery. This test may thus be a measure of the metabolic response to surgery.

Boberg, J., Carlson, L. A., and Hallberg, D. (1969), *J. atheroscler. Res.*, **9**, 159.

Lewis, B., Boberg, J., Mancini, M., and Carlson, L. A. (1972), *Atherosclerosis*, **15**, 83.

69. Studies of the Precision and Accuracy of Gastric Secretory Tests for the Determination of Acid Reduction following Vagotomy: W. LORENZ, H. TROIDL, H. ROHDE, G. ACKER, and W. SEIDEL, Division of Experimental Surgery and Pathological Chemistry, University Surgery Clinic, Marburg/Lahn, Germany.

After vagotomy a medium reduction of the maximum acid output (M.A.O.) of about 50–70 per cent was observed, but in a few cases, some with insulin-negative responses, there was almost no reduction. Since these exceptions could be caused by technical errors or biological variations, studies on the precision and accuracy of gastric secretory tests in non-operated duodenal ulcer patients were carried out as follows:—

1. *Quality control for the titration*: Using mixed gastric juice from 50 patients 10-ml. portions were frozen at −20° C. and the acid was determined daily over 6 months. Average and range control charts were constructed according to Gooszen (1960).

2. *Duplicate gastric tests in 80 patients*: The M.A.O. in response to 6 μg. pentagastrin per kg. i.m. was recorded according to Baron (1970).

3. *Dose–response curves with pentagastrin*: In 40 of the patients studied under (2) the response to 6, 12, and 15 μg. pentagastrin per kg. was recorded.

Within a single day the coefficient of variation for the titration was only 1·2 per cent ($n = 10$) and within 6 months it was 0·8 per cent ($n = 112$), indicating a high precision of the test. Also the reproducibility of the pentagastrin test (6 μg. per kg.) was excellent for the whole group (test 1: 251 ± 98 ml. per hour and 29·2 ± 14·1 mEq. per hour; test 2: 243 ± 100 ml. per hour and 29·5 ± 16·7 mEq. per hour) but not for single patients, since 15 per cent of the subjects showed differences of more than 40 per cent (maximum 84 per cent). Furthermore, the accuracy of M.A.O. was not guaranteed, because 38 per cent of the patients secreted 18–33 per cent more acid following 12 μg. pentagastrin per kg. than after 6 μg. per kg.

BARON, J. H. (1970), *Scand. J. Gastroent.*, suppl., **6**, 9.
GOOSZEN, J. A. H. (1960), *Clin. chim. Acta*, **5**, 431.

70. The Role of a High-residue Diet in the Treatment of Diverticular Disease of the Colon: T. G. PARKS, Department of Surgery, The Queen's University, Belfast.

Gastro-intestinal transit rates were measured in 24 patients with diverticular disease of the colon while on a low-residue diet containing less than 3 g. daily of indigestible fibre. Subsequently the transit rates were reassessed in the same patients when stabilized on a high-residue diet incorporating a bran supplement. The fibre content of this régime was 12 g. daily. The technique described by Hinton et al. (1969) of using radio-opaque polythene pellets for assessing intestinal transit rate was modified in the present study, and for comparison simultaneous measurements were made using ^{51}Cr-labelled sodium chromate.

The time interval from ingestion to recovery of the first markers, and of 20, 50, and 80 per cent of the markers was assessed. The mean transit time while on the low-residue diet was 43·6 hours compared with 37·2 while on the high-residue régime ($P < 0·01$). The mean wet weight of faecal residue was 96 g. daily on a low-residue diet compared with 176 g. on a high-residue diet ($P < 0·001$). The corresponding mean daily dry weights were 19·6 and 34·2 g. respectively.

It is concluded that a diet incorporating a high-fibre content leads to a significant increase in the transit rate as well as in the bulk of the faeces.

HINTON, J. M., LENNARD-JONES, J. E., and YOUNG, A. C. (1969), *Gut*, **10**, 842.

71. Human and Computer-aided Diagnosis of Lower Gastro-intestinal Disorders in 468 Patients: F. T. DE DOMBAL, D. J. LEAPER, J. C. HORROCKS, J. R. STANILAND, S. E. CLAMP, and A. P. MCCANN, University Department of Surgery and the Centre for Computer Studies, University of Leeds.

This paper reports a comparison between various diagnostic modes in respect of lower gastro-intestinal disorders, such as large-bowel cancer, diverticular disease, Crohn's disease, and ulcerative colitis. In a retrospective series of 300 patients the computer's overall accuracy was 79·7 per cent, and subsequently a prospective unselected consecutive series of 168 patients was studied. For each patient we recorded the initial clinical diagnosis, the final preoperative diagnosis after full investigation, the computer's diagnostic prediction based largely upon the house-surgeon's case notes, and the final histopathological diagnosis.

Overall, in 168 patients the computer's diagnostic prediction proved accurate in 89·5 per cent. This compares with an initial clinical diagnostic accuracy of 69·5 per cent and a final accuracy after full investigation of 87·6 per cent. Most of the computer's errors were in misclassifying Crohn's disease and ulcerative colitis, and in predicting cancer the computer was 95·7 per cent accurate.

These results suggest that using a simple diagnostic-aided system inexperienced surgeons may approach the diagnostic effectiveness of their more experienced colleagues.

SHORT NOTES OF RARE OR OBSCURE CASES

PRIMARY RETROPERITONEAL HYDATID CYST

BY S. MUKERJEE, M. NIGAM, AND J. C. SARAF
WILLINGDON HOSPITAL, NEW DELHI, INDIA

SUMMARY

A case of a primary retroperitoneal hydatid cyst in an Indian adult which was treated by marsupialization is described. Attention is drawn to the rarity of the lesion, the probable mode of spread, and the difficulties encountered in its diagnosis.

THE word *Echinococcus* is of Greek origin and means hedgehog berries because the multiple cysts resembling berries and hooklets seen on laboratory examination present a bristling appearance. The word 'hydatid' is also of Greek origin and means a drop of water. It was first applied by Rudolphi in 1810.

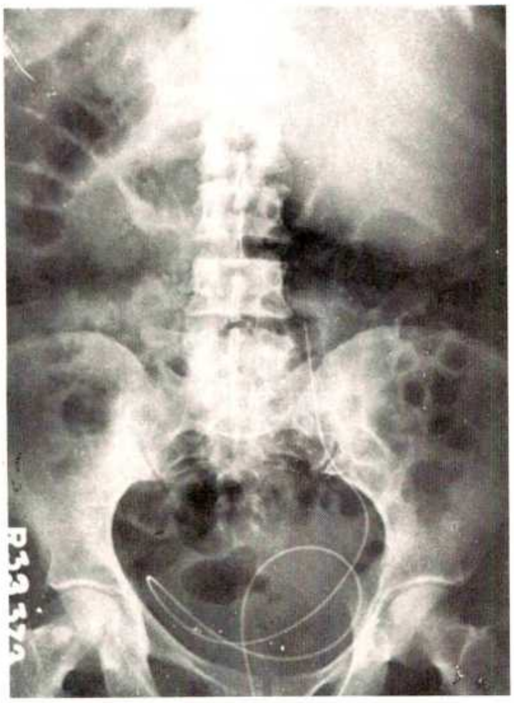

FIG. 1.—Plain radiograph of the abdomen showing a circumscribed soft-tissue shadow in the left hypochondrium and loin.

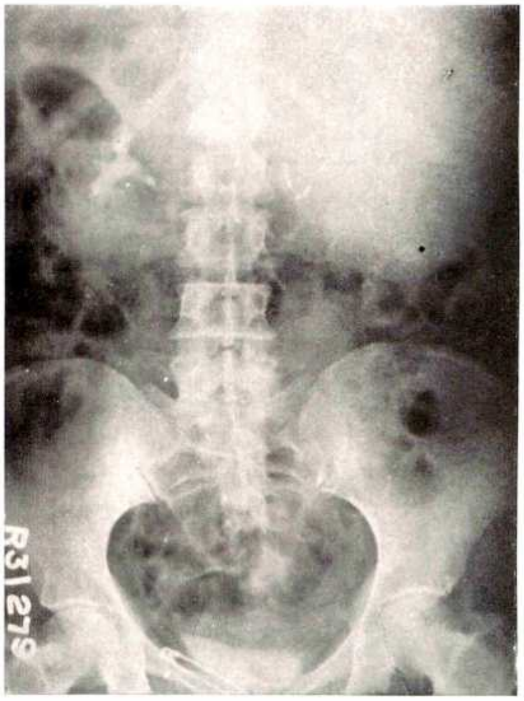

FIG. 2.—Intravenous pyelogram showing a non-functioning left kidney.

Redi in 1664 first suspected the animal origin of hydatid cysts. The course of these cysts was not known until 1782, when Goeze and later Batsch (1786) recognized under the microscope the small taenias armed with a crown of hooklets in the granulated cyst fluid. They proposed the name of *Echinococcus granulosus*. In 1821 Bremser from Vienna first reported a case of hydatid disease in a human patient who was operated upon by Kern. In 1853 Von Siebold proved that *Taenia echinococcus* was the producer of this disease. The life history of the parasite was first described by Naunyn in 1863. At the end of the past century and at the beginning of the present one Deve made a complete study of hydatidoses.

Echinococcus granulosus lives attached to the villi of the small intestine of the dog and other definitive hosts, such as wolves and foxes. When an ovum is swallowed by an intermediate host such as a pig, sheep, cow, or human the protective membrane is dissolved and the embryo penetrates the mucosa of the duodenum and the first part of the jejunum and enters the venous channels of the portal system, thus reaching the liver. Some, however, may pass through the liver and enter the inferior vena cava, thereby gaining access to other organs and tissues. The ova then forms a hydatid cyst of the liver or other viscera. Some investigators believe that the embryo may gain access to the lymphatics of the intestine, thus explaining the occurrence of hydatid cysts at sites other than the liver (Jidejian, 1957).

According to Barret and Thomas (1952) 55–60 per cent of the cysts are formed in the liver, 30 per cent in the lungs, and 2·5 per cent in the kidneys. Of the cysts at other sites, 2·5 per cent are primary cardiac cysts, 2 per cent occur in bones, 1 per cent in muscles, 0·5 per cent in the brain, and 1·5 per cent in other organs such as the spleen. Several cases of cysts of the pancreas (Anderson and Peebles, 1959) have been reported. Cysts of the omentum (Maccagno, 1955), ovary, parametrium, and pelvis (Morris, 1952), thyroid and orbit (Dew, 1928), mediastinum (Rakower and Milwidsky, 1960), and different muscles have also been observed.

Primary retroperitoneal hydatid cysts, however, are very rare while peritoneal and secondary

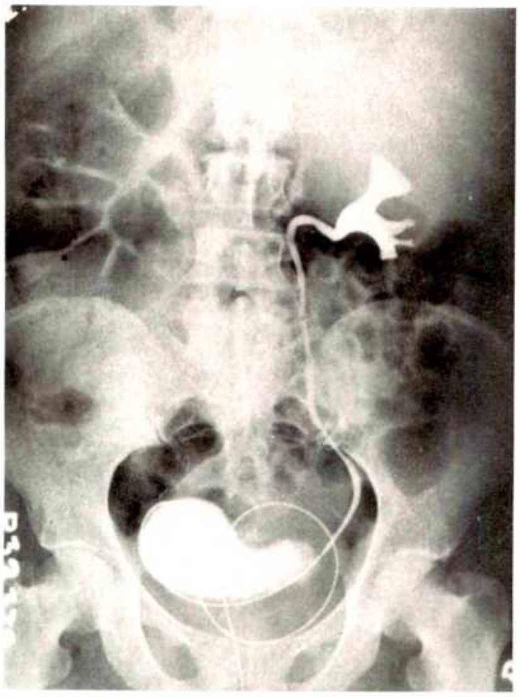

FIG. 3.—Retrograde pyelogram of the left side showing the left kidney to be pushed downwards by a mass.

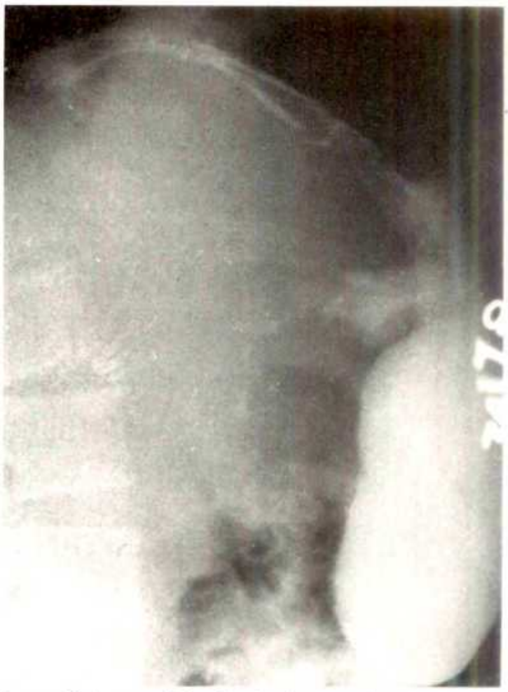

FIG. 4.—Barium-meal film showing the stomach to be displaced anteriorly by a mass.

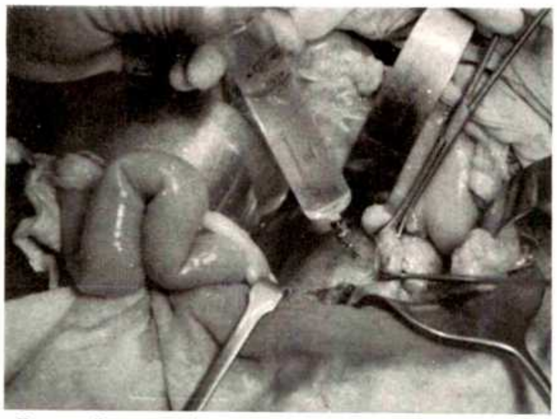

FIG. 5.—Cyst exposed at operation. Clear fluid is aspirated in the syringe.

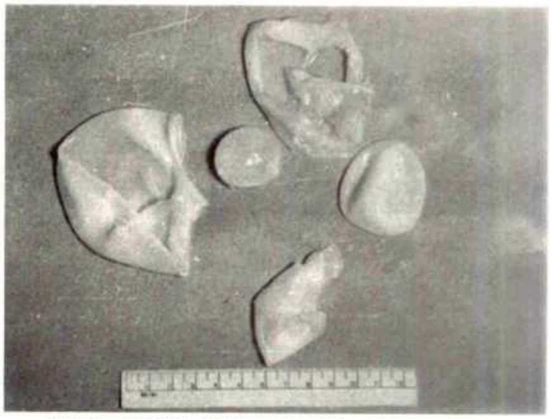

FIG. 6.—Daughter cysts evacuated from the hydatid cyst.

retroperitoneal cysts are not uncommon. Only 8 cases of primary retroperitoneal hydatid cyst have been recorded in the literature. A case of primary retroperitoneal hydatid cyst in an Indian adult is described here. Attention is drawn to the difficulty in diagnosis and management of such a lesion.

CASE REPORT

B. B., a 45-year-old woman, was admitted on 4 Aug., 1971, to Willingdon Hospital, Delhi, with a 3-month history of a lump in her abdomen. This had gradually increased in size. There was no pain, vomiting, diarrhoea, urinary complaint, fever, or loss of weight.

On examination the patient was a middle-aged female of average build. There was no anaemia, cyanosis, jaundice, oedema, or lymphadenopathy. On abdominal examination a swelling, measuring 15 × 15 cm., was felt in the left hypochondrium. The lower margin was well defined, while the upper limit could also be felt although not distinctly. The swelling did not move with respiration. It was a firm ballotable mass which was dull to percussion. The liver and spleen were not felt. There was no free fluid in the abdomen. The respiratory, cardiovascular, and central nervous systems were normal on examination.

On investigation the haemoglobin was 12 g. per cent, and the total leucocyte count was 8000 per c.mm., with polymorphs 58 per cent, lymphocytes 30 per cent, eosinophils 10 per cent, and monocytes 2 per cent. The blood-urea was 40 mg. per cent and the blood-sugar 76 mg. per cent. Albumin and sugar were absent on routine urine examination. However, on microscopic examination 10–12 pus cells and red-blood cells per c.mm were seen. Urine culture was sterile. A plain radiograph of the abdomen showed a circumscribed soft-tissue shadow in the left hypochondrium and left loin (*Fig.* 1). An intravenous pyelogram showed a non-functioning left kidney (*Fig.* 2). On a retrograde pyelogram the left-kidney pelvis was seen to be of normal calibre but the left ureter was kinked and the kidney appeared to be pushed downwards (*Fig.* 3). Barium-meal examination showed the stomach to be displaced anteriorly and to the right side (*Fig.* 4). From this it was concluded that the swelling was most probably a hydatid cyst of the spleen. Casoni's test could not be done because there was no free hydatid fluid available. A chest radiograph was normal.

An exploratory laparotomy was done via a right paramedian incision. The stomach was displaced anteriorly. The gastrocolic omentum was opened and a large cyst was found occupying the lesser sac (*Fig.* 5). The stomach and the pancreas were adherent to the anterior surface of the cyst. Clear fluid was aspirated with a syringe. Ten per cent formalin was injected into the cyst. Posteriorly the cyst was adherent to the aorta and the inferior vena cava. The splenic vessels were also adherent to it. Excision of the cyst *en masse* was not feasible in view of the dense adhesions of the cyst to major blood-vessels. The cyst was opened and fluid was aspirated. Daughter cysts were evacuated and the laminated membrane was removed (*Fig.* 6). A large Malecot catheter was left in the cyst and brought outside the skin via a separate stab incision in the left loin. The liver lobes were normal. The postoperative course was uneventful and the catheter was removed 3 weeks after operation. The patient regularly attends the follow-up clinic. She still has a sinus discharging a little fluid. A sinogram done 3 months postoperatively showed a small residual cavity. In July, 1972, when last examined the patient had no other cystic swellings.

DISCUSSION

Lockhart and Sapinza (1958), on the basis of 2 cases of hydatid cysts of the lumbar fossa and after careful study of the clinical, radiological, and operative findings, confirmed the existence of an anatomico-clinical entity of retroperitoneal hydatid cyst. Razdan, Grewal, and Rai (1963) described a case of hydatid cyst in the retroperitoneal tissues presenting clinically as an iliac abscess. Ghooi and Sikdar (1963) encountered a case of hydatid cyst arising from the sheath of the psoas major muscle and which was intimately adherent to the uterus, bladder, common iliac vessels, inferior vena cava, and lower part of the ureter. The patient succumbed to anaphylactic shock during closure of the wound. In another case of retroperitoneal hydatid cyst, described by Mathur, Bhatt, Garg, and Sharma (1969), a biopsy was taken at the first operation in the mistaken diagnosis of renal neoplasm. This patient also died of anaphylactic shock during the second operation aimed at removal of the retroperitoneal hydatid cyst.

An echinococcal cyst of the retroperitoneal cellular tissue infiltrating the inguinal and femoral areas was described by Thackuk (1967). Similar lesions of the retroperitoneal space have been described by Assonad (1964), Bernard (1965), Brardino (1969), and Uraberski (1969).

The probable mode of spread of the hydatid embryo to the retroperitoneal space is either via the lymphatics from the gastro-intestinal tract or via the portal system of the liver.

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VILLOUS PAPILLOMA OF THE RECTUM (WITH UNUSUAL COMPLICATIONS)

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SUMMARY

A case is reported in which a villous papilloma of the rectum was complicated by severe electrolyte losses and acute renal failure. Successful management by peritoneal dialysis and early surgery is described.

THE occasional complication of severe fluid and electrolyte loss from villous papillomas of the rectum is now well recognized (Hoffman, 1959; Davies, Seavey, and Sessions, 1962; Lee and Keoun, 1970). Rarely intrinsic reversible renal failure is an added complication (Kille, Blainey, Dawson-Edwards, Elkington, and Hulme, 1967).

A further such case is reported here, illustrating unusual clinical and biochemical features. The successful management by peritoneal dialysis and early resection of the tumour is described.

CASE REPORT

A 51-year-old housewife was admitted as an emergency following a 3-day history of vomiting, muscle cramps, and general malaise. On the night prior to admission her husband had helped her to the toilet no less than 20 times to pass watery mucoid fluid per rectum.

On direct questioning she had noticed recent thirst and weight-loss but initially denied any alteration in bowel habit. Later, on persistent questioning she admitted to passing two loose bowel actions a day for about 12 months previously and the occasional passage of 'water' preceding her bowel action. (She had not previously sought medical advice.)

On admission she was extremely ill and severely dehydrated with sunken facies, cold cyanosed peripheries, and clammy skin with loss of skin turgor. Her pulse was 100 per minute and thready, and her blood-pressure was 'difficult to record'. Fasciculation of the calf muscles was observed. Rectal examination revealed a rubbery frond-like tumour at 7 cm.

Immediate investigations showed a haemoglobin of 21·9 g., total protein 12·6 g., and blood-urea 320 mg. per cent (*Fig.* 1). Serum hyperviscosity made measurement of the serum electrolytes impossible.

Immediate resuscitation included intravenous infusion of 7·4 litres of normal saline (1140 mEq. of sodium), 1 litre of 5 per cent dextrose, and 220 mEq. of potassium supplements over the first 24 hours. This was followed by clinical improvement, with the supine blood-pressure rising to 120/80 and skin turgor returning towards normal. With rehydration the haemoglobin fell to 16·2 g. and the total protein to 6·4 g. She passed 625 ml. of urine. However, her blood-urea rose to 350 mg. per cent whilst the serum sodium and chloride remained extremely low (*Fig.* 1). Intravenous therapy was stopped and oral fluids were encouraged on the second day after admission.

Throughout this period the patient continued to pass rectal fluid and a further 500 ml. were released during a sigmoidoscopy which confirmed the diagnosis of villous papilloma.

Three days after admission she began to deteriorate again with vomiting, tachycardia, and signs of increasing dehydration. Only 200 ml. of urine had been passed over 24 hours and her blood-urea had risen to 400 mg. per cent whilst the serum sodium (112 mEq./l.) and chloride (80 mEq./l.) were still very low. Intravenous therapy was restarted and a further 3 litres of normal saline with 80 mEq. of potassium chloride were given. Her deterioration continued over the next 36 hours and she became confused, semi-comatose, and increasingly breathless. Clinically and radiologically she had pulmonary oedema although she appeared dry with cold peripheries and her serum sodium and chloride levels remained extremely low. The pressure in her neck veins was not elevated and there was no peripheral oedema. The blood-urea was now 470 mg. per cent with unrecordably high serum uric acid and phosphate levels. She was transferred to the Wessex Regional Renal Unit on the fifth day of admission with established acute intrinsic reversible renal failure and severe electrolyte abnormalities.

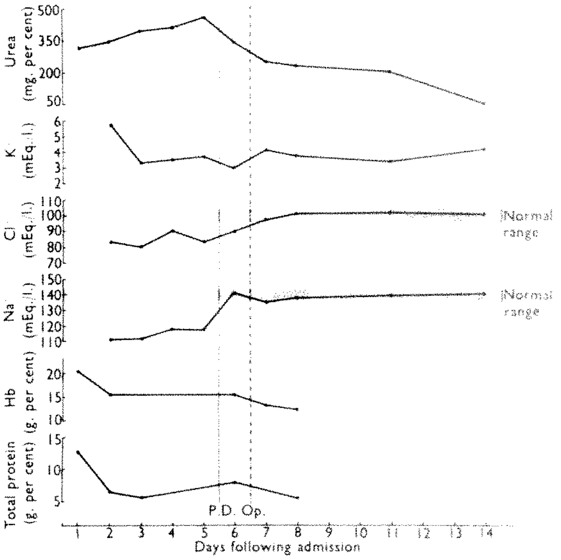

FIG. 1.—Urea, serum-electrolytes, haemoglobin, and total protein levels during the period after admission. P.D., Peritoneal dialysis. Op., Operation.

Peritoneal dialysis was immediately started. Alternating Dialaflex solutions 1·36 per cent and 6·36 per cent were given at a rate of 2 litres per hour supplemented initially by 5 mEq. and later by 7 mEq. of potassium chloride per litre. After eight exchanges a negative fluid balance was achieved with a 3-kg. weight-loss and clinical resolution of the pulmonary oedema. One litre of double-strength plasma was given to maintain serum oncotic pressure, and 300 ml. of 4·2 per cent sodium bicarbonate for correction of severe metabolic acidosis. Hydrocortisone, 10 mg. i.v., was given empirically on two occasions when unaccountable hypotension occurred. Intravenous lignocaine was given to suppress ventricular ectopics probably caused by electrolyte disturbances.

By the sixth day after admission her conscious level had improved, she was free of pulmonary oedema, her blood-pressure had risen to 140/90, and her blood-urea had fallen to 350 mg. per cent. The serum sodium had dramatically risen to 141 mEq./l. However, she remained oliguric and continued to lose enormous quantities of watery mucoid fluid per rectum (probably over a litre every 12 hours) which contained 141 mEq. of sodium per litre and 40 mEq. of potassium per litre. Control of the metabolic disturbance seemed impossible as long as the tumour remained in situ and therefore an emergency operation was decided upon. The tumour was found to be too extensive to be removed per rectum and therefore an anterior resection of the rectum was carried out. An end-to-end rectosigmoid anastomosis was carried out with temporary left iliac colostomy. The tumour measured 8 × 18 cm. and histologically there was no suggestion of malignancy.

Postoperatively the patient was given parenteral nutrition and peritoneal dialysis was continued. On the fourth postoperative day (tenth day after admission) a diuresis began and dialysis was discontinued. Thereafter, apart from thrombophlebitis of the right leg she made an uneventful recovery, renal function returning entirely to normal, and the colostomy was closed 3 months later.

Table I.—DETAILS OF CASES OF RECTAL VILLOUS PAPILLOMAS REPORTED IN THE LITERATURE

AUTHOR	AGE AND SEX OF PATIENT	PRESENTATION	BIOCHEMISTRY		DEHYDRATION PER SE OR ESTABLISHED A.I.R.R.F.*	MANAGEMENT
			Highest Blood-urea (mg. per cent)	Lowest Serum Sodium (mEq./l.)		
Fitzgerald (1955)	57 F.	Diarrhoea for 4 years	205	119	Dehydration alone	Infusion, i.v. Excision of tumour after 28 days
Jordan and Erickson (1958)	56 M.	Diarrhoea for 2 years	—	115	Dehydration alone	Intensive i.v. infusion. Abdominoperineal resection to include tumour 'at later date'
Popovsky (1965)	82 F.	Diarrhoea for 6 years	86	124	Dehydration	Infusion, i.v. Anterior resection of rectosigmoid after 15 days
Babior (1966)	69 F.	Diarrhoea for 2 months	142 (after i.v. infusion)	120	Dehydration	Infusion, i.v. Resection of tumour 'at later date'
Kille and others (1967)	56 M.	Diarrhoea for 6 years	700	112	A.I.R.R.F.	Haemodialysis. Abdominoperineal resection of rectum and tumour after 18 days
	60 M.	Diarrhoea for 4 years	560	—	? A.I.R.R.F. (inconclusive)	Haemodialysis (fluid only infused after dialysis). Resection of recto-sigmoid junction after 20 days
Hammer (1969)	74 F.	'Chronic' diarrhoea	278	104	Dehydration	Infusion, i.v. Resection of tumour 'at a later date'
Lee and Keown (1970)	74 F.	Watery rectal discharge for 2 years	255	127	Dehydration	Inadequate i.v. infusion delayed until third day. Transrectal excision of tumour after 21 days
	77 M.	Diarrhoea over 'indefinite period'	475	113	Dehydration	Infusion, i.v. Transcoccygeal resection of rectal tumour after 8 days
Present series (1973)	51 F.	Acute 'watery rectal discharge' (slight looseness of bowel actions for 12 months)	470	'Unrecordable'†	A.I.R.R.F.	Intensive i.v. infusion, peritoneal dialysis, emergency laparotomy, and resection of tumour 24 hours after admission to renal unit (5 days after admission to hospital)

* A.I.R.R.F., Acute intrinsic reversible renal failure.
† After 7 litres of normal saline, 111 mEq./l.

DISCUSSION

This case illustrates a number of points. The presentation was dramatic with little preceding evidence suggesting the presence of the tumour. In almost all the previously described cases (*Table I*) acute presentation had been preceded by colitis-like symptoms lasting on average for 5 years. Popovsky (1965), in his review of the literature, stated: '*sine qua non* condition for the appearance of the "low salt syndrome" complication is a long interval (over five years) of symptoms common to villous papilloma (pseudo-diarrhoea and sero-mucoid discharge from the rectum)'.

In spite of energetic fluid and electrolyte repletion which clinically corrected the pre-renal factor the serum-sodium and chloride levels remained extremely low. Probably this continued hyponatraemia occurred because the total-body sodium was still low with perhaps relative water excess. Possibly, however, a 'sick-cell syndrome' may have developed, causing inappropriate distribution of electrolytes, the sodium pump having failed at cell-membrane level, thus allowing sodium into the cells at the expense of extracellular levels. The subsequent development of pulmonary oedema precluded further saline infusion. The pulmonary oedema may have been caused by myocardial failure due to a combination of factors such as hypokalaemia, acidosis, and hypoxia before total fluid and electrolyte repletion. Conceivably, increased permeability of pulmonary capillaries in this uraemic state (Crosbie, Snowdon, and Parsons, 1972) may have contributed.

This is the first such case reported in which peritoneal dialysis has been used, and the total correction of serum electrolytes (particularly sodium, chloride, and potassium) was rapid. Intravenous therapy alone had failed to achieve this. Peritoneal dialysis is considered a particularly safe self-regulatory method of giving potassium in an extremely precarious situation (anuric renal failure and immeasurable potassium losses).

Removal of the offending tumour was undertaken much earlier than has hitherto been customary and at a time when the patient was still clinically and biochemically unstable. It was considered that metabolic equilibrium would not have been achieved as long as the tumour, the source of the enormous electrolyte losses, remained in situ. Postoperatively the situation was relatively easy to control. Kille and others (1967) suggested that 'surgery should not be attempted until all repletion of electrolytes and fluid had been corrected', but to do this may result in such a delay that the patient perishes.

Finally, it should again be emphasized that the majority of these patients at presentation have a pre-renal uraemia secondary to the enormous fluid, protein, and electrolyte losses, especially of sodium and chloride, and will not require dialysis provided that early intensive intravenous replacement, inclusive of plasma, is given.

Acknowledgements.—I would like to thank Dr. Ralph Moore for referring this case, Mr. J. D. Younghusband for his timely surgical intervention, and Dr. Harry Lee for his supervision, advice, and permission to publish details of this case.

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FAECAL FISTULA DUE TO LONG-STANDING EXTRA-UTERINE PREGNANCY

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LONG-STANDING extra-uterine pregnancies are uncommon; for them to be complicated by a faecal fistula must be even more uncommon. Various causes of enterocutaneous fistula have been documented (Aird, 1957; Edmunds, Williams, and Welch, 1960), but intra-abdominal pregnancy as a cause does not appear to have been previously encountered. Two cases are presented from Mulago Hospital, Kampala, Uganda, in each of which a long-standing extra-uterine pregnancy led to the formation of a faecal fistula. In one case the small intestine and in the other the large intestine was involved.

CASE REPORTS

Case 1.—The patient was a 20-year-old Luo woman from Western Kenya. She had had a normal delivery of a full-term female child in August, 1971, and had subsequently been in good health. Her periods, however, had not started again following the delivery. Just over a year later in September, 1972, she had developed a swelling in the right groin. This was painful and had gradually increased in size. The swelling had burst spontaneously 1 month later and she had started discharging faeces through the groin. She had lost weight and her general health had deteriorated.

On admission the patient was in a poor condition. She was wasted, with a haemoglobin of 10·5 g. per 100 ml. There was a fistula in her right groin just above the inguinal ligament, 4 cm. from the pubic tubercle, discharging faeces. She held her right hip in 50° flexion. A radiograph of the right iliac region showed a collection of foetal bones (*Fig.* 1).

With the help of glycerine suppositories she had normal bowel actions per rectum. After suitable preoperative preparation including sterilization of the bowel contents and blood transfusion she was operated on in November, 1972. Just under the skin in the right groin there was a cavity about as big as a clenched fist. It contained well-formed foetal bones, including skull, ribs, and long bones. The bones were removed and a formal laparotomy was carried out. There was a defect, 4 × 2·5 cm., in the antimesenteric border of the ileum about 45 cm. from the ileocaecal junction. This communicated with the cavity in the groin which also had the right ovary and tube as posterior relations (*Fig.* 2). The small gut was dissected free from the cavity. The defect in the ileum was closed transversely with two layers of catgut. The uterus and left tube appeared normal. There was no other abnormal finding and the abdomen was closed. The cavity in the groin was packed with eusol-soaked ribbon gauze. The patient made an uneventful postoperative recovery. The cavity became smaller with daily dressings and she was discharged after 4 weeks. She was seen 3 months after operation, by which time the wounds were completely healed and she had started to gain weight.

Case 2.—This patient was a 19-year-old Muganda girl. She had been well until 8 months before admission, when she had stopped menstruating and she had thought that she was pregnant for the first time. Four months later she had felt continuous central abdominal pain which had persisted in spite of treatment. She had had a scanty period about 1 month before admission. About this time she had noticed a swelling just to the right of the umbilicus.

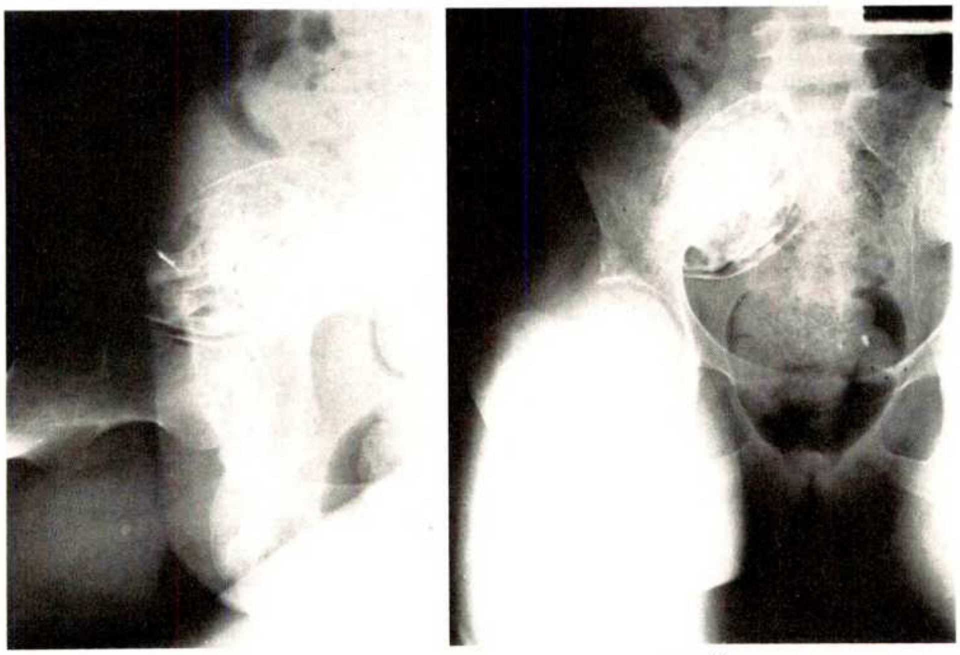
A B

FIG. 1.—*Case* 1. Radiographs of the abdomen. A, Lateral view. B, Anteroposterior view

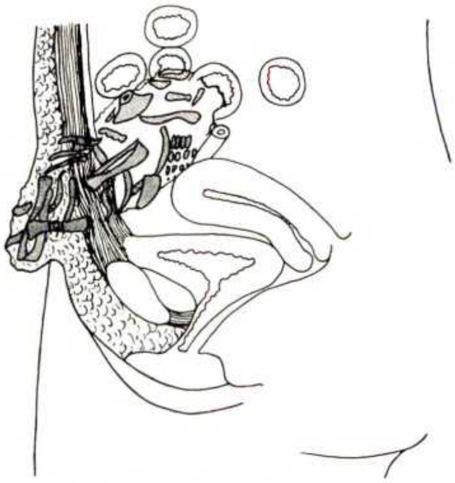
FIG. 2.—*Case* 1. Diagrammatic representation of the pathological process showing involvement of the small bowel and extrusion of foetal bones through the skin of the anterior abdominal wall.

This had subsequently burst and she had begun to discharge foul-smelling pus through the abdominal wall, 1 cm. proximal to the umbilicus in the midline.

On admission she was in good general condition. There was a slightly mobile mass 10 cm. in diameter to the right of the umbilicus and proximal to it. It was tender, smooth, and crepitant. The associated sinus discharged gas and faeculent pus. A pregnancy test was negative. Anaerobic organisms were grown from the pus in the discharging sinus. An abdominal radiograph showed a collection of foetal bones corresponding in position to the abdominal mass (*Fig.* 3).

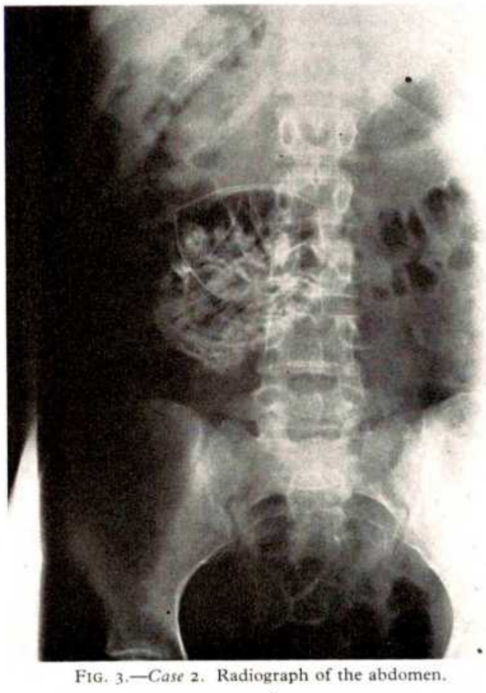
FIG. 3.—*Case* 2. Radiograph of the abdomen.

After suitable preparation including sterilization of the bowel contents she underwent operation. Laparotomy confirmed the presence of a necrotic advanced extra-uterine pregnancy. There was a marked inflammatory reaction around the foetal parts which were attached to the uterus, caecum, transverse colon, liver, gall-bladder, and anterior abdominal wall. A spicule of bone had perforated the transverse colon. The foetal parts were dissected free and the small defect in the transverse colon was closed with catgut and an omental patch. The patient made an uneventful recovery and was able to leave hospital on the ninth postoperative day.

DISCUSSION

The first recorded case of intra-abdominal pregnancy is usually attributed to Albucasis (1013–1106), the distinguished Arabian physician of Cordova. Since his time numerous references to isolated but interesting examples of extra-uterine pregnancy have been made. These historical reports have been well reviewed by Jarcho (1949) and King (1954).

Primary intraperitoneal pregnancy is extremely rare (Cavanagh, 1958) and the usual cause is an early rupture of a tubal pregnancy. Consequently a history suggestive of the accident can be obtained in many cases, as in *Case* 2. However, in *Case* 1 no such history was obtained, and the patient had had no periods since delivery 15 months previously. It is interesting to speculate when this process took place in this case. It could have occurred at the time of her pregnancy in 1971. The coexistence of an intra-uterine and extra-uterine ('combined') pregnancy is very uncommon (Novak, 1926), and the uterine pregnancy rarely goes to term (Burkhart, Mule, Begneaud, and Kohen, 1963). Alternatively, she could have become pregnant shortly after delivery in August, 1971, this pregnancy being extra-uterine.

An extra-uterine pregnancy very rarely goes to term; much more commonly foetal death occurs. The subsequent course is then variable and has been well discussed by King (1954) with illustrative examples. Frequently the gestation sac becomes infected, with suppuration and fistulation to the skin or to the neighbouring hollow viscera—vagina, bladder, or the intestines. Foetal parts may occasionally be discharged through these fistulae (Schumann, 1921). Our 2 cases are interesting in that they each presented initially with a faecal fistula and the presence of an intraperitoneal pregnancy was recognized in the course of investigation. In both cases suppuration of the gestation sac had resulted in its communication first with the intestine and later with the skin. That this is not a more common occurrence must be due to the fact that surgical interference usually takes place before this stage is reached. Douglass and Kohn (1947) and Beacham, Hernquist, Beacham, and Webster (1962) found that advanced abdominal pregnancy was more common in Negroes than in whites by sixteen and twenty times respectively. As early surgery is not always available to these patients extra-uterine pregnancy should be kept in mind as an occasional cause of enterocutaneous fistula.

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REVIEWS AND NOTICES OF BOOKS

The Care of your Colostomy. By J. C. GOLIGHER, Professor of Surgery, University of Leeds, and MURIEL POLLARD, Appliance Officer, The General Infirmary at Leeds. 8 × 5 in. Pp. 31, with 41 illustrations. 1973. London: Baillière Tindall. 15p.

The Care of your Ileostomy. By J. C. GOLIGHER, Professor of Surgery, University of Leeds, and MURIEL POLLARD, Appliance Officer, The General Infirmary at Leeds. 8 × 5 in. Pp. 27, with 32 illustrations. 1973. University Department of Surgery at Leeds. 20p.

THESE two booklets have been brought up to date, the present versions being based on previous publications from the University Department of Surgery at Leeds and similar booklets published by other hospitals. They have been written to give to the patients concerned and contain sound advice about the day-to-day management of a colostomy and of an ileostomy from a practical point of view and without sentimentality. Although written for the patient to read and refer to, many surgeons will want to have copies of these books, for they contain many practical tips about which surgeons are frequently asked by their patients, and so that they can be given to their patients.

Both books provide helpful advice about day-to-day living, diet, baths, etc., and with good practical information about the many appliances now available on the British market. The names and addresses of the manufacturers and agents for the supply of these appliances are given in the appendixes. The management of many of the appliances is illustrated with clear line drawings. There is a particularly good section in the ileostomy booklet on the management of skin soreness which many surgeons and ward sisters will find invaluable.

Professor Goligher and Muriel Pollard are to be congratulated on two excellent booklets which will be a great help and solace to many patients.

Osteosynthese in der Handchirurgie. By ALFRED PANNIKE, Tübingen. 9¾ × 6½ in. Pp. 124+xi, with 167 illustrations. 1972. New York: Springer-Verlag. DM.48.

THIS book describes the use of internal fixation in relation to fractures of the bones of the hand and fingers. The previously used methods of pinning and wiring such fractures are given but the author's preference is for miniature plates and screws. The necessary surgical armamentarium is described and the different problems are well illustrated by diagrams and excellent radiographs. The author reviews over 200 such open reductions and claims results which are very much better than those using conservative means.

This volume should be of considerable interest to all surgeons involved in hand surgery and the extensive and excellent diagrams make a knowledge of German almost unnecessary in following the text.

Intensivpflege Intensivtherapie. By A. WAHLIN, L. WESTERMARK, and A. VAN DER VLIET, Stockholm; translated by H. GOERKE and edited by G. A. NEUBAUS. 9¾ × 6½ in. Pp. 223+xv. Illustrated. 1972. Berlin: Springer Verlag. DM.48.

THIS book on intensive therapy was originally published in Swedish in 1968 and has now been translated into German. It is primarily aimed at medical students, nurses, and others working in intensive-care units and is based on the experience of the intensive-care unit run by the Department of Anaesthesiology at the Karolinska Hospital. The book is full of useful advice and explains in detail but at the same time in simple terms the various procedures which may be performed in an intensive-care unit. The reasons for performing each procedure are clearly stated, and the book is well illustrated throughout by photographs and line diagrams.

An appendix lists the equipment, drugs, and infusion solutions which should be stocked in an intensive-care unit and even gives the normal values of the commoner haematological and biochemical investigations.

This is an excellent volume and could well be read with benefit by anyone involved in intensive care.

Blood Flow Measurement. Edited by COLIN ROBERTS, King's College Hospital Medical School, London. Pp. 184. Illustrated. 1972. London: Sector Publishing Ltd. £4·20.

THIS book contains 34 contributions from more than 50 authors, and comprises the bulk of the material presented at an international conference on the theory and practice of blood-flow measurement organized by the Biological Engineering Society and the Biochemical Engineering Department of King's College Hospital Medical School. It is therefore not the comprehensive manual of blood-flow methodology which the title might suggest but rather a useful guide to recent developments in some particular fields, notably the use of ultrasound and electromagnetic techniques. For those who are using or propose to use these methods, and who are familiar with their physical bases, the book will be very valuable. Nine of the chapters deal helpfully with aspects of assorted thermal and peripheral techniques.

The general medical reader will find the inevitably technical and mathematical sections leavened by chapters on the value of the measured quantities in clinical assessment.

As a contribution towards increasing, by interdisciplinary collaboration, the precision of the measurements on which clinical judgements and diagnoses are made this book is to be most warmly welcomed.

BOOK NOTICES

[*The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.*]

The Anesthesiologist and the Surgeon. By JOHN P. BUNKER, M.D., Stanford, California. 8¼ × 5½ in. Pp. 158+xix. 1972. Edinburgh: Churchill Livingstone. £4.

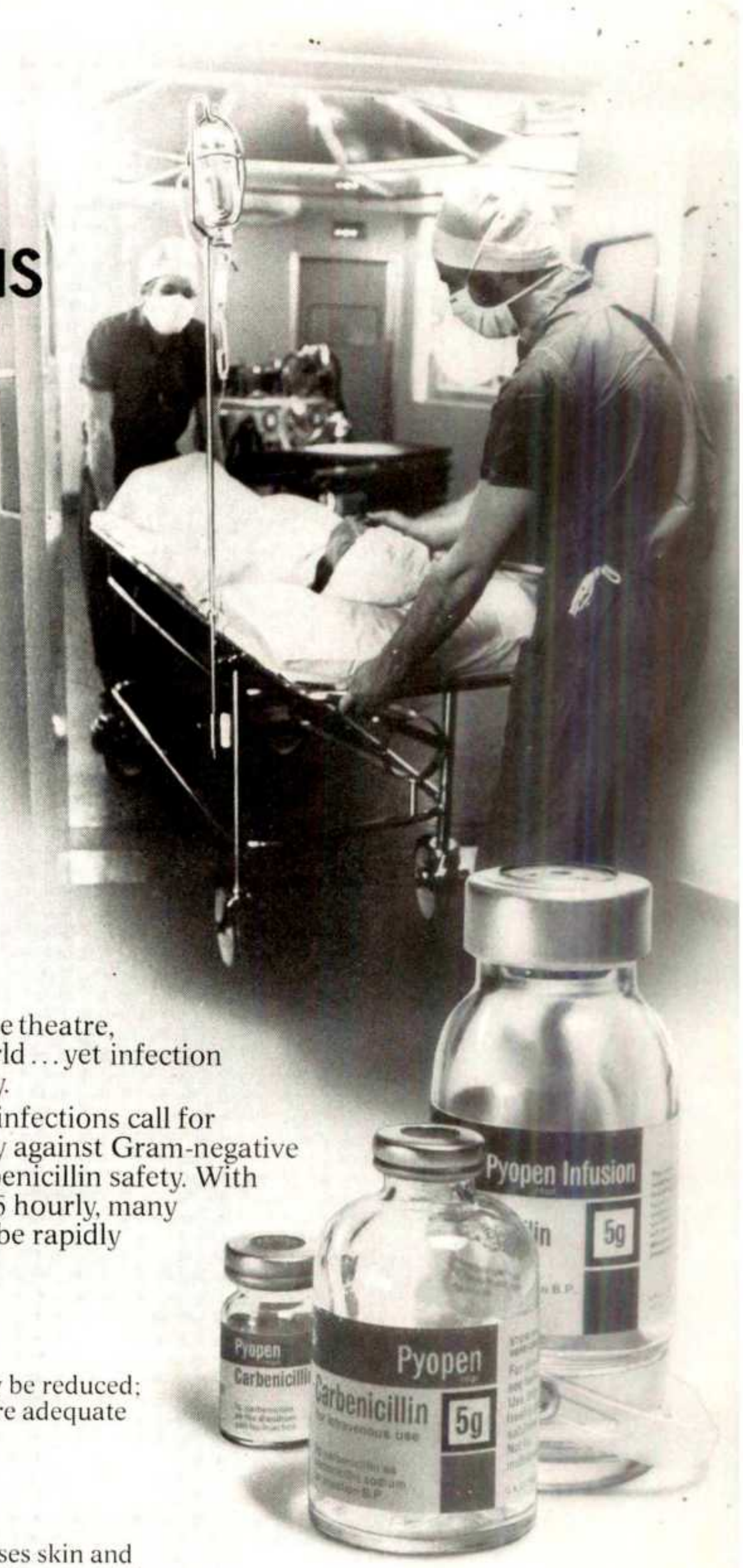
Techniques of Abortion. By SELIG NEUBARDT, M.D., F.A.C.O.G., F.A.C.S., New York, and HAROLD SCHULMAN, M.D., F.A.C.O.G., New York. 8¼ × 5½ in. Pp. 172+xi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £5.

Cardiac Surgery. Edited by JOHN C. NORMAN, M.D. Boston. 9½ × 6½ in. Pp. 703+vii. Illustrated. 1972. New York: Appleton-Century-Crofts. $18.95.

Manual of Fracture and Orthopaedic Surgery. By K. S. BOSE, M.S. (Cal.), F.A.M.S., Calcutta. 8½ × 5½ in. Pp. 262+xii. Illustrated. 1972. Calcutta: Kamala Books. Price not given.

Metabolic, Degenerative, and Inflammatory Diseases of Bones and Joints. By HENRY L. JAFFE, M.D., New York. 10 × 7 in. Pp. 1101+xi, with 1066 illustrations. 1972. London: Henry Kimpton. £15·75.

Angiography of Trauma. By WHEI-RUNG FU, M.D. Washington. 9 × 6 in. Pp. 106+vii, with 32 illustrations. 1972. Springfield, Ill.: Charles C. Thomas. $11.75.



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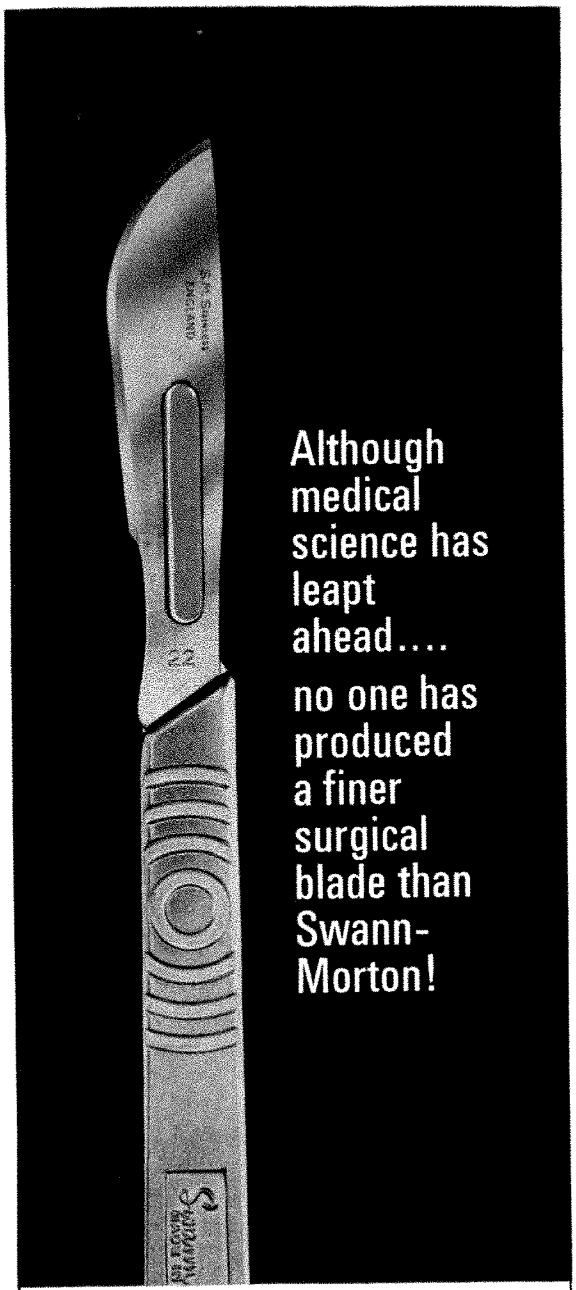
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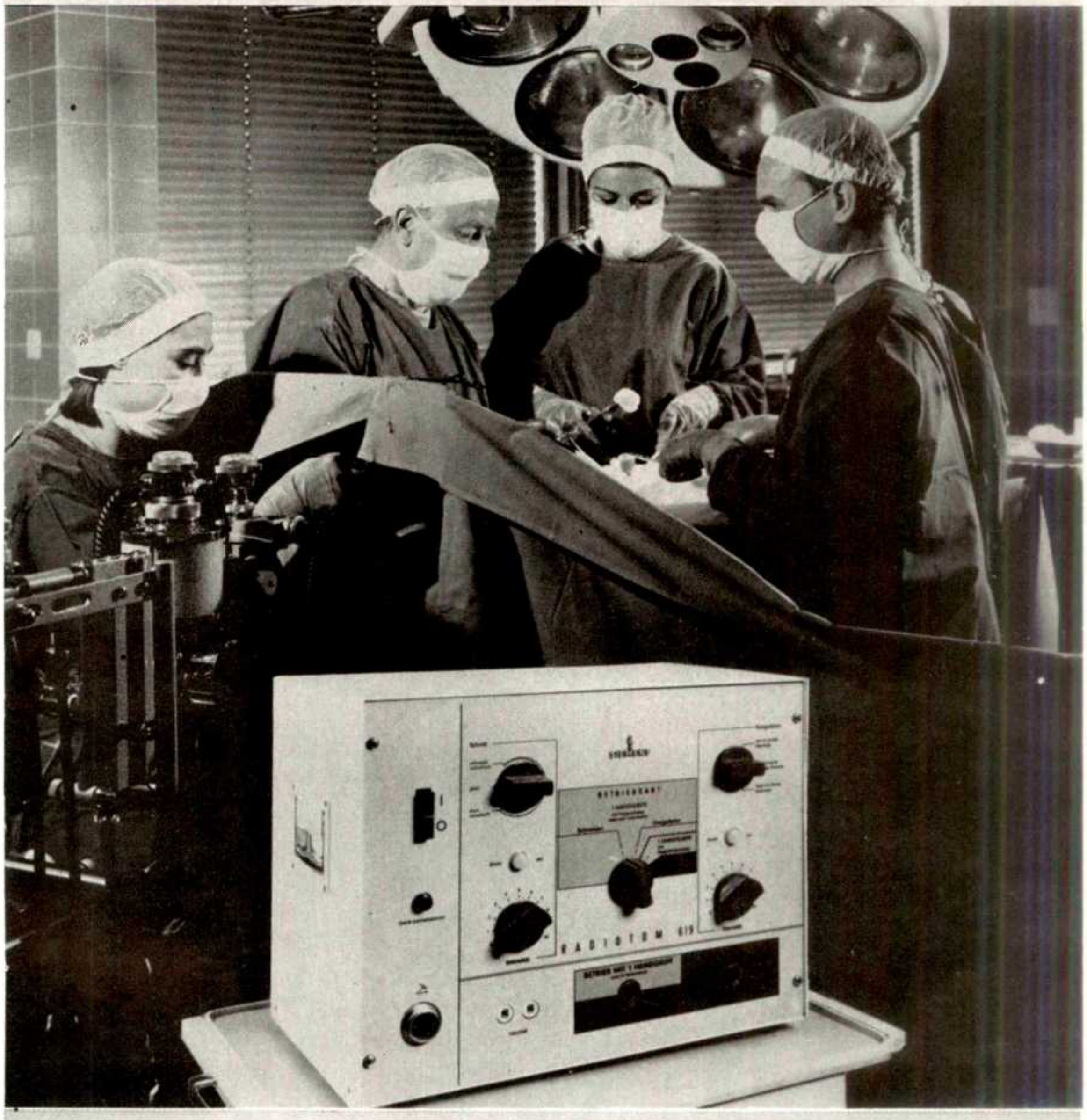

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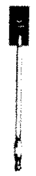

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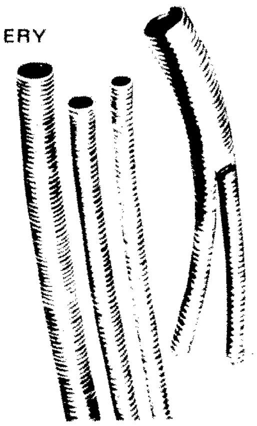

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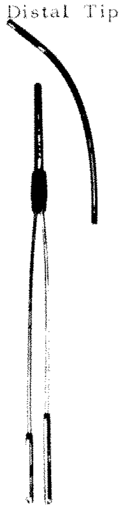

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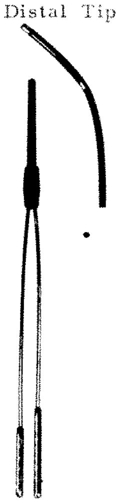

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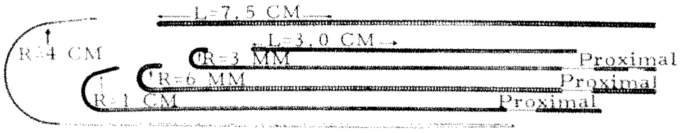

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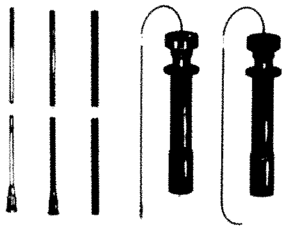

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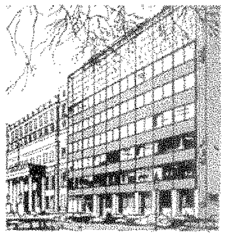

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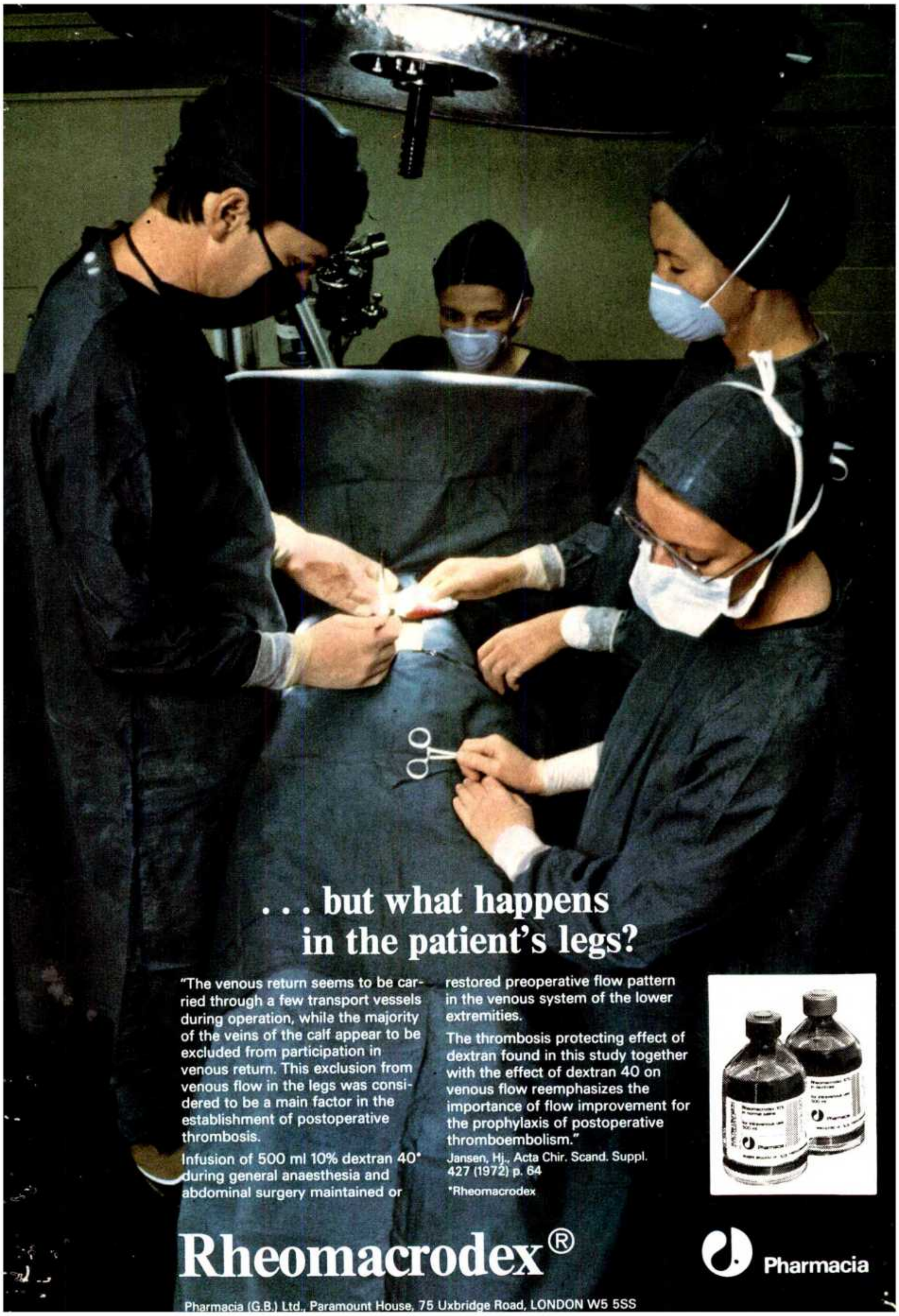

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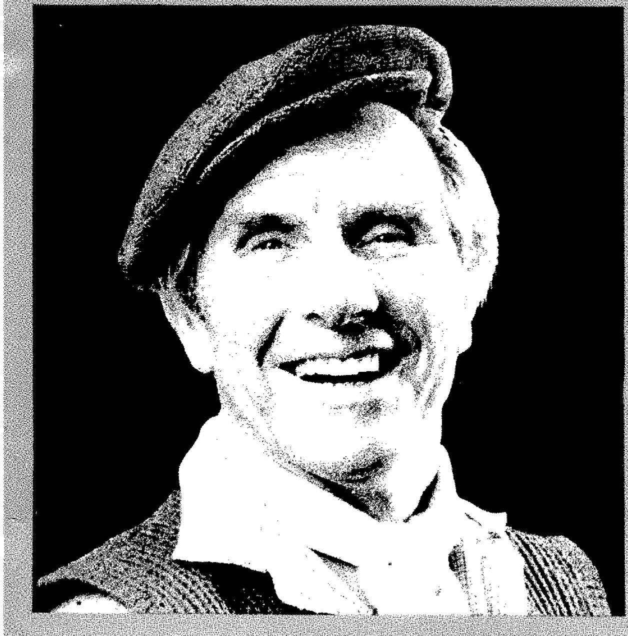

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1 *Brit med J*, (1969), **4**, 470
2 *Postgrad med J*, (1969), **45**, Supplement (November), 91
3 *S Afr med J*, (1970), **44**, Supplement (August), 12
4 *Med J Austr*, (1971), **1**, 526

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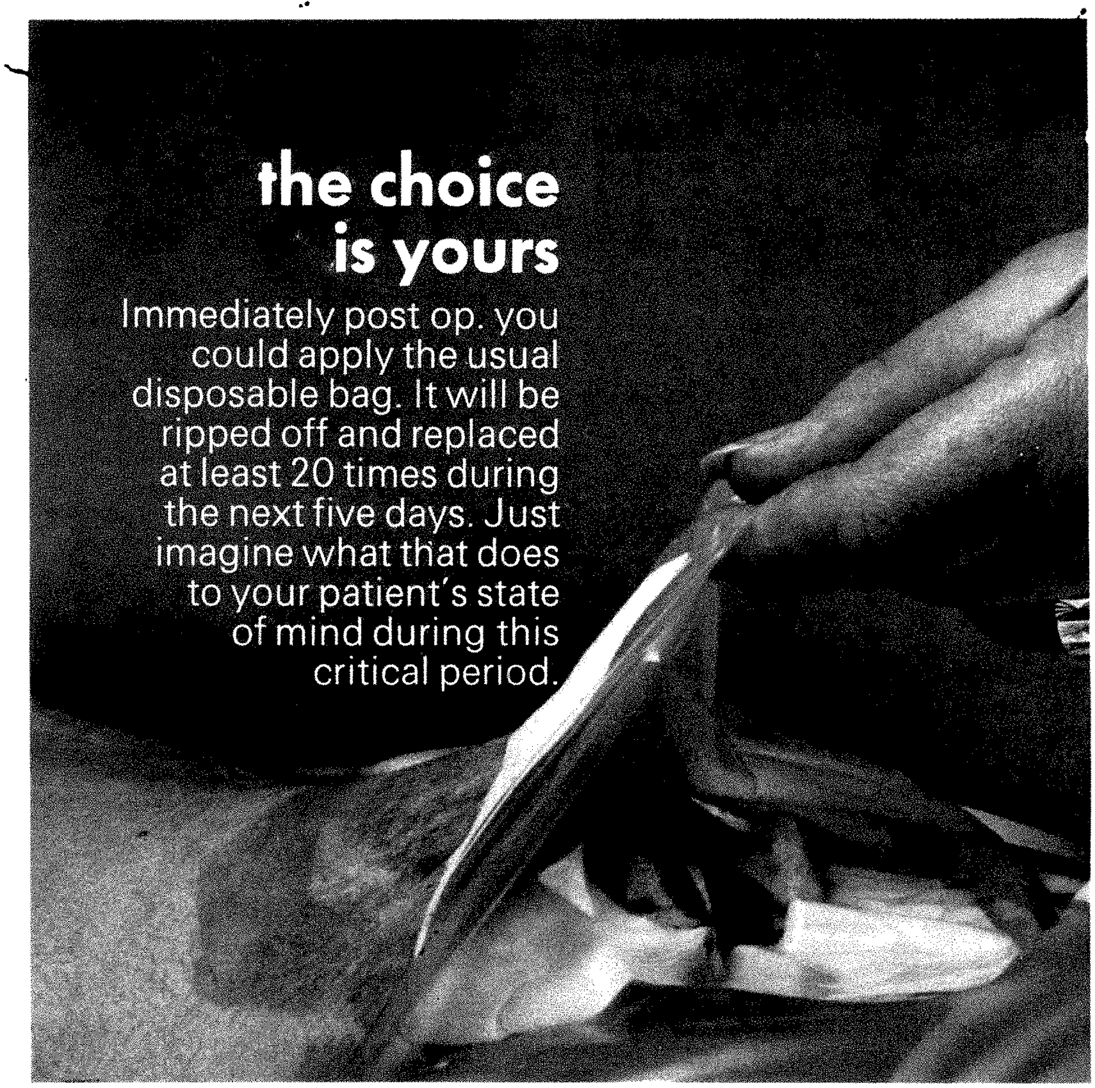

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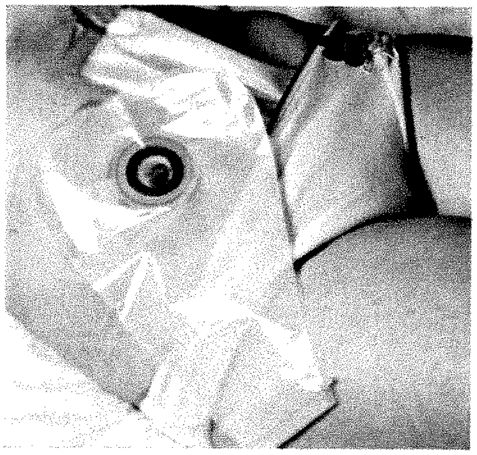

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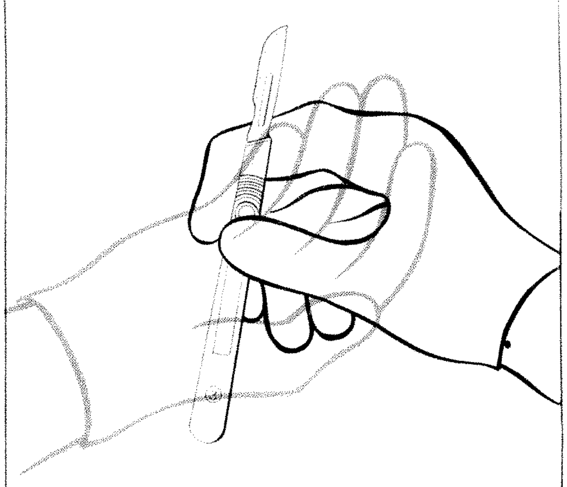

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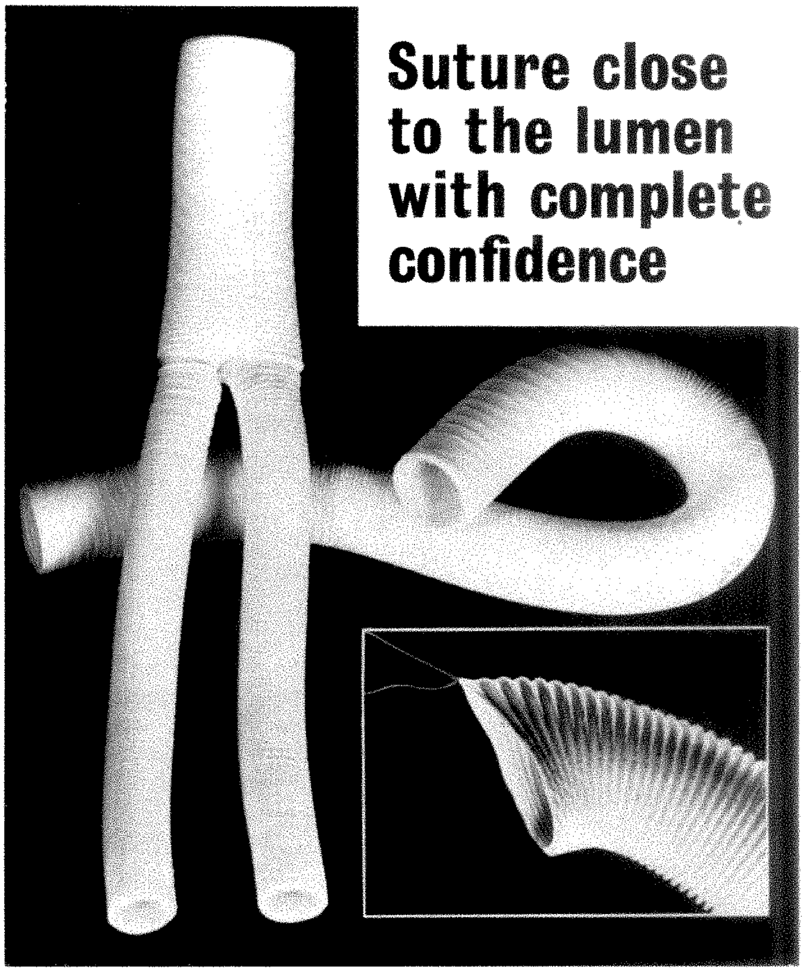

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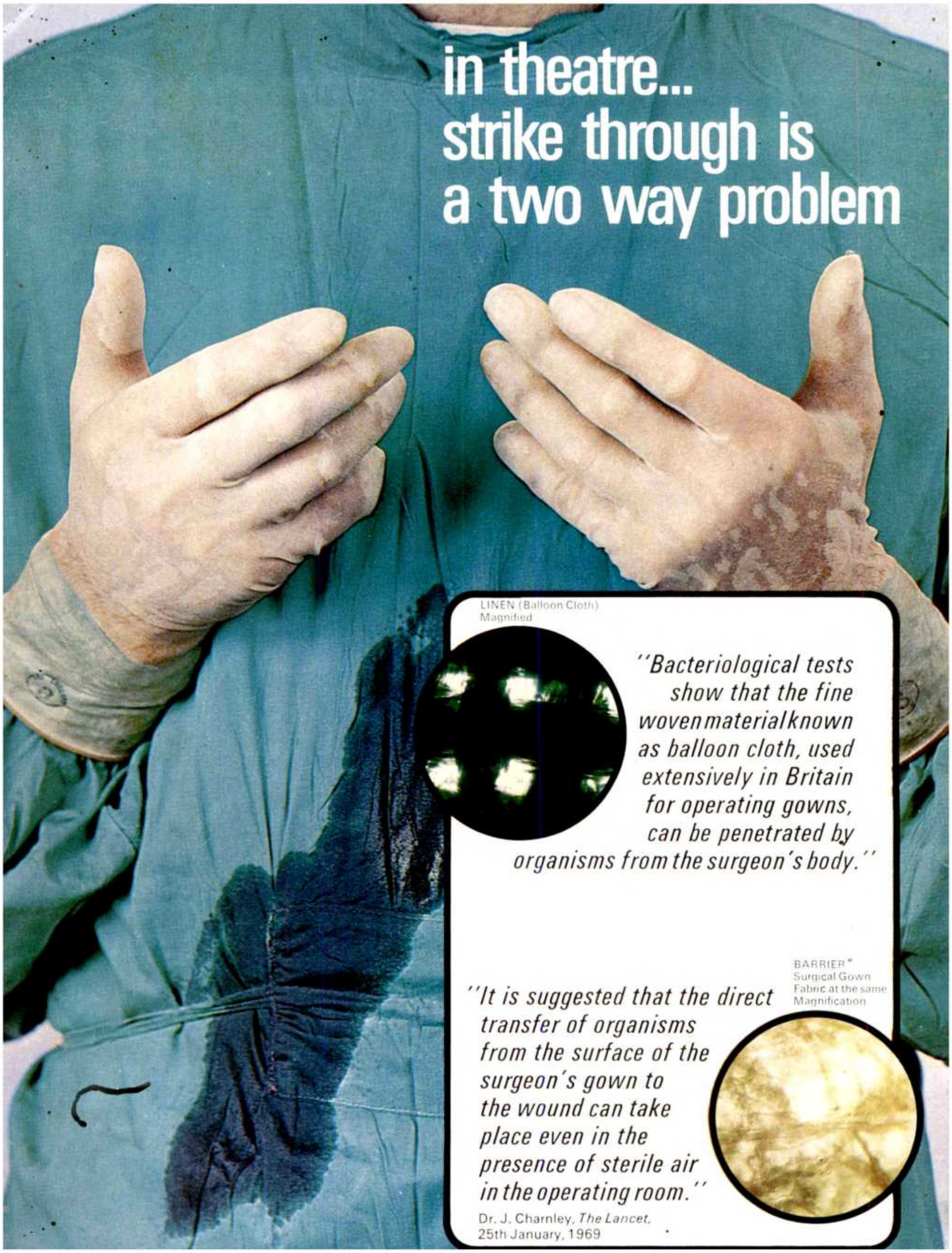

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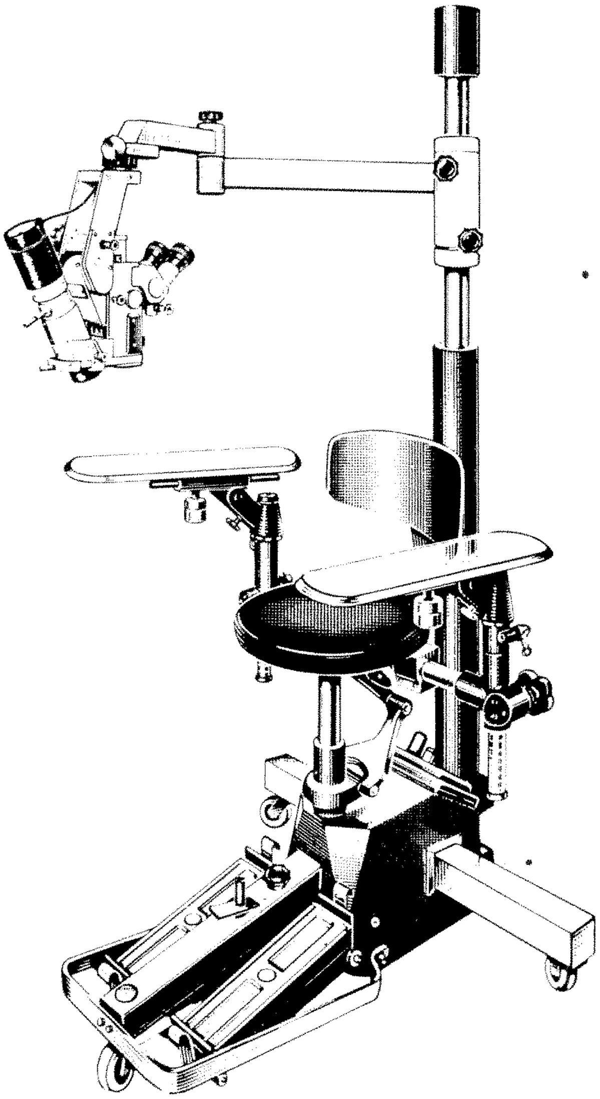

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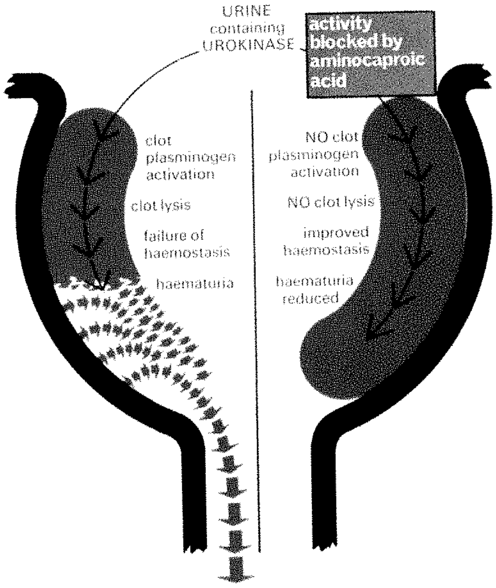
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THE
BRITISH JOURNAL OF SURGERY

Vol. 60 DECEMBER, 1973 No. 12

EDITORIAL

As we stand at the threshold of 1974 with all its portents for the Health Services of Great Britain, we would wish our readers to know about changes that are being introduced with the January number of the BRITISH JOURNAL OF SURGERY. Since it first appeared in July 1913 there have been only three changes of format, and the Editorial Committee has decided that the time has come to introduce a number of changes in style and lay-out. In future every article will begin on a new page. This we hope will improve the appearance of the Journal, as well as making it easier to present a more attractive reprint production. Spare space will be used, where appropriate, for short items of selected material of topical, historical, or philosophical interest; the Editorial Committee hopes that readers will contribute items for this purpose, and their help will be welcome.

Volume 61 will differ from the present one in several other ways. The names of the authors of an article will alternate with the title of the article at the top of each page. The full journal reference will appear at the beginning of each article. This should help with the identification of reprints and photocopies. Authors will have their appointments at the time of submitting their article printed as a footnote on the first page. There will be important alterations in the citation of references; these are explained in the Changes to Instructions to Authors, which have already been distributed as loose inserts in recent numbers of the Journal.

Headings will be clearer and the lay-out of tables will be 'cleaner'. The type face will in future be Times for the text material and Grotesque bold for the article headings instead of the present Plantin. The portrait of Lister will return to the cover, which itself has been completely redesigned.

It has been decided to publish in the Journal a limited number of review articles; some of these will be by invitation, but if authors wish to submit articles of this nature they will be welcome and will be considered by the Editorial Committee in the usual manner. Book reviews will appear over the name of the reviewer and it is intended in future to list those of less particular value to our readers. Obituary notices will be limited to those who have made outstanding contributions to surgery. Rare cases will no longer be accepted unless they are of exceptional interest or importance. In future all articles should be sent to the Editorial Secretary at the Bristol address.

We are grateful to our Publishers for their willing and enthusiastic co-operation in the redesign of the Journal and with them we share the hope that the changes now due to take place may be acceptable to our readers and will improve the value of the work in future issues.

H. H. G. EASTCOTT
Editorial Secretary

ORIGINAL PAPERS

A HYPOTHESIS ON SOME FACTORS GOVERNING THE BEHAVIOUR OF SHORT SEGMENTS OF THE SMALL BOWEL

By D. H. R. JENKINS*

DEPARTMENT OF CLINICAL SURGERY, UNIVERSITY OF EDINBURGH

SUMMARY

A hypothesis is advanced in which it is argued that variations in the extrinsic autonomic innervation of short small-bowel segments are responsible for the unpredictable behaviour of such segments. Experimental evidence is offered to substantiate the hypothesis.

THE use of reversed intestinal segments in the treatment of the short-bowel syndrome is well established, but the optimum length of the segment is yet to be determined. Reports of both experimental work (Singleton, 1954; Hammer, Seay, and Johnson, 1959; Baldwin-Price and Singleton, 1965) and actual application of antiperistaltic segments in the control of the short-bowel syndrome in the human (Gibson and Blackman, 1962; Sako and Blackman, 1962; Ellis and Coll, 1968) have been made. It is accepted that the resection of more than three-quarters of the small bowel will lead to weight-loss, hypoproteinaemia, steatorrhoea, and malabsorption (Jenesius, 1945; Jackson, 1958; Ellis and Coll, 1968). Antiperistaltic segments will produce incomplete intestinal obstruction with delay in intestinal transit time and retention of carbohydrate and protein, and to a lesser extent fat, leading to their greater absorption and they thus reverse, in part at least, the effect of the loss of a large percentage of the small bowel (Shepherd, 1966).

By trial and error it has been established that a 7·5–10-cm. segment of terminal ileum interposed in an antiperistaltic manner in the human will significantly delay intestinal transit time (Editorial, 1971).

Not only does the optimum length of reversed segment need to be established, but also the site from which such a segment should be taken. Furthermore, an understanding of the mechanism involved in the behaviour of such segments is required if a rational approach, based on physiological reasoning, is to be adopted. Review of the literature has revealed that there is little to suggest that such mechanisms have been fully examined.

Torbey (1960) and Torbey and Waddell (1961) noted that some short segments of the ileum supplied by one vascular pedicle exhibited a high degree of tone and remained contracted after isolation from the gut. This finding has been confirmed in rabbits (Jenkins and Macleod, 1970), and later work in rabbits and dogs by the same authors (Jenkins and Macleod, 1972) indicated mechanisms which might be involved. As a result of their experiments Jenkins and Macleod suggested that the vagus was uniformly distributed to the whole of the small bowel, serving to maintain tone. On the other hand, the jejunum had no extrinsic sympathetic supply and the ileum had one distributed in an irregular manner only. The suggestion was made that when there was both a sympathetic and a parasympathetic component, reaching the segment in question via the main branches of the superior mesenteric artery, a regular and predictable response could be expected from such a segment placed in either an iso- or an antiperistaltic manner. When a high degree of tone was noted in a short segment of distal ileum this was thought to be due to the uninhibited effect of the vagus on that particular segment. From the results it was argued that the variations in the extrinsic autonomic supply were responsible for the peculiarities in behaviour observed.

If these suggestions are correct they clearly have relevance to the question of the selection of a segment for reversal in the treatment of the short-bowel syndrome.

In order to test the hypothesis outlined, experiments were performed on dogs in which a prediction was made of the behaviour of a particular segment of distal ileum following its isolation but before its insertion in continuity with the gut. If the predicted behaviour could be shown to occur then rules could be established from the physiological and anatomical basis of variation in the extrinsic autonomic supply governing the selection of segments of the small bowel for their use in a therapeutic situation.

MATERIALS AND METHODS

In 6 adult mongrel dogs, weighing between 10·0 and 14·5 kg., the abdomen was opened by a midline incision. The ileum was identified and an estimate was made of its length. A segment of distal ileum, 10 cm. from the ileocaecal junction, supplied by one or by two vessels and 10 cm. in length was selected and marked with fine silk sutures. The distal half of the remainder of the ileum was excised. The selected 10-cm. segment was anastomosed in continuity with the remaining bowel in either an anti- or isoperistaltic manner. Single-layer interrupted 000 Dexon sutures were used with the suture line everted in all cases.

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The defects in the mesentery were closed and the abdomen was re-sutured in layers. In 2 other dogs 20-cm. lengths of distal ileum were selected and reanastomosed in the manner described. Both were supplied by two vessels.

Initially the dogs were drip fed with a glucose/saline solution but when they were fully conscious and ambulant they were given food of a standard proprietary brand. All the dogs, irrespective of weight, received ample food in excess of the manufacturer's recommendations. The dogs were weighed frequently. The intestinal transit time was assessed by observing the mouth-to-anus time of methylene blue. Post-mortem examinations were performed on all the animals.

RESULTS

In dogs II, V, and VI (*Table I*) the single-vessel distal ileal segment contracted visibly following isolation and it was anticipated that some degree of obstruction would result following interposition of such segments. Dog II (antiperistaltic interposition) and dog V (isoperistaltic interposition) gained weight before death and dog II remained well for 83 days. Dog V was put down on day 20 when clinical signs of intestinal obstruction developed which was confirmed at autopsy. Obstruction also occurred at the site of the interposed segment in dog VI and he was put down on day 8, having lost 0·4 kg. in weight.

In dogs I, III, and VIII double-vessel segments were interposed in an isoperistaltic manner. It was anticipated that there would be no obstruction due to the interposed segments and that weight-loss would ensue. Weight-loss was seen in all 3 dogs and led to dog VIII being killed at an early date.

In dogs IV and VII double-vessel segments were interposed in an antiperistaltic manner and a large weight-loss was predicted and was, in fact, observed.

Intestinal transit times, measured by an admittedly crude method, were increased in the dogs in which single-vessel segments had been interposed.

It has been predicted that the excision of the distal half of the small bowel would lead to weight-loss, decreased intestinal transit time, and eventually death. It was anticipated that the interposition of

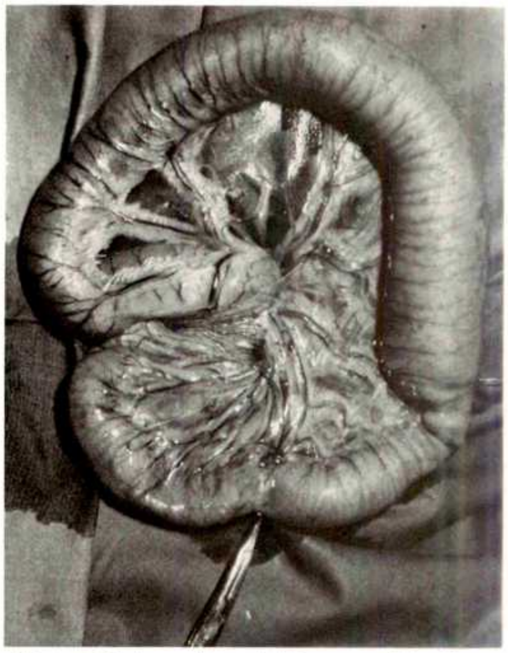

FIG. 1.—A single-vessel isoperistaltic segment of distal ileum in continuity with the remaining small bowel. Its position is shown by the forceps. Dilatation of the bowel proximal to the high-tone short segment is clearly shown.

Table I.—DETAILS OF THE RESULTS OF INTERPOSITION OF SHORT SEGMENTS OF SMALL BOWEL IN DOGS

	DOG							
	I	II	III	IV	V	VI	VII	VIII
Preoperative weight (kg.)	13·7	11·7	13·6	14·2	10·0	14·5	14·2	14·5
Weight at death (kg.)	12·6	11·71	11·95	7·6	11·1	14·1	12·0	12·5
Weight-loss (kg.)	1·1	0·01	1·65	6·6	Gain 1·1	0·4	2·2	2·0
Lowest weight recorded (kg.)	12·5	10·6	11·5	7·6	9·8	14·1	11·9	12·1
Number of vessels supplying segment	2	1	2	2	1	1	2	2
Segment length (cm.)	10	10	10	10	10	10	20	20
Iso- or antiperistaltic	Iso	Anti	Iso	Anti	Iso	Iso	Anti	Iso
Prediction	Weight-loss; no obstruction	No weight-loss; obstruction	Weight-loss; no obstruction	Some weight-loss; slight obstruction	No weight-loss; obstruction	No weight-loss; obstruction	Some weight-loss; some obstruction	Weight-loss; no obstruction
Survival time prior to sacrifice (d.)	75	83	78	65	20	8	36	26
Intestinal transit time (hr.)	6	12	4	10	12	18	8	4
Stenosis	No	Yes	No	Slight	Yes	Yes	Slight	No
Anastomosis	Satisfactory	Satisfactory	Satisfactory	Small abscess	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Pre-segment dilatation	No	Yes	No	No	Yes	Yes	No	No
Post-mortem appearance of small bowel	Normal	Proximal dilatation	Normal	Normal	Proximal dilatation	Proximal dilatation	Normal	Normal

single-vessel segments would, contrary to the results of interposing double-vessel segments, cause a degree of obstruction, increasing the intestinal transit time and thus promoting further absorption of intestinal contents. The expected outcome was observed in the small numbers studied.

It is of interest that the interposition of a short antiperistaltic double-vessel segment did not alter the behaviour of the small bowel and resulted in a similar weight-loss and decreased intestinal transit time as in the isoperistaltic double-vessel segment animals.

DISCUSSION

The question of adrenergic innervation of the smooth muscle of the small intestine is still not fully answered. Youmans (1972), in his presentation of the arguments for and against a significant role for the sympathetic system, concluded that it does have a marked influence on small-bowel motility.

Celender (1959) suggested that in the cat there are no extrinsic inhibitory nerves to the jejunum, and other workers (Kock, 1959; Kerwenter, 1965) have agreed with him. Celender's (1959) argument was that the sympathetic inhibition of smooth muscle was due to 'spill-over' of transmitter from the adrenergic vasoconstrictor nerves. There is no doubt about the action of both parasympathetic and sympathetic nerves on the vessels of the bowel (Padula, Noble, and Camishon, 1967, 1968) and their presence has been proved anatomically (Silva, Ross, and Osborne, 1971). While Silva and others (1971) disagreed with Celender (1959) and indicated that there are clearly demonstrable inhibitory nerves of sympathetic origin, they also noted that the chief projection of the extrinsic adrenergic fibres is upon blood-vessels. They showed, using the histochemical fluorescence technique (Falck and Owman, 1965), that the adrenergic sympathetic fibres occurred in greater concentration in association with arteries and arterioles than with veins. The discussion is further complicated by the known existence of inhibitory fibres within the vagus which are preganglionic, distinct from the sympathetic fibres, and non-adrenergic (Paton and Vane, 1963; Martensen, 1965; Campbell, 1966). The question of species difference may be of importance since the majority of the work quoted has been on cats. However, the primary, secondary, and tertiary plexuses in the myenteric plexus of the cat are similar to those demonstrated in the rabbit (Richardson, 1958) and in our earlier work we noted similar behaviour of gut segments in the rabbit and dog.

Whether the observations recorded are due to true anatomical variation or to a physiologically altered balance in inhibitory and stimulatory fibres is not clear. That the predicted behaviour was the observed behaviour of the segments examined suggests that the hypothesis of variable extrinsic autonomic innervation and the part that it plays in the behaviour of such segments may be correct, in the dog at least. If this is so then rules governing the use of such segments begin to emerge.

It is suggested that very short segments of the distal ileum supplied by one vascular pedicle should be observed following their isolation. If they visibly contract and remain contracted they will behave as if they are supplied by parasympathetic fibres only with no modifying sympathetic component and should, therefore, be avoided since they may cause a degree of obstruction, whether placed in an iso- or antiperistaltic manner, out of all proportion to their short length. Single-vessel distal ileal segments which do not contract and are, therefore, exhibiting low tone may be supplied by both parts of the extrinsic autonomic system and may then exhibit a low degree of obstruction when interposed in an antiperistaltic manner in keeping with their short length. We did not find, however, any such segments in the small group examined here.

Whenever two or more vessels supply a segment its behaviour will be predictable and will depend primarily on the length of the segment, since both components of the autonomic system will be represented.

If 7·5–10 cm. is the correct segment length in the human it should not be a high-tone single-vessel segment if a large degree of obstruction is to be avoided.

Acknowledgements.—Special thanks are due to Professor Sir John Bruce and Professor A. P. M. Forrest for the use of facilities of the Department of Clinical Surgery, University of Edinburgh, and to Mr. I. B. Macleod for his help and advice during the course of the experimental study.

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STRANGULATED EXTERNAL HERNIA ASSOCIATED WITH GENERALIZED PERITONITIS

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SUMMARY

Thirteen patients are described in whom strangulated external hernia was associated with generalized peritonitis. The causes of this combination are discussed.

Although the features of peritonitis are usually quite distinguishable from those of an uncomplicated strangulated hernia, in virtually all the cases previously reported in the literature the presence of peritonitis was not recognized until operation for the hernia was undertaken. Increased awareness of this complication and a conscious effort to exclude it resulted in the correct preoperative diagnosis in 4 of our patients.

When the peritonitis is recognized preoperatively it is suggested that a laparotomy should be performed to deal with the intraperitoneal lesion, and that the associated groin hernia should be repaired by a preperitoneal approach through the laparotomy incision.

CRONIN and Ellis (1959) drew attention to the occasional occurrence of a collection of pus in an empty hernial sac in the course of a generalized peritonitis. They reported 5 cases of their own and reviewed another 27 instances collected from the world literature, all of which were diagnosed preoperatively as strangulated hernia. Maurath and Frauke (1966), in their review, stated that failure to recognize the associated acute abdominal disease in such cases results in a mortality of 60–70 per cent. At Mulago Hospital, Kampala (the National Hospital of Uganda), strangulated external hernia is by far the commonest emergency surgical condition (McAdam, 1961), and in a review of the cases seen in the past 2 years three different causes of the combination of strangulated hernia and peritonitis were encountered in 9 patients. Recently a special effort has been made to recognize the presence of peritonitis in patients presenting with strangulated hernia, and this has resulted in a correct preoperative diagnosis being made in 4 patients. This paper presents these two groups of patients and discusses the problem of preoperative diagnosis and treatment.

CASE REPORTS

Case 1.—N. A., a 40-year-old female, had had an umbilical swelling for 3 months. Four days before admission she developed severe colicky pain at the umbilicus which later became generalized and was associated with progressive abdominal distension. On examination her temperature was 38·2° C., pulse-rate 100 per minute, and blood-pressure 100/70 mm. Hg. There was generalized abdominal distension and tenderness, and a tender irreducible umbilical hernia, 5 cm. in diameter, was present.

At operation the umbilical hernia contained strangulated omentum, but thin greenish pus poured out of the peritoneal cavity. The incision was then extended and exploration of the abdomen revealed a generalized peritonitis resulting from a ruptured right tubo-ovarian abscess. The pus was drained and the abdomen was closed with drainage to the pouch of Douglas. The patient made a steady recovery, although she developed severe wound infection. Secondary suture was performed on the twenty-first postoperative day.

Case 2.—G. M., a 48-year-old male, had had a right inguinal herniorrhaphy 3 years previously. A lump had appeared in the left groin 9 months later but had been reducible and painless until 3 days before admission, since when the patient had had severe generalized abdominal pain and vomiting. On examination he was toxic and dehydrated. His temperature was 39·0° C., pulse 100 per minute, and blood-pressure 100/60 mm. Hg. There was generalized abdominal tenderness with diminished bowel-sounds, and a very tender irreducible left inguinal hernia was present. A diagnosis of strangulated inguinal hernia was made.

At operation the hernial sac was slightly thickened and haemorrhagic and contained only blood-stained fluid. A loop of bowel was retrieved from the peritoneal cavity and was found to be congested but viable. It was noted that the peritoneal cavity contained a large quantity of haemorrhagic fluid but this was attributed to the spontaneously reduced incarcerated loop of bowel. The patient failed to improve postoperatively and 2 days later the abdomen was more distended and remained tender and silent. The patient was thought to have peritonitis due to gangrenous bowel but at laparotomy acute haemorrhagic pancreatitis was found. After a stormy course a pancreatic pseudocyst became apparent on the fourteenth postoperative day. This was drained by cystogastrostomy on the twenty-fifth day, following which the patient made a satisfactory recovery. All his wounds healed by primary intention and he was discharged home after 35 days in hospital.

Case 3.—P. L., a 45-year-old male, gave a 2-day history of colicky abdominal pain and pain in the right inguinal region with vomiting and progressive abdominal distension. He had had a lump in the right groin for 12 years but this had not previously been tender. On examination he was in a satisfactory general condition. The abdomen was distended, there was marked guarding and rebound tenderness, and bowel-sounds were absent. There was a very tender irreducible right inguinal hernia.

On exploring the hernia the sac was found to be oedematous with areas of haemorrhage. It contained a loop of small bowel which was congested but viable. As a large quantity of blood-stained fluid poured out of the peritoneal cavity the abdomen was explored through a right paramedian incision, revealing the presence of acute haemorrhagic pancreatitis. The peritoneal exudate was sucked out, the peritoneum lavaged with normal saline, and the abdomen closed with non-absorbable sutures. Herniorrhaphy was performed. The ascites reaccumulated postoperatively but slowly cleared on treatment. The patient was discharged on the eighteenth postoperative day with no further complications.

Case 4.—C. K., a 47-year-old male, was admitted with a 3-day history of vomiting and a painful, irreducible inguinal lump; this lump had been present for 4 years but hitherto had been reducible. On examination the patient was febrile and dehydrated. The pulse-rate was 80 per minute and blood-pressure 120/90 mm. Hg. There was generalized abdominal tenderness and guarding and a tender, tense, and irreducible left inguinal hernia was present.

When the patient arrived in the operating theatre another hernia was discovered in his right groin and this was also tense, tender, and irreducible. A synchronous exploration was undertaken by two surgeons using two separate incisions, and on opening both hernial sacs copious pus poured out from the peritoneal cavity. The incisions were then converted into a low laparotomy incision and the peritoneal cavity was explored. No cause for the peritonitis was identified and the abdomen was closed with drainage. After initial improvement the patient's condition progressively deteriorated. Post-mortem examination was refused.

Case 5.—D. N., a 40-year-old male, had had a reducible right inguinal swelling for several years. At 10 p.m. on the day before admission he had had a sudden attack of colicky abdominal pain and the inguinal swelling became irreducible and rapidly enlarged. Vomiting started 2 hours after the onset of the abdominal pain and had been copious. On examination the patient was obviously in severe pain and was dehydrated; there was a large tender irreducible right scrotal hernia, and the abdomen showed visible peristalsis with rebound tenderness and guarding in the right iliac fossa.

Table I.—DETAILS OF PATIENTS WITH STRANGULATED EXTERNAL HERNIA ASSOCIATED WITH GENERALIZED PERITONITIS WHICH WAS NOT RECOGNIZED PREOPERATIVELY

CASE	AGE AND SEX	SITE OF HERNIA	SOURCE OF PERITONITIS	DURATION (d.)	TREATMENT	OUTCOME
1	40 F.	Umbilical	Ruptured right pyosalpinx	4	Laparotomy; drainage of pyosalpinx	Severe wound infection, secondary suture. Survival
2	48 M.	L.I.H.	Acute pancreatitis	3	Herniorrhaphy. Exploratory laparotomy. Cystogastrostomy	Survival
3	45 M.	R.I.H.	Acute pancreatitis	2	Herniorrhaphy. Exploratory laparotomy	Survival
4	47 M.	B.I.H.	Undetermined	3	Herniorrhaphy. Exploratory laparotomy	Death
5	40 M.	R.I.H.	Small-bowel volvulus	2	Herniorrhaphy. Laparotomy: resection and anastomosis	Wound infection, drainage. Survival
6	30 M.	L.I.H.	Gangrenous Richter's hernia	14	Herniorrhaphy. Laparotomy: resection and anastomosis	Survival
7	31 F.	Umbilical	Gangrenous Richter's hernia	14	Laparotomy: cardiac arrest	Death
8	60 M.	R.I.H.	Gangrenous Richter's hernia	3	Herniorrhaphy. Laparotomy: resection and repair	Wound infection, secondary suture. Survival
9	60 F.	R.F.H.	Gangrenous Richter's hernia	10	Herniorrhaphy. Laparotomy: resection and repair	Wound infection. Survival

L.I.H., Left inguinal hernia R.I.H., Right inguinal hernia. B.I.H., Bilateral inguinal hernias. R.F.H., Right femoral hernia.

Table II.—DETAILS OF PATIENTS WITH STRANGULATED EXTERNAL HERNIA ASSOCIATED WITH GENERALIZED PERITONITIS WHICH WAS RECOGNIZED PREOPERATIVELY

CASE	AGE AND SEX	SITE OF HERNIA	SOURCE OF PERITONITIS	DURATION (d.)	TREATMENT	OUTCOME
10	65 M.	R.I.H.	Perforated typhoid ulcers terminal ileum	2	Laparotomy and suture. Hernia sac contained pus only	Strangulated R.I.H. on fourth postoperative day. Herniorrhaphy. Survival
11	32 M.	R.I.H.	Appendicitis	3	Appendicectomy. Preperitoneal herniorrhaphy	Uneventful. Survival
12	60 F.	L.F.H.	Gangrenous Richter's hernia	10	Laparotomy: resection and suture. Purse-string suture to neck of sac	Hernial sac abscess, drainage. Survival
13	55 M.	R.I.H.	Afferent loop strangulation (Philip, 1967), late stage	4	Laparotomy: resection and anastomosis. Purse-string suture to neck of sac	Gross scrotal abscess, drainage. Secondary suture. Survival

See footnote to *Table I* for key to abbreviations.

At operation the hernial sac contained two separate loops of small bowel which could not be reduced, and blood-stained fluid drained from the peritoneal cavity. The abdomen was then explored through a right paramedian incision, revealing volvulus of the small bowel with gangrene of 73 cm. of intestine. This was treated by resection and end-to-end anastomosis, the abdomen was closed, and herniorrhaphy was performed. Both wounds became infected postoperatively, requiring drainage. The patient was able to go home on the twenty-third postoperative day to continue wound dressings as an outpatient.

Case 6.—Y. K., a 30-year-old male, was admitted with a 2-week history of a painful lump in the left groin and anorexia. The pain had been somewhat worse since the morning of admission and the abdomen had been more distended. On examination his pulse-rate was 90 per minute, blood-pressure 130/90 mm. Hg, and he was slightly dehydrated. The abdomen was generally distended and tender but no rebound tenderness was elicited. There was a small, tender, irreducible, left inguinal hernia.

On exploration he was found to have a left direct inguinal hernia of the Richter's type through a defect in the conjoint tendon. The involved segment of the small bowel was gangrenous and adherent to the sac and a perforation had occurred at the level of the constriction ring. The abdomen was then opened through a right paramedian incision and a purulent peritonitis was discovered. The involved portion of ileum was resected and peritoneal toilet was performed. The abdomen was closed without drainage and herniorrhaphy was carried out. The patient made an uncomplicated recovery. A review of the abdominal radiographs revealed that apart from dilated loops of small bowel and multiple fluid levels, free gas was present under the right diaphragm and had been missed preoperatively.

Case 7.—N. E., a 31-year-old female, gave a 2-week history of colicky abdominal pain, vomiting, and constipation. On examination she was very dehydrated and shocked, with a pulse-rate of 140 per minute and a systolic blood-pressure of 55 mm. Hg. The abdomen was distended and tender and bowel-sounds were absent. There was a small peri-umbilical mass, which had not been previously noticed by the patient. Nasogastric aspiration yielded faeculent material. The patient was resuscitated with intravenous fluids, including 1 litre of blood, and at the time of operation her blood-pressure was 110/70 mm. Hg and pulse 120 per minute. She was found to have a small narrow-necked umbilical hernial sac which was distended with pus, and there was gross peritoneal soiling with intestinal contents. A formal laparotomy incision was made but the patient developed a cardiac arrest and could not be resuscitated. At post-mortem examination the generalized peritonitis was confirmed. There was fat necrosis around the umbilical site, and 45 cm. from the ileocaecal valve there was a circumscribed necrosis of the antimesenteric border of the ileum with central perforation. The final diagnosis was generalized peritonitis resulting from a strangulated umbilical hernia.

Case 8.—B. M., a 60-year-old male, complained of the sudden onset of generalized colicky abdominal pain and vomiting starting 3 days before admission, the pain later settling in the lower abdomen. He had not noticed a swelling in the right groin until the onset of the abdominal pain. On examination the patient was obviously very ill and was dehydrated and toxic. The pulse was 120 per minute and the blood-pressure was 140/90 mm. Hg. The abdomen was distended, tense, and generally tender with marked guarding, and the bowel-sounds were diminished. A tense irreducible right direct inguinal hernia was present.

At operation the defect was found to be in the conjoint tendon and the sac was distended with pus which was welling up from the peritoneal cavity. The abdomen was then opened and gross purulent peritonitis was discovered. A patch of the caecum close to the base of the appendix was gangrenous and perforated; this was thought to have been caused by strangulation followed by spontaneous reduction of a Richter's hernia involving the caecum. The gangrenous portion of the caecum and the adjacent appendix were excised, the defect was repaired in two layers, and peritoneal toilet was carried out. The abdominal wound was closed with drainage, and herniorrhaphy was performed. Both wounds became infected and had to be laid open; secondary suture was performed on the twenty-eighth postoperative day with satisfactory results.

Case 9.—N. E., a 60-year-old female, was admitted with a 10-day history of colicky abdominal pain, vomiting, and painful swelling in the right groin. On examination she was dehydrated, her pulse was 100 per minute, and blood-pressure 100/60 mm. Hg. The abdomen was generally distended, rigid, and tender with visible and palpable peristalsis. There was a small right femoral hernia which was hot, tender, and irreducible.

At operation the hernia was found to contain a gangrenous knuckle of the antimesenteric border of the ileum which was excised and repaired in two layers. However, copious amounts of pus flowed out of the general peritoneal cavity, and the abdomen was therefore explored through a right paramedian incision. This revealed a generalized purulent peritonitis but no other intraperitoneal lesion was discovered. Peritoneal toilet was carried out, the abdomen was closed without drainage, and a Lotheisen-Cooper herniorrhaphy was performed. Infection of the groin wound required removal of skin sutures for drainage. The patient was able to leave hospital on the eighteenth postoperative day and the wound subsequently healed satisfactorily.

The findings in these 9 patients are summarized in *Table I*. In addition, in 4 patients the presence of peritonitis in association with a strangulated hernia was recognized preoperatively and the details of these patients are summarized in *Table II*.

DISCUSSION

These cases demonstrate three different ways in which strangulated hernia and peritonitis can coexist. Zuckerkandl (1891) reported the case of a 55-year-old man with a 6-day history of a painful irreducible hernia, which on exploration contained pus only, secondary to a generalized peritonitis arising from a perforated acutely inflamed appendix. Since this report several similar instances have been reported (Cronin and Ellis, 1959). Seven of our patients (*Cases* 1–5, 10, and 11) belong to this category. In the reported cases in which the cause of the peritonitis was identified this included perforated peptic ulceration, pyosalpinx, and pneumococcal peritonitis, but perforated acute appendicitis accounted for the majority of cases—no doubt a reflection of its relative importance in the aetiology of generalized peritonitis. On the other hand, the rarity of appendicitis in our list (1 in 7 cases) may be explained on a basis of its relatively lower incidence in our patient population. The association of acute pancreatitis and strangulated hernia has not been previously reported, and although acute pancreatitis is an even less common cause of acute abdomen than appendicitis in Uganda it accounted for 2 of our 7 cases. Our cases support the finding of Cronin and Ellis (1959) that the presence of a large amount of fluid in the peritoneal cavity and delay in the treatment of the peritonitis are the factors which favour the development of this complication.

In 5 of our patients (*Cases* 6–9 and 12) the generalized peritonitis was caused by extension of infection from the gangrenous loop of bowel in the strangulated hernia. All 5 hernias were of the Richter's type: 2 inguinal (both direct), 2 femoral, and 1 umbilical hernia. The increased proneness to strangulation in direct hernias in the African has been noted by Cole (1964), and a high proportion of these are of the Richter's type. Gangrene of the knuckle of the bowel is a well-recognized feature of strangulated Richter's hernia because of the less severe symptoms that it produces. Bacterial invasion of the dying contents of the sac occurs if the obstruction is unrelieved. This is initially limited to the sac for days and sometimes for weeks; it usually terminates as a superficial abscess and is an occasional cause of external intestinal fistula. Generalized peritonitis may supervene because of extension of infection from the sac to the general peritoneal cavity, as in *Case* 9. More commonly, however, the necrosis of the hernial contents results in a perforation at the line of demarcation or spontaneous reduction, with free leakage of intestinal contents into the peritoneal cavity. The operative findings and the radiological demonstration of gas under the diaphragm in one of our patients confirm this sequence of events.

The most important factor in the development of this complication is the duration of the obstruction, and the fact that Richter's hernias produce relatively less severe symptoms often results in the patient not seeking medical help until severe complications ensue. In the case involving the caecum the duration of symptoms was 3 days, while in the 4 cases involving the small bowel symptoms had been present for 10 days or longer.

A third way in which generalized peritonitis coexists with strangulated external hernia is when the gangrenous loop of bowel lies in the peritoneal cavity. A rare but well-recognized example of this is Maydl's hernia (hernia-in-W). Philip (1967) has described a less known presentation in which the intra-abdominal portion of the small intestine proximal to the site of hernial obstruction in right inguinal hernia becomes obstructed by the caecum. He described 4 illustrative cases and claimed that 14·4 per cent of strangulated hernias in Tanzania were of this variety. Only 1 of our own cases conformed to this description (*Case* 13) and in this case the presence of peritonitis was recognized preoperatively. However, as the mortality from all types of strangulated hernia in Mulago Hospital is 3·0 per cent (McAdam, 1961) it is unlikely that cases of this presentation have passed unrecognized.

A correct preoperative diagnosis is notoriously difficult to make. None of our first 9 cases nor those reviewed by Cronin and Ellis (1959) was diagnosed correctly preoperatively. As the latter authors stated, 'it might appear surprising that difficulty should have arisen in differentiating between a peritonitis and a strangulated hernia, but the presence of a painful lump, about which the patient complains bitterly, makes it difficult for the surgeon to entertain any other diagnosis'. In all our patients the clinical picture in retrospect clearly suggested the presence of a generalized peritonitis, and it would appear that the failure of the surgeon to entertain any other diagnosis is the main obstacle to correct diagnosis. This state of affairs is not helped by the fact that whereas strangulated external hernia is a very common emergency its association with peritonitis is relatively rare. Nevertheless, failure to recognize this association when it occurs is an unjustifiable lapse in clinical acumen. Recently, by ensuring that every diagnosis of strangulated hernia is qualified with 'no evidence of generalized peritonitis' or otherwise, 4 such cases have been recognized preoperatively (*Table II*). As strangulated hernia is mostly dealt with by junior hospital doctors the adoption of this policy has proved successful in drawing attention to the possibility of this complication. Any patient with strangulated external hernia whose symptoms have lasted for more than 48 hours requires careful history-taking and examination to elucidate the sequence of events and to exclude the presence of generalized peritonitis.

Clearly a laparotomy is the best procedure when the presence of peritonitis is recognized preoperatively. This permits primary treatment of the intraperitoneal lesion and adequate peritoneal toilet. However, no conclusive evidence for the most satisfactory method of treating the hernia has emerged from these cases. In the 2 cases in whom peritonitis was due to acute pancreatitis the herniorrhaphy wounds healed primarily. On the other hand, only in 1 of the cases not recognized preoperatively in which the peritonitis was purulent did the wounds heal without complication. It can therefore be inferred from these results that a formal repair of the groin hernia through a separate incision is only justified when the associated peritonitis is not of the purulent type.

Three different methods were employed in the management of the hernia in the 4 patients who had primary laparotomy. In 1 patient the inguinal defect was left untreated and a formal repair was envisaged at a later date. However, the hernia reappeared on the fourth postoperative day with features of obstruction, and an emergency herniorrhaphy had to be performed. Strangulation of a pre-existing external hernia in the postoperative period has been described by Maurath and Frauke (1966) and Pfeffermann and Freund (1972).

In 2 patients the peritoneal connexion to the hernial sac was obliterated with a purse-string suture at the neck of the sac. In both patients the sac subsequently developed collections of pus requiring drainage, and in 1 patient with a scrotal hernia this was the source of prolonged morbidity. It is interesting that in 2 of the cases reported by Cronin and Ellis (1959) there were late collections of pus in the hernial sac following a generalized peritonitis. Although it is uncertain what is the ultimate recurrence rate following this method of treatment it has the advantage that it should prevent the possible occurrence of strangulation in the early postoperative period with the attendant risks of reoperation. However, it would appear that if this procedure is to be undertaken in the presence of purulent peritonitis the hernial sac should be drained through a separate stab incision.

In 1 patient the hernia was repaired through a pre-peritoneal approach to the internal ring (Nyhus, 1964) without complications. A separate incision was unnecessary as access to the pre-peritoneal space was achieved through the low abdominal incision. This procedure is technically easy, it offers a permanent cure for the inguinal hernia and is a minor addition to the operation. It is likely that the outcome from this approach will be superior to other methods and its further evaluation is indicated.

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PANCREATIC REFLUX DURING OPERATIVE CHOLEDOCHOGRAPHY

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SUMMARY

Reflux of dye into the pancreatic duct was studied during operative choledochography performed in 211 conservative cases undergoing elective cholecystectomy. Reflux occurred with the same frequency whether the dye was injected by hand or by a constant-flow electrically driven pump. The outlined pancreatic duct was abnormal in 27 per cent of cases where a pancreatogram was obtained. No association was found between ductal stones and reflux of dye into the common bile-duct. Pancreatic reflux was associated with a low biliary pressure and segmental duodenal activity.

THE significance, if any, of reflux of contrast medium into the pancreatic duct during operative choledochography remains undecided. Its reported incidence varies from 8 to 32 per cent (Schulenberg, 1966; Whitaker, Parkinson, and Howell Hughes, 1968; Cuschieri, Howell Hughes, and Cohen, 1972). There is little doubt that this is a phenomenon which is usually obtained under highly uncontrolled conditions. Most published work on this subject has been done without due regard to such variables as the rate of injection of dye, pressure of injection, type of anaesthesia, and the use of premedicating drugs. This paper deals with the incidence and significance of pancreatic reflux in 211 consecutive cases undergoing elective cholecystectomy where an operative choledochogram was performed using either hand or pump injection of dye.

MATERIALS AND METHODS

Patients undergoing cholecystectomy were studied. The age range was 28–72 years. In the last 45 patients no drugs were administered for 10 hours before operation in all but 2 cases. Anaesthesia was carried out with thiopentone, nitrous oxide, and oxygen, a combination which has no effect on biliary pressures (Mallet-Guy, 1952). Muscle relaxation was achieved with D-tubocurarine. Each patient had an operative choledochogram through a Portex cannula inserted into the common bile-duct via the cystic duct. Dye (sodium diatrizoate, 40 per cent) was injected by hand (3–9 ml.) in the first 166 cases and by an electrically driven pump in the last 45 patients. The delivery of the pump was adjusted to a constant rate of 6 ml. per minute. The pressure exerted by the pump varied with the resistance to flow in the tubing but it averaged 25 mm. Hg. This method of manometric choledochography has been previously reported (Cuschieri and others, 1972) and the apparatus is shown in *Fig.* 1. It allows common bile-duct pressure monitoring during the injection of dye together with simultaneous intraduodenal pressure monitoring.

RESULTS

1. Incidence of Pancreatic Reflux.—Reflux of contrast medium into the pancreatic duct occurred in 23 out of 166 cases of hand injection (13·9 per cent) and in 8 out of 45 consecutive cases of pump injection (17·7 per cent). The overall incidence of pancreatic reflux was 15·4 per cent.

2. Incidence of Acute Pancreatitis.—Out of the total 211 cases, 1 patient developed acute pancreatitis after surgery with a rise in the serum amylase of 2050 Somogyi units per 100 ml. This patient did not have pancreatic reflux of sodium diatrizoate during operative choledochography.

3. The Outlined Pancreatic Duct.—Eight out of the 31 pancreatograms obtained showed an abnormal pancreatic duct. In all these the duct was dilated (diameter $>0·3$ cm.) and in 1 case calculi were present in the dilated pancreatic duct (*Fig.* 2). Three of these patients had chronic pancreatitis which was confirmed at operation.

4. Associated Choledochal Pathology.—In this series there were 18 cases of ductal stones and pancreatic reflux was present in only 1 of these. Moreover, in another case pancreatic reflux only occurred after removal of a stone from the lower end of the bile-duct (*Fig.* 3). The common bile-duct showed no radiological abnormality in 23 reflux cases with a normal pancreatic duct. Dilatation of the common bile-duct ($>1·0$ cm.) was present in 3 cases of pancreatic reflux where the outlined pancreatic duct was abnormal.

5. Dynamics of Reflux.—Reflux of sodium diatrizoate into the pancreatic duct was observed in 8 cases where dynamic pressure changes could be monitored simultaneously in the common-bile-duct and second part of the duodenum. In these cases pancreatic reflux was associated with a low resting choledochal pressure (mean 2·3 mm. Hg, range 0–6·0 mm. Hg). The average choledochal resting pressure for the 45 consecutive pump injection cases was 6·3 ± 4·0 mm. Hg. Reflux into the pancreatic duct occurred during injection but after the entry of dye into the duodenum in 6 cases and in these the choledochal sphincter was hypotonic as shown by the filling/pressure curve (*Fig*. 4). In the other 2 cases pancreatic reflux occurred after the injection of dye at a time when the duodenum showed gross segmental activity (*Fig*. 5).

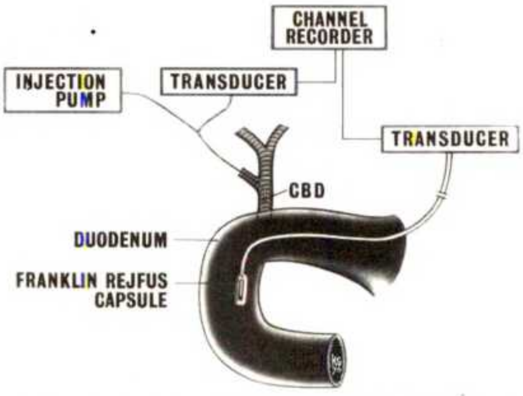

FIG. 1.—Apparatus used for manometric choledochography which allows dynamic pressure monitoring during operative choledochography using sodium diatrizoate (40 per cent) and a constant-flow injection pump.

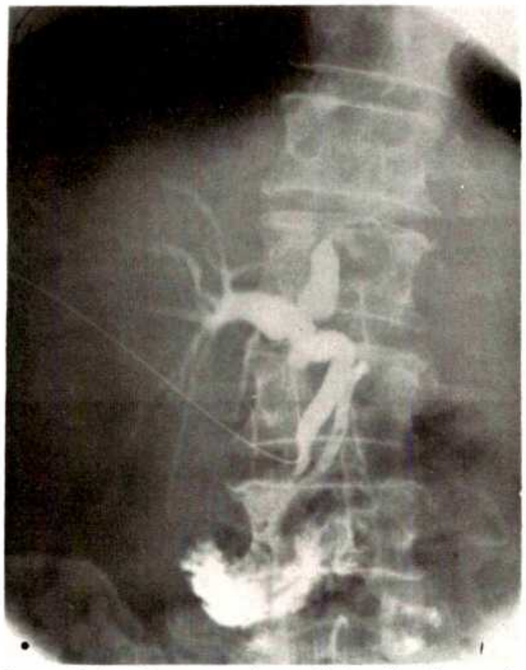

FIG. 2.—Reflux of contrast medium outlining a dilated pancreatic duct containing at least one calculus.

6. Follow-up of Patients.—All the cases of pancreatic reflux have been carefully followed up for periods extending from 14 to 46 months. Three were known to have chronic pancreatitis at operation and have required several hospital admissions for attacks of pancreatitis. One patient has developed a relapsing pancreatitis since her cholecystectomy 2 years previously. A barium-meal examination done at this stage showed reflux of barium into both the common bile-duct and the pancreatic duct (*Fig*. 6). None of the 23 cases with a normal outlined pancreatic duct has developed evidence of pancreatitis after operation.

DISCUSSION

Pancreatic reflux during operative choledochography occurred with the same frequency when dye was injected into the common bile-duct by a constant-flow pump at physiological pressure ranges as when injected by hand where excessive pressure peaks are known to be created.

Schulenburg (1966) considered pancreatic reflux as having no clinical importance and regarded it as an incidental finding at operative choledochography. The present authors, whilst agreeing that this is true in the majority of cases, consider it to be an overstatement as cases with an abnormal outlined pancreatic duct may have or subsequently develop chronic pancreatitis, as did 4 out of 8 cases with abnormal pancreatograms in the present series.

Following isolated reports of acute pancreatitis resulting from the use of lipiodol and water-soluble dyes (Zech, 1949), Howell and Bergh (1950) found a positive correlation between biliopancreatic reflux of contrast medium and elevation of the serum amylase. However, their work was done on postoperative T-tube choledochograms where the problem of sepsis complicates the picture, and the contrast media used were Thorotrast and Diodrast. The only case in the present series of 211 operative choledochograms that developed acute postoperative pancreatitis did not have pancreatic reflux during

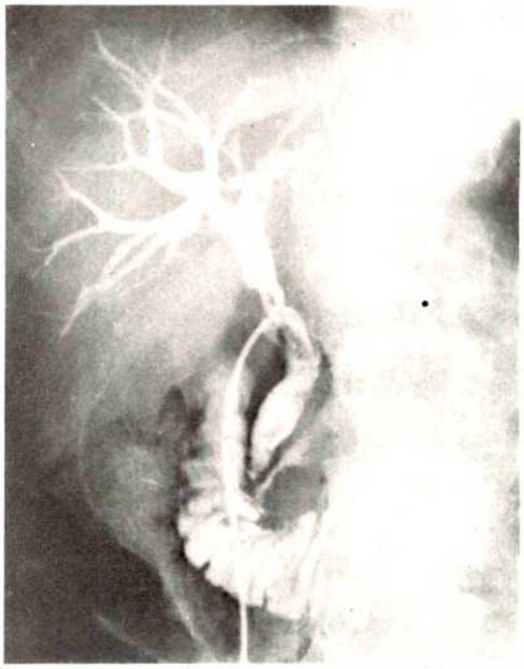

FIG. 3.—Pancreatic reflux of contrast medium seen after removal of a stone from the lower end of the common bile-duct.

operative choledochography. The present authors are in agreement with Schulenberg (1966) in considering postoperative pancreatitis after operative choledochography as extremely uncommon unless a large amount of dye is injected under pressure.

Experimental work in dogs suggests that reflux of dye into the pancreatic duct indicates biliary hypertension. Thus, Parry, Hallenbeck, and Grindlay (1955) have shown that in the dog the pressures in the common bile-duct are lower than those in the pancreatic duct during a fasting period, and this relationship existed in the majority of cases after meals. However, the anatomy of the periampullary region in the dog differs considerably from that of the

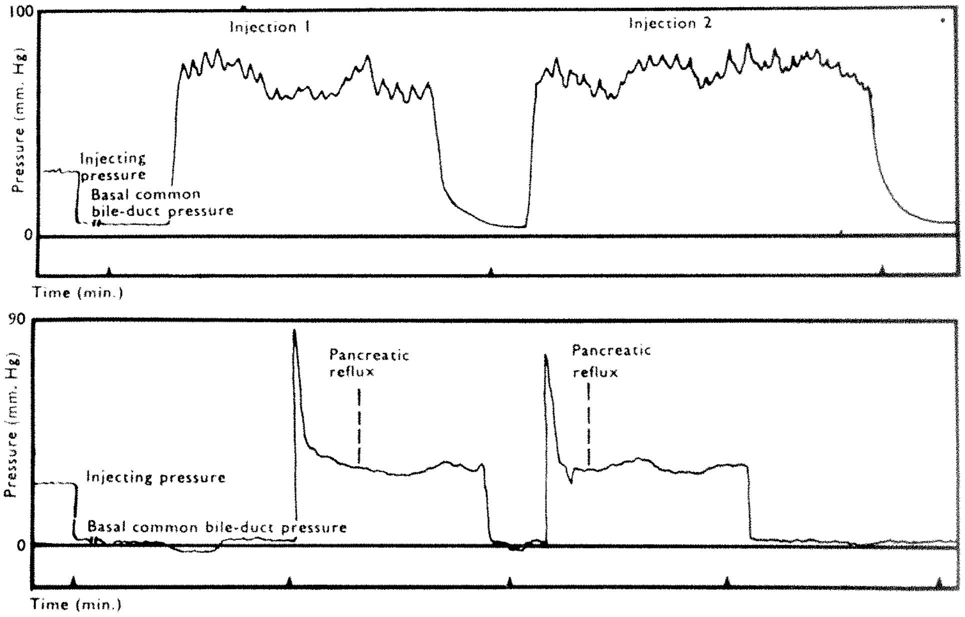

FIG. 4.—Pressure/filling curve in a case showing pancreatic reflux during injection of dye (*below*), compared with a normal choledochal pressure/filling curve (*above*). In the reflux case the common bile-duct pressure during injection of dye was similar to the pressure of injection. This indicates that the choledochal sphincter was offering little or no resistance to the flow of dye into the duodenum.

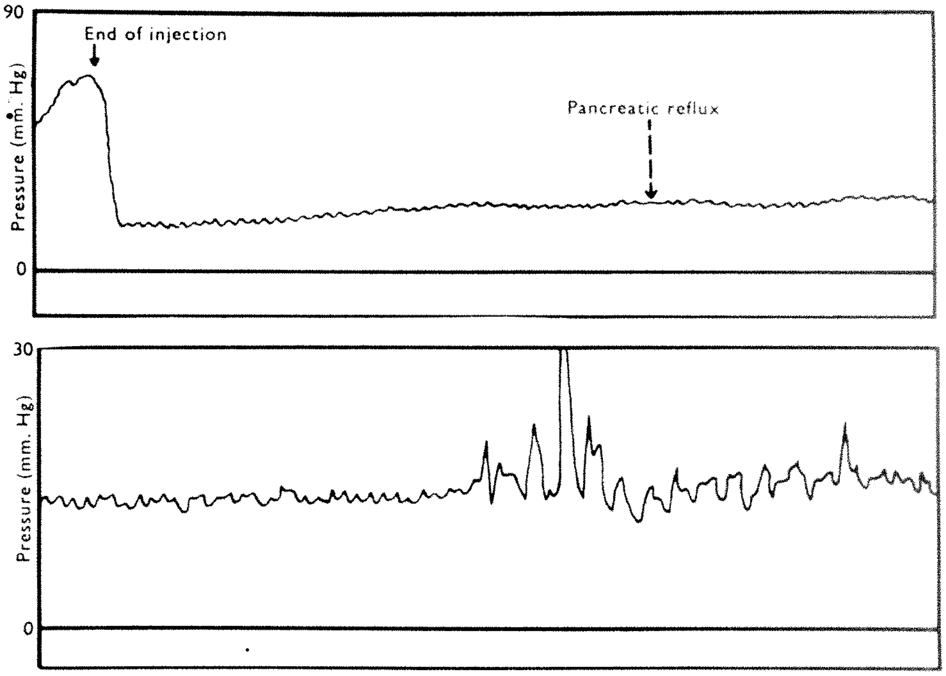

FIG. 5.—Pancreatic reflux occurring after injection at a time when the duodenum exhibited gross segmental activity. *Above*, common bile-duct pressure tracing. *Below*, duodenal pressure tracing.

human and findings from such animal experimentation are not therefore applicable to man. Our findings show that reflux of dye into the pancreatic duct is not associated with obstructive lesions of the choledochus and that the resting common bile-duct pressure in reflux cases is not elevated from the normal range. Reflux of contrast medium into the pancreatic duct can only occur when the choledochal sphincter is relaxed and this is in support of the work of Kune (1970).

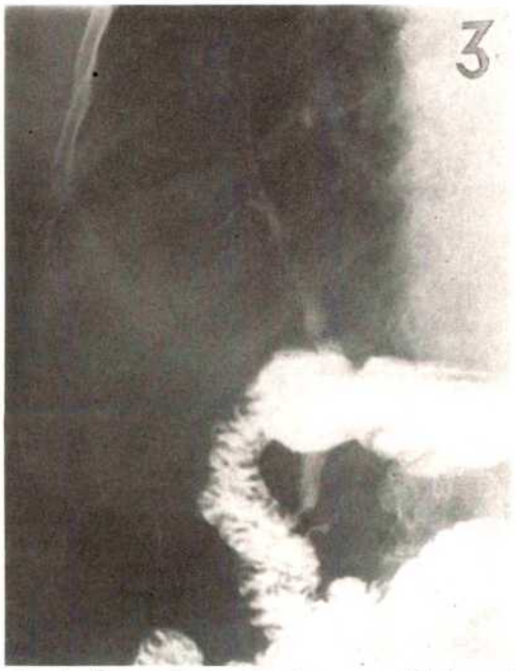

FIG. 6.—Reflux of barium into the common bile-duct and pancreatic duct during a barium-meal examination in a patient with chronic pancreatitis.

Analysis of the pressure/filling curves in reflux cases indicates the presence of a hypotonic choledochal sphincter in some cases where reflux of the dye occurred during injection, i.e., choledochopancreatic reflux.

Duodenopancreatic reflux was encountered in cases showing segmental duodenal activity and occurred after the injection of dye had stopped. One of the 2 patients exhibiting this type of reflux developed chronic pancreatitis and refluxed barium into both the pancreatic and common bile-ducts during a barium-meal examination carried out some months after cholecystectomy. This may be of some significance in view of reports (Muller-Weiland, 1963; McCutcheon, 1964; Anderson, 1967) of abnormal duodenal motility patterns in patients with chronic pancreatitis. It would seem that the normal choledochal sphincter guards against reflux of duodenal contents into the pancreaticobiliary tree and this reflux is potentiated by a hypotonic choledochal sphincter and/or the high pressure that can be generated by segmental activity in the duodenum. The suggestion of McCutcheon (1964) that such reflux may be the prime cause of pancreatitis requires further investigation. Other evidence in support of this hypothesis includes the report of Dreiling, Kirschner, and Nemser (1960) of a series of patients who developed pancreatitis in association with lesions producing distal duodenal obstruction. Experimentally, a closed-loop duodenal obstruction in dogs results in a severe necrotizing pancreatitis (Pfeffer, Stasior, and Hinton, 1957).

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EARLY AND DELAYED OPERATION IN ACUTE GALL-STONE DISEASE

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Summary

In a review of 157 patients admitted to hospital as emergencies with acute gall-stone disease it was found that 52 cases (33·1 per cent) had undergone definitive operation for gall-stones during the emergency admission in spite of an overall conservative policy in relation to operation. The results of these early operations are compared with those of operations delayed to a second admission in other patients of this series. There was no significant difference in mortality or morbidity, but there was a saving on average of 5 days in hospital for those patients who were operated on at the first admission.

The clinical manifestations of gall-stones can properly be referred to as 'gall-stone disease'; in this account we confine ourselves to manifestations arising in the biliary tract, thereby excluding the extra-biliary complications of pancreatitis and gall-stone ileus.

In the management of any acute episode of gall-stone disease conservative treatment is commonly preferred, no matter whether inflammatory or mechanical factors predominate. The policy of conservatism, aimed primarily at inflammatory disease, derives from the early part of this century and has been described as reserving surgical intervention within the first few days for uncertain diagnosis or uncontrolled infection (Till, 1963); acute symptoms usually subside, and operation necessary to deal with stones is planned as a delayed elective procedure at a later date. This view is based on the premiss that operation during the acute phase may be difficult or even dangerous; as a policy it succeeds in that the resulting mortality is generally low. Nevertheless, the timing of operation remains controversial and many have argued that early definitive operation without planned delay will avoid a waiting period, which is not entirely free from further painful attacks, and allow the patient to resume a normal life sooner; if operation is carried out in the first few days symptoms are at once abolished and further spread of inflammation beyond the gall-bladder is prevented (Devine, 1940; Glen and Thorbjarnson, 1963; Smith and Sherlock, 1964; Essenhigh, 1966; Payne, 1969; Van der Linden and Sunzel, 1970). It cannot be denied that these are strong arguments against delay.

The management of our own patients has been based on a conservative policy. Even so, considerable numbers of patients for various reasons have had early operation, defined here as operation during the emergency admission. We have compared the results in these patients with the results in those treated conservatively followed by delayed operation at a later admission in a group of patients all of whom were admitted initially as emergencies. If early operation is fraught with difficulties its results might be expected to compare poorly with delayed operation when a conservative policy is in operation, because patients selected for early operation will tend to be those in whom the disease is worse and has failed to respond to conservative management. It is not intended to suggest that all cases of acute gall-stone disease present the same management problem, for the spectrum is wide. Operation is of necessity early, even urgent, in some cases, but in the majority it can safely be postponed to a second admission. The question is whether postponement offers any advantage to this majority of patients.

THE SERIES

The patients presenting as emergencies with acute gall-stone disease admitted to two surgical units of the Royal Infirmary, Glasgow, during the years 1966–9 were surveyed. The units had similar admission arrangements and both adopted a conservative policy. All the patients were shown to have gall-stones either by operation or by radiology. The composition of the group of cases from each unit was very similar and they are therefore considered together, the total number of patients being 157 (45 men and 112 women).

The patients have been placed in three treatment groups in relation to the definitive operation, by which is meant cholecystectomy and, when required, operations to clear stones from the ducts, as distinct from simple emergency drainage operations of the gall-bladder or ducts.

Group 1: *Delayed Operation* (60 patients; 38·2 per cent).—Orthodox conservative management of the acute attack and discharge from hospital, followed by readmission at a later date and definitive surgery. The mean age of this group was 58 years (range, 21–81 years) and there was a male : female ratio of 17 : 43.

Group 2: *Early Operation* (52 patients; 33·1 per cent).—Definitive operation during the first (emergency) admission. The mean age was 56 years (range, 17–80 years) and the male : female ratio was 17 : 35.

Group 3: *No Operation* (45 patients; 28·7 per cent).—The patients in this mixed group either died without operation (3) or after cholecystostomy alone (1), declined operation (5), or failed to return after initial conservative treatment and discharge from hospital (11). A further 25 patients were considered unfit for definitive operation (15·9 per cent of the series). The mean age was 63 years (range 23–87 years) and the male : female ratio was 15 : 30.

The reasons for early operation are shown in *Table I*.

Of the 52 early operations, 8 were performed within 24 hours of admission and 7 more within the first 4 days, an incidence of 9·6 per cent of the whole series. The remaining 37 operations took place between 5 days and 4 weeks after emergency admission. This group is characterized by a high incidence of duct stones, which were found in 40 per cent of patients; ducts were explored in 56 per cent of the early operations. Acute cholecystitis, on the other hand, was present in 29 per cent compared with 45 per cent of the patients in group 1. Duct stones were found in 13 per cent of the patients in group 1, 28 per cent of the ducts being explored.

RESULTS

Three aspects have been examined in this survey: mortality in hospital, postoperative morbidity, and length of total hospital stay. In patients readmitted for delayed operation the total hospital stay is the sum of all the periods spent in hospital; there were usually two admissions, but in a few cases there were intermediate admissions for recurring acute episodes before the final admission for delayed operation.

Mortality.—*Table II* shows that after delayed operation (group 1) there was 1 death (1·8 per cent of the group). A man of 54 years died 3 days after cholecystectomy; no cause of death was apparent at the post-mortem examination. After early operation (group 2) there were 2 deaths (3·9 per cent of the group). One man of 65 years died from myocardial infarction on the second postoperative day and a woman of 72 years died with a stone obstructing the lower end of the common bile-duct 5 weeks after cholecystectomy without duct exploration. There is no statistically significant difference between the mortalities of groups 1 and 2 at the 5 per cent level.

The highest mortality was in the patients who had no definitive operation (group 3) where there were 4 deaths (8·9 per cent of the group). One death from renal failure in a man of 77 years followed cholecystostomy for empyema of the gall-bladder. Two men of 72 and 73 years respectively died from cardiopulmonary failure, and a woman of 58 died from massive pulmonary embolism; she was found at post-mortem examination to have also a carcinoma of the pancreas. The last 3 patients had no operation and they all died within 4 weeks of emergency admission.

The total number of deaths in the series of 157 patients was 7, an incidence of 4·5 per cent. There were 3 operative deaths in the 112 definitive operations (2·7 per cent), and there were 3 deaths during conservative treatment in 104 patients (2·9 per cent).

Postoperative Morbidity.—In a retrospective survey of this kind there was no set pattern for recording postoperative complications. The complications noted have been extracted from the case records and summated in *Table II*. The proportion of patients having recorded complications was about the same following delayed and early operation; for group 1, 30·0 per cent, and for group 2, 27·7 per cent.

As would be expected, and considering all the operative cases together, wound infection and pulmonary infection occurred most often, in 13·1 and 10·7 per cent of patients respectively. Cardiac and renal problems were the next most frequent complications, occurring in 6·3 and 5·4 per cent of patients respectively. Other complications, including postoperative peritonitis, haemorrhage, wound disruption, and jaundice, were infrequent, the incidence of none of these complications exceeding 4·5 per cent. No special note of deep-vein thrombosis had been made; it was only recorded twice when it resulted in marked swelling of the leg.

Postoperative stay in hospital (*Table III*) was slightly less on average after delayed operation (14 days) than after early operation (17 days).

Table I.—REASON FOR EARLY OPERATION

	No. of Cases
Continuing pain	29
Jaundice	12
Severe sepsis	5
Laparotomy for acute abdominal symptoms	4
Palpable obstructed gall-bladder	2
	52

Table II.—MORTALITY AND POSTOPERATIVE MORBIDITY

	GROUP 1		GROUP 2		GROUP 3	
	No.	Per cent	No.	Per cent	No.	Per cent
Patients dying in hospital	1	1·8	2	3·9	4	8·9
Patients with complications of operation	18	30·0	20	27·7	—	—

Table III.—HOSPITAL STAY

HOSPITAL STAY (d.)	GROUP 1		GROUP 2		GROUP 3	
	Mean	Range	Mean	Range	Mean	Range
Postoperative	14	3–34	17	3–50	—	—
Total	30	14–55	25	7–62	14	7–50

Table IV.—SUMMARY OF THE FINDINGS IN 54 CASES OF ACUTE CHOLECYSTITIS

	GROUP 1	GROUP 2
No. of patients	39	15
Mortality	1 (2·6 per cent)	1 (6·7 per cent)
Morbidity	12 (30·8 per cent)	5 (33·3 per cent)
Mean total hospital stay (d.)	29	26
Difficult operations	5	0

Total Hospital Stay.—The patients in group 1 accepted advice to return for definitive surgery, having been treated conservatively at the emergency admission. While awaiting elective readmission 6 patients (10 per cent) were readmitted with further acute episodes of gall-stone disease; all these patients were later discharged when the acute episode had subsided.

The mean total hospital stay for group 1 patients (*Table III*), including the emergency and elective admissions and any intermediate admissions, was 30 days (range, 14–55 days). For group 2 patients, in whom surgery was completed at the first admission, the mean total hospital stay was 25 days (range, 7–62 days).

DISCUSSION

The results may be summarized as follows. Among the patients surveyed with acute gall-stone disease there was no statistically significant difference in the operative mortality between the patients who were operated on during the emergency admission (group 2) and those having delayed operation at a second admission (group 1), despite the general application of a conservative attitude to operation. Likewise, the frequency of recorded postoperative complications was nearly the same in both groups. The postoperative hospital stay, however, was a little longer in the patients who were operated on early; despite this, and of more importance, the total hospital stay was reduced by 5 days by early operation. Furthermore, 1 in 10 of the patients awaiting delayed operation was readmitted during the waiting period because of further attacks of pain; there must also have been others in whom attacks recurred but who did not require hospital admission. It should be added that 11 patients in group 3, in whom no operation was done because they failed to return for delayed surgery, would presumably have benefited from operation carried out during the emergency admission.

These findings are in keeping with those of Van der Linden and Sunzel (1970) in Sweden, who found the total hospital stay to be shortened by 8 days as a result of early operation. There were no deaths in their series after early operation, which was carried out during the emergency admission on the next convenient day after the diagnosis had been clearly established and the patient had been assessed as fit for surgery. They then examined sickness insurance payments and concluded that return to work was delayed by a factor of 50 per cent after delayed operation compared with early operation. Glen and Thorbjarnson (1963) and Essenhigh (1966) also commented on a saving of time in hospital achieved by early operation, without increased mortality.

Apart from the importance of the fitness of the patient (in our series 15·9 per cent of patients were considered to be unfit for surgery), a major question is the difficulty of operation and liability to complications in early surgery when florid acute cholecystitis is present. *Table IV* sets out the findings in our cases of acute cholecystitis. There was 1 postoperative death in both group 1 and group 2, while the frequency of postoperative complications was the same in the two groups. A survey of the operation notes suggests that none of the early operations was considered unduly difficult by the operator, whereas 5 were considered difficult after a waiting period and delayed surgery. Smith and Sherlock (1964) pointed out that difficulty at delayed surgery after a severe attack of acute cholecystitis is accepted by the surgeon though in fact if the operation had been done earlier it might have been found easier. In Payne's (1969) series of 398 patients with acute cholecystitis operation was performed within a few hours of admission in one-third of the cases without mortality. Smiddy (1970) undertook emergency cholecystectomy on the day of admission in 100 consecutive patients with clear-cut acute cholecystitis who were considered to be fit for surgery, and there were 3 deaths; these occurred in patients with a mean age of 75 years. This mortality compares favourably with 4 deaths in a series of 100 cases who were treated conservatively. However, it is possible that some of the latter cases might have been unfit for emergency surgery. The postoperative stay was greatly prolonged after emergency operation and Smiddy saw no place for routine emergency surgery in these circumstances. None of our patients who were operated on within 4 days of admission died.

The experience of the operator is of importance in any consideration of early operation, a point which is brought out by Van der Linden and Sunzel (1970). In our series almost all the early operations were done by consultant surgeons, whereas surgeons in training carried out one-third of the delayed operations of group 1.

The analysis of the cases of acute gall-stone disease presented here indicates that, given experienced surgeons, early definitive surgery after proper assessment of the patient is safe and offers some advantage over surgery delayed on conservative principles. Advancing the time of surgery has not interfered with full exploration of the ducts, which were explored in over half the cases operated on during the emergency admission.

Acknowledgements.—We are grateful to our colleagues, in particular Mr. J. Hutchison, for allowing us to survey their patients, and to Dr. P. W. Macfarlane for the statistical calculations.

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MEASUREMENT OF STOMA SIZE FOLLOWING CHOLEDOCHODUODENOSTOMY BY TRANSDUODENAL CHOLANGIOGRAPHY

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SUMMARY

Previous reports concerning the operation of choledochoduodenostomy have stressed the importance of an 'adequate' stoma. However, there does not appear to have been an attempt to measure the stoma size by some objective method.

The results with a new technique for the assessment of the stoma and duct system postoperatively are reported. The method involves the use of a transnasal guided catheter system with selective catheterization of the common bile-duct via the stoma. Accurate delineation of the stoma and ducts is then possible.

The stoma was successfully catheterized in 13 out of 16 attempts, and satisfactory radiographs were obtained in 1 other patient by a modification of the technique. The measurements of the maximum diameter of the stoma were considerably less than those reported previously; despite this the clinical result in the short term was good in all except the 2 patients in whom the stoma could not be demonstrated.

THE operation involving side-to-side anastomosis between the common bile-duct (or common hepatic duct) and the proximal duodenum has been termed 'external choledochoduodenostomy' (Capper, 1961), 'biliary fenestration' (Magarey, 1966), and 'side-to-side choledochoduodenostomy' (Degenshein and Hurwitz, 1967). These terms refer to basically similar procedures although there are some differences in technique. The operation is increasingly accepted as a useful procedure in patients with a variety of biliary disorders, and may be considered in patients with multiple or recurrent stones in the common bile-duct and in patients with carcinoma or benign lesions obstructing the distal common bile-duct. It has even been advised as a routine procedure in patients with common bile-duct stones (Magarey, 1966).

All previous reports stress the importance of an adequate stoma in order to avoid the complication of ascending cholangitis. Johnson and Stevens (1969) have compared two groups of patients with a stoma greater or less than 2 cm. in diameter with particular reference to the incidence of cholangitis. They concluded that a stoma size greater than 2 cm. was essential to the success of the operation. Other authors (Capper, 1961; Magarey, 1966; Burgess and Kidd, 1967) have drawn similar conclusions. In these papers it appears that the size of the stoma was assessed by the surgeon at operation, and presumably this assessment was based on the length of the incision in the common bile-duct. Unfortunately such a method, even if accurately performed, does not necessarily provide a correspondingly accurate measurement of the stoma after the anastomosis is completed.

We report here our initial results with a new method for the postoperative radiological assessment of the stoma and biliary tract following choledochoduodenostomy. The report deals only with patients having the operation for choledocholithiasis. The stoma is catheterized via a transnasal tube, the principle of the technique being similar to that of selective arteriography. A preliminary report of the method has been published (Sorby and Ham, 1972).

MATERIAL AND METHODS

Patients.—The procedure was performed 16 times in 15 patients. Their ages ranged from 24 to 81 years, all except 1 being over 50 years. All had jaundice due to choledocholithiasis, and 8 patients presented with clinical evidence of cholangitis. Cultures of bile taken at operation were positive in each of these 8 patients.

Table I.—MAXIMUM DIAMETERS OF THE COMMON BILE-DUCT AND STOMA IN THE PRESENT SERIES

CASE No.	DIAMETER OF COMMON BILE-DUCT (mm.)		DIAMETER OF STOMA (mm.)
	Preoperative	Postoperative	
1	?	15	9
2	?	15	15
3	26	16	10
4	28	12	11
5	30	20	10
6a	18	—	Failed
6b	13	13	11
7	20	11	11
8	25	14	14
9	30	20	10
10	22	14	23
11	25	16	19
12	20	8	13
13	21	—	Failed
14	40	14	20
15	29	16	25
Mean	24·1	14·6	14·4

The single young patient (*Case* 6, *Table I*) presented with the clinical features of oriental cholangiohepatitis, and in this instance the biliary stones were largely intrahepatic. This patient had two operations; at the first numerous stones were removed, intrahepatic strictures of the right and left hepatic ducts were dilated, and a choledochoduodenostomy performed. Five months later jaundice and cholangitis recurred. The second operation involved further dilatation of the strictures, removal of intrahepatic stones, and reconstruction of the choledochoduodenostomy.

All the procedures were performed between 12 and 20 days postoperatively.

Operative Technique.—The incision in the common bile-duct (or common hepatic duct) is oblique or vertical and as long as possible. The duodenum is mobilized and a similar oblique incision is made in its first part or near the junction of the first and second parts. The anastomosis is performed with continuous chromic catgut; an external layer of interrupted black silk sutures is added if the wall of the duct is markedly thickened.

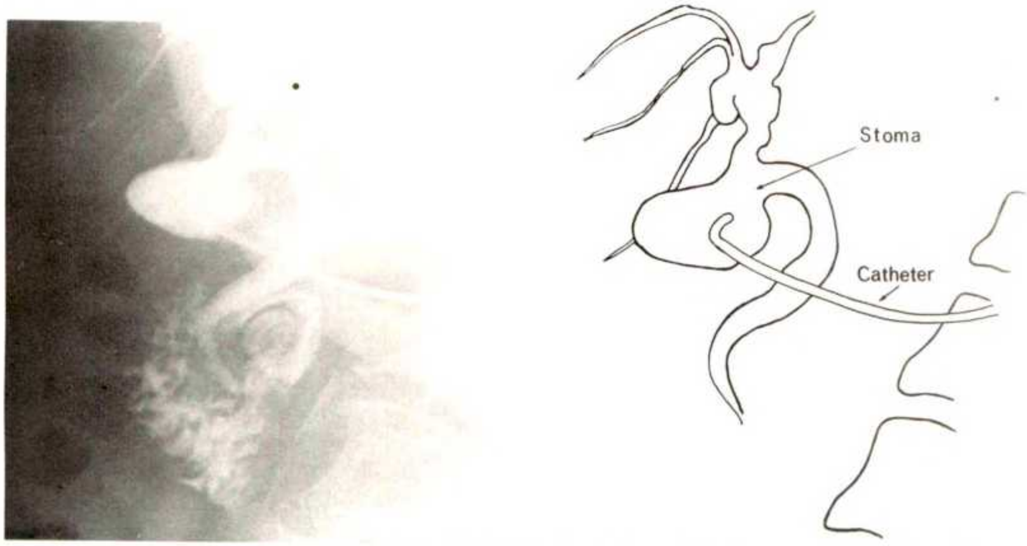

FIG. 1.—*Case* 3. Oblique view of the catheter in the duodenal cap, with dye outlining the stoma, bile-ducts, duodenum, and a duodenal diverticulum.

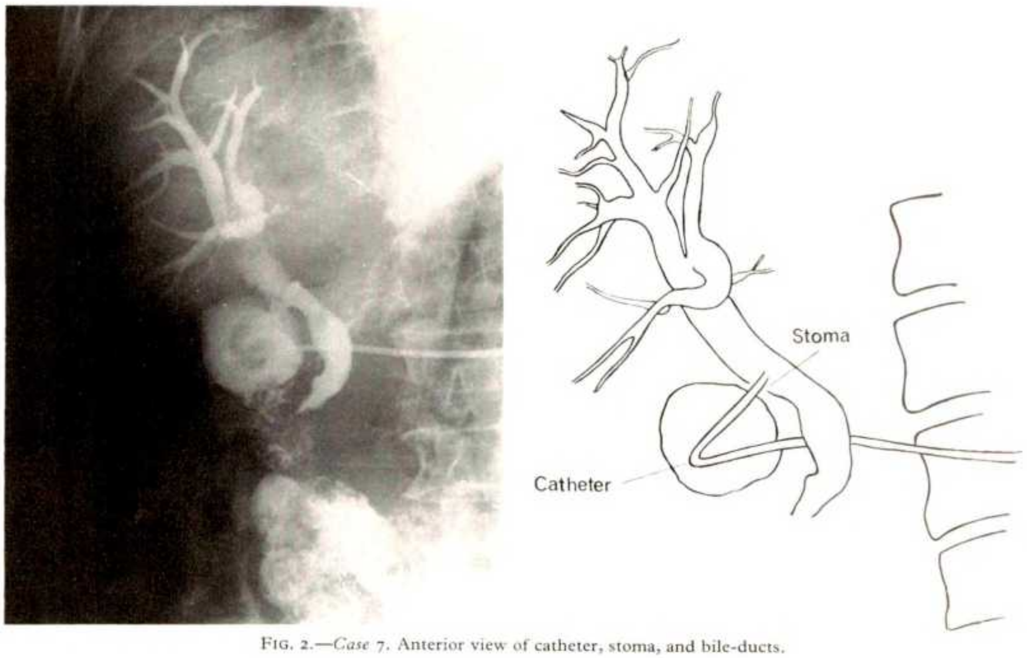

FIG. 2.—*Case* 7. Anterior view of catheter, stoma, and bile-ducts.

In most patients the surgeon estimated the stoma to be at least 20 mm. in diameter. The exceptions were the patient with oriental cholangiohepatitis, in whom the stoma was recognized to be small after each operation, and *Cases* 10 and 15, in whom the stoma was thought to be at least 25 mm. in diameter.

Radiological Technique.—The equipment consists of a Muller-USCI Guide System (United Catheter and Instrument Corporation), a remotely controlled guide-wire and catheter system originally designed for selective and superselective arterial catheterization for arteriography. A guide-wire tip may be flexed from 0° to 180° by a remote handle and a catheter with a soft flexible tip can be advanced out over it. The combined catheter/guide-wire assembly can be rotated 360° around its longitudinal axis.

The patient is premedicated with intravenous diazepam, 5–10 mg., on the radiological screening table and the nasal cavity is anaesthetized locally. The catheter/guide-wire assembly is passed transnasally through the stomach to the duodenum. The tip is flexed superiorly and rotated slightly posteriorly to 'seek' along the margin of the duodenum. When it engages in the stoma the soft tip of the catheter can be advanced over the stationary flexed guide-wire and up into the bile-duct.

Contrast (Urografin 60) is then injected to fill the biliary system and pass through the stoma into the duodenum. Films are taken in the following projections: supine, right oblique, left oblique, and lateral. Cine-films may be performed to show distension filling of the duct system with duodenal peristalsis.

An alternative technique if the stoma cannot be catheterized is to intubate the duodenal cap and inject denser contrast (Urografin 76). The procedure usually takes half to three-quarters of an hour and is well tolerated by the patients.

Measurement of Duct and Stomal Sizes.—The size of the common bile-duct before operation is measured on films obtained by intravenous or percutaneous transhepatic cholangiography. The maximum diameters of the common bile-duct and stoma after operation are measured on the transduodenal cholangiograms. The measurements are expressed to the nearest millimetre and no allowance is made for magnification factors.

RESULTS

Measurement of Duct and Stomal Sizes.—Catheterization of the stoma and transduodenal cholangiography were successful in 13 of the 16 attempts (*Table I*). One failure followed the first operation in the patient with oriental cholangiohepatitis. In this patient (*Case* 6) the diameter of the common bile-duct was at the upper limit of normal preoperatively and construction of an adequate stoma was more difficult than in the other patients. Catheterization of the stoma was unsuccessful in 2 other patients (*Cases* 1 and 13), but adequate films were obtained in *Case* 1 by the alternative method described above.

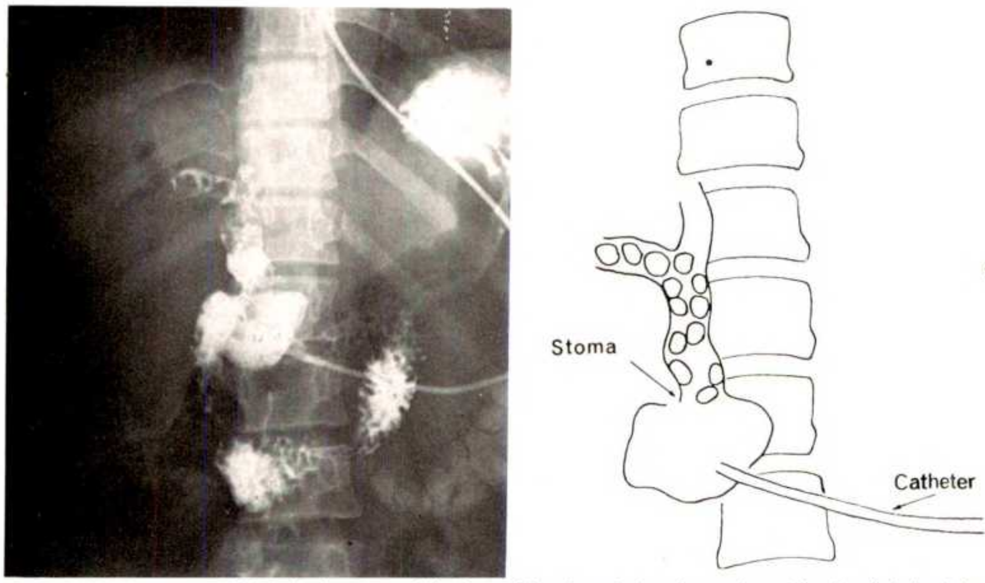

FIG. 3.—*Case* 6. Multiple stones and debris in the common bile-duct and intrahepatic ducts in a patient with oriental cholangiohepatitis.

The mean diameter of the common bile-duct before operation was 24·1 mm. (range, 13–40 mm.); after operation it was reduced to 14·6 mm. (range 8–20 mm.). The mean diameter of the stoma was 14·4 mm. (range 9–25 mm.). The largest diameter of the stoma was usually seen on an oblique or lateral film. Representative transduodenal cholangiograms are shown in *Figs*. 1, 2, and 3.

Clinical Results.—These operations have been performed over the past 2½ years and the period of follow-up is therefore short. Two patients have had clinical episodes of cholangitis. The first was the patient with oriental cholangiohepatitis (*Case* 6); presumably, the cholangitis was related in part to the small stoma and in part to recurrence of the intrahepatic strictures and stones. In the past 18 months he has had two further mild episodes of cholangitis which have subsided spontaneously within 6 days. *Case* 13, in whom transduodenal cholangiography was also unsuccessful, has had one episode of cholangitis which settled with antibiotics. It is anticipated that re-exploration will be necessary.

DISCUSSION

A choledochoduodenostomy stoma is usually regarded as 'adequate' if air is visible in the biliary tree on a plain film or if barium refluxes into the bile-duct from the duodenum during a barium-meal examination (Capper, 1961; Johnson and Stevens, 1969). Magarey (1966, 1971) has used aerated water with or without barium and recommends these methods for the assessment of the stoma and ducts. In our experience the presence of gas in the biliary tree does not necessarily permit measurement of stoma size or assessment of residual pathology in the bile-ducts, although it does of course indicate that the stoma is patent.

The barium-reflux test has three problems: first, reflux does not always occur even though the stoma is patent; secondly, the presence of large amounts of contrast in the stomach and duodenum may make it difficult to visualize the stoma and biliary tree; thirdly, the barium filling of the duct may be so dense as to obscure calculi or may be discontinuous and thus simulate them.

The present technique permits some precision in the demonstration of the stoma and ducts, in that small amounts of contrast can be injected serially. It was possible in this initial study to cannulate the stoma in 13 of 16 attempts. In 1 of the 3 failures an alternative technique—injection of dye into the duodenum adjacent to the stoma—was successful.

The method has permitted direct measurement of the stoma size in more than one projection, so that estimates of its maximum diameter were obtained. In all instances the stoma was considerably smaller than might have been predicted on the basis of the length of the incision in the common bile-duct. In most patients the stoma size was less than the figure of 20 mm. stated to be essential by previous writers. Despite this the clinical result in the short term has been good in all but 2 patients; in 1 of these (*Case* 6) the cholangitis was due to a combination of unusual factors, but both were presumed to have stomas which were too small.

It might be suggested that the reason for these marked differences in stoma size lies in the operative technique used in the present patients. This may be so; however, our technique appears to be similar in all essential respects to those reported previously, and is exactly the same as that reported by Hurwitz and Degenshein (1964). The use of the two-layer anastomosis in some patients could theoretically result in a reduction in stoma size; however, this addition to the technique was only used if the common bile-duct was markedly thickened. Thus, it is likely that the reason for the discrepancy between this and other reports is related to the differences in the methods of assessing the stoma. The reports of Capper (1961) and Madden, Chun, Kandalaft, and Parekh (1970) demonstrate that good clinical results may be obtained if the incisions in the common bile-duct and duodenum are sufficiently long (at least 25 mm.) and the anastomotic technique is satisfactory. However, the present results suggest that in these and other reports the size of the stoma in many patients may be considerably less than the 20 mm. quoted as essential. It is unlikely that the stoma will be much larger than the maximum diameter of the common bile-duct, and there may be little or no advantage to the patient in trying to achieve a stoma larger than this. It is important to note that the common bile-duct was reduced in size after operation in all our patients, but it is uncertain whether this reduction had any influence on the stoma. Finally, it is also uncertain whether a stoma which is adequate as a biliary by-pass for the patient with malignant obstruction is also adequate for the patient with a chronically dilated, thickened, and inflamed common bile-duct associated with calculi.

These questions will only be resolved by objective assessment of the stoma and biliary system soon after operation and subsequent long-term follow-up. The present technique provides the means for such objective assessment. In addition, it may also be useful in the investigation of the patient who presents with recurrent symptoms following choledochoduodenostomy; with the knowledge of the normal range of stoma size or of the postoperative stoma size of that particular patient an accurate diagnosis of stenosis of the stoma may be made.

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SELECTIVE OR TRUNCAL VAGOTOMY?

FIVE-YEAR RESULTS OF A DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL

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SUMMARY

The 5-year results of a double-blind, randomized, controlled trial of selective versus truncal vagotomy, each with pyloroplasty, are reported. Of 100 patients entering the trial, 95 are available for study. There were 4 suspected or proven recurrent ulcers in the truncal group and 1 suspected but no proven recurrence in the selective group. The incidence of episodic diarrhoea was significantly less in the selective group; 4 mild and no severe cases compared with 11 mild and 2 severe cases among the truncal vagotomies. There was no severe dumping; mild symptoms were more common in the selective group but not significantly so. Miscellaneous dyspeptic symptoms were a little more common in the truncal group. Taking all these symptoms into consideration, the Visick clinical status of the selective group was superior. Weight changes, haemoglobin levels, and calcium levels were similar and satisfactory in each group. Selective vagotomy is superior to truncal vagotomy when each is combined with pyloroplasty.

THE operation most frequently used in Great Britain today for chronic duodenal ulcer is truncal vagotomy, combined with some form of pyloroplasty. During the 1960's the modification, introduced in 1948 by Franksson in Sweden and Jackson in the U.S.A. and called by them 'selective vagotomy', in which denervation is limited to the stomach, was strongly advocated by Griffith (1966) in the U.S.A., Burge (1964) in the U.K., Grassi (1970) in Italy, and Amdrup, Clemmesen, and Andreassen (1967) in Denmark. The main benefit claimed for the selective operation was a marked decrease in the incidence of episodic post-vagotomy diarrhoea. Both Marckmann, Baden, and Amdrup (1968) and Sawyers, Scott, Edwards, Shull, and Law (1968) claimed better gastric denervation and a lower incidence of positive insulin tests after the selective procedure.

A number of trials have been published in which the results of selective vagotomy have been compared with those of truncal vagotomy (Kraft, Fry, Wilhelm, and Ransom, 1967; Mason, Giles, Graham, Clark, and Goligher, 1968; Sawyers and others, 1968; Kronborg, Malmstrom, and Christiansen, 1970), but in none of these was the drainage procedure standardized and the follow-up conducted blindly. In an attempt to assess accurately the merits and demerits of these two vagotomies we have organized a prospective, double-blind, controlled trial.

PATIENTS AND PROCEDURE

During 1966 and 1967, 100 of our duodenal ulcer patients coming to elective operation were admitted to a prospective trial, 50 patients having truncal vagotomy and 50 having selective vagotomy, each with a Finney-type pyloroplasty (Kennedy and Connell, 1969). Patients were admitted to the trial only after the abdomen had been opened and the feasibility of vagotomy and of pyloroplasty had been confirmed. All patients with other significant gastro-intestinal disease, such as gastric ulcer, gall-stones, or pancreatitis, were automatically excluded. Patients having emergency operations and those inadequately assessed or unlikely to be available for follow-up were also excluded. At this stage a card was drawn by a nurse from a box containing 50 cards marked 'S' and 50 marked 'T' and the appropriate operation was performed. Selective vagotomy involved preservation of the hepatic branches of the anterior vagus and the coeliac branch of the posterior vagus. The pyloric branch of the hepatic nerve was not divided but both anterior and posterior nerves of Latarjet were divided. Eighty-one of the operations were performed by the same surgeon and the remainder by three other surgeons personally trained in the technique. The two groups were comparable in that there were 11 females in the selective group and 10 in the truncal group; the mean age of the groups was 47 and 45 years respectively. The severity of the ulcer diathesis, as judged by preoperative complications and by levels of gastric acidity, was comparable in the two groups. Annual follow-up was conducted by a physician who had no knowledge of which operation had been used in any individual patient. Careful inquiries and measurements were made in relation to pain, possibility of recurrence of the ulcer, nausea, vomiting of food or bile, dysphagia, heartburn, dumping, food intolerance, flatulence, weight change, alteration in bowel habit, diarrhoea, and patient satisfaction. Each patient was given a clinical grading using a simplification of the Visick grading as follows:—

1. No symptoms: a perfect result.
2. Mild symptoms: not troublesome.
3. More severe symptoms: some degree of disability.
4. Severe symptoms: recurrent ulcer, disabling side-effects, or reoperation.

Attention was particularly concentrated upon dumping and diarrhoea, which were graded + when quite trivial and often not complained of spontaneously, or + + when more severe and a significant nuisance to the patient. A patient was considered to be dumping when he complained of two or more of the following: fullness or discomfort in the epigastrium, nausea, sweating, weakness, palpitations, and the need to lie down after a meal, either large or small. Diarrhoea was defined as the passage of loose watery stools with urgency and sometimes incontinence, recurring at regular intervals of days or weeks. Sometimes there were only two or three motions in an attack; nevertheless the fear of incontinence, sometimes inhibiting the individual from going to work, could merit a ++ rating. The frequency of bowel habit, in motions per week, was recorded in each patient at the start of the trial and changes recorded at annual follow-up. All of these data depended upon the patient's statement. More objective data were provided by records of weight before operation and subsequently by haematological and biochemical studies at the end of 5 years.

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RESULTS

Two positive findings emerged from our early follow-up studies which have already been published. First, there was a significantly lower incidence of positive insulin tests in the selective group, which led us to predict that there would ultimately be a lower incidence of recurrent ulcer. Secondly, at the end of 2 years there was a significantly lower incidence of episodic post-vagotomy diarrhoea (Kennedy and Connell, 1970). The object of the present paper is to publish the results of this trial 5 years after the last operation was performed.

Table I.—AVAILABILITY FOR FOLLOW-UP

TYPE OF VAGOTOMY	AT 5 YEARS			AT 2–4 YEARS		ORIGINAL TOTAL AT ENTRY TO SERIES
	Personal Interview	Postal Questionnaire	Total Available	Dead	Lost	
Selective	46	3	49	1	0	50
Truncal	44	2	46	2	2	50

Table II.—CLINICAL STATUS AT 5 YEARS

TYPE OF VAGOTOMY	MODIFIED VISICK GRADING					
	1	2	Successes	3	4	Total Failures
Selective	27	20	47	0	2	2
Truncal	29	11	40	2	4	6

P = 0·1506 (not significant).

All the 100 patients survived operation and all have been interviewed at least once since operation. Since operation 3 patients (1 in the selective, 2 in the truncal group) have died; 2 with bronchial carcinoma and 1 with congestive heart failure. An additional patient survives with a treated breast cancer. It has been difficult to trace patients and to arrange personal follow-up in the Belfast area during the past 3 years, so that it is scarcely surprising that 2 patients have been lost to follow-up (*Table I*), both from the truncal group; they were last seen at 2 years and 3 years after operation respectively. Forty-nine of the selective group and 46 of the truncal group have been followed up at 5 years, all of whom were personally interviewed at this time except 5 patients (3 in the selective group and 2 in the truncal group) for whom we have relied upon information supplied by questionnaires filled in by the patient or his family doctor. Each of these patients had been seen at earlier follow-up and the postal evidence simply confirmed the previous findings. Many patients have been seen after 6 and 7 years, but we have ignored these data as we wished to compare the status of all the patients at the same point in time—5 years after operation.

In the analysis of the results Fisher's exact probability test has been used throughout.

Clinical Grading.—Using the modified Visick grading described, we have found 2 failures (grades 3 and 4) in the selective group and 6 failures in the truncal group (*Table II*). Of the absolute failures (grade 4) in the truncal group, all were cases of suspected or proven recurrent ulcer, whereas 1 in the selective group came to reoperation because of a malfunctioning pyloroplasty with no ulcer recurrence. The two grade 3 patients in the truncal group each had severe episodic diarrhoea. Visick gradings for the 5 patients who had either died or been lost to follow-up are available for 2 or 3 years after operation. The patient in the selective group was graded 1; in the truncal group two patients were graded 1, one patient graded 2, and one patient graded 3.

Recurrent Ulceration.—The object of any vagotomy is to cure the original duodenal ulcer and to avoid recurrent ulcer. At 5 years there were 3 recurrent ulcers which had been proven at operation as well as a fourth suspected recurrence in the truncal group, compared with only 1 suspected recurrence in the selective group (*Table III*). This difference was predictable in the early stages of the trial because of the lower incidence of positive insulin tests after selective vagotomy already reported, only 2 of 45 tests after selective operation being positive compared with 9 of 45 tests after truncal vagotomy. The recurrence after selective vagotomy and 2 of the truncal cases presented during the first year after operation, with the 2 others presenting in the third and fourth years. The overall incidence of suspected and proven recurrence of 5·4 per cent (2 per cent after

Table III.—ULCER RECURRENCE AT 5 YEARS

TYPE OF VAGOTOMY	NO. OF CASES	RECURRENCE		
		Suspected	Proven	Total
Selective	49	1	0	1
Truncal	46	1	3	4

P = 0·1097 (not significant).

Table IV.—EPISODIC DIARRHOEA AT 5 YEARS

TYPE OF VAGOTOMY	NO. OF CASES	DIARRHOEA		
		+	++	Total
Selective	49	4	0	4
Truncal	46	11	2	13

P = 0·0156 (significant).

selective vagotomy) may well rise with the passage of time.

Diarrhoea.—We have not been concerned with diarrhoea in the early postoperative period but rather with persisting episodes of explosive watery diarrhoea, sometimes with incontinence, recurring at intervals of days, weeks, or months. Diarrhoea has occurred in 13 patients after truncal vagotomy and in 4 patients after selective vagotomy, a statistically significant difference. In only 2 patients, both in the truncal group, was the diarrhoea sufficiently severe to be a major disability (*Table IV*). Occasionally this curious episodic diarrhoea phenomenon does not manifest itself until some years after operation, while other patients with episodic diarrhoea at earlier follow-up may lose their symptoms when they discover provocative articles of diet and learn to avoid them. It is impossible to measure the precise severity of this symptom in each case, but 6 patients in the truncal group and only 1 in the selective group had attacks more often than once a month, and 4 patients in the truncal group and none in the selective group had more than four motions per day during an attack. Loose watery motions were produced at the rate of 1558 per annum by the truncal group compared with 300 per annum by the selective group.

Table V.—DUMPING AT 5 YEARS

TYPE OF VAGOTOMY	NO. OF CASES	DUMPING		
		+	++	Total
Selective	49	13	0	13
Truncal	46	5	0	5

$P = 0·0677$ (not significant)

Table VI.—MISCELLANEOUS SYMPTOMS AT 5 YEARS

TYPE OF VAGOTOMY	FLATULENCE	HEART-BURN	DYS-PHAGIA	NAUSEA	VOMITING	
					Food	Bile
Selective	8	2	0	6	1	2
Truncal	15	3	2	6	2	2

Table VII.—WEIGHT CHANGE AT 5 YEARS

TYPE OF VAGOTOMY	NO. OF CASES	GAINED WEIGHT	MEAN WEIGHT CHANGE OF WHOLE GROUP (kg.)
Selective	49	37	+4·5
Truncal	46	32	+4·0

$P = 0·6458$ (not significant).

Bowel Habit.—In each case the preoperative bowel habit was expressed in motions per week, and the same information was sought at the 5-year follow-up, episodes of diarrhoea being excluded. In both groups the majority of patients stated that there was an 'improvement', with a mean increase of 2·3 motions per week in the selective group and 2·0 in the truncal group, not a significant difference. Constipation was not a problem at this stage; only 4 patients in the selective group and 7 in the truncal group claimed a decrease in bowel frequency. These results were similar to those found at the first annual review.

Dumping.—One of the principal reasons for adopting vagotomy instead of partial gastrectomy as the operation of choice for duodenal ulcer was the high incidence of dumping after gastrectomy. It was disappointing, therefore, at our first review to find dumping in nearly 40 per cent of this series; at that time no less than 17 patients were given a ++ rating, indicating symptoms sufficiently severe to be a nuisance. At 5 years the position had improved, probably because patients had learnt to adjust their diets appropriately and thus diminished both the frequency and the severity of this symptom complex.

Table VIII.—HAEMATOLOGY AT 5 YEARS

TYPE OF VAGOTOMY	NO. OF CASES	HAEMOGLOBIN (g. per cent)		MEAN CORPUSCULAR VOLUME (cu. μ)	
		Mean	No. under 13 g.	Mean	No. over 100
Selective	36	14·8	3	92·5	2
Truncal	37	14·6	3	91·7	2

Table IX.—CALCIUM AND ALKALINE PHOSPHATASE AT 5 YEARS

TYPE OF VAGOTOMY	NO. OF CASES	MEAN CALCIUM LEVEL (mg. per cent)	ALKALINE-PHOSPHATASE LEVEL (K.A. units)	
			Mean	No. over 15 K.A. units
Selective	34	9·4	8·7	2
Truncal	36	9·0	15·6	4

There were now no cases meriting ++ grading, but the continuing incidence of 27 per cent in the selective group is disturbing (*Table V*); the difference is not statistically significant. It must be stressed that this high incidence is directly related to the diligence of the interviewing physician. Many patients did not make any spontaneous complaint, and the dumping only came to light after close and careful questioning. The same is true of the other dyspeptic symptoms investigated.

Miscellaneous Dyspeptic Symptoms (*Table VI*).—By far the commonest of these was flatulence, and this was seen more often in the truncal group; it was hardly ever considered to be an important problem. Nausea, with or without vomiting, was not sufficiently common to cause comment. Bile vomiting occurred in only 2 patients of each group and was probably a product of the pyloroplasty rather than of the vagotomy. Gall-stones were not diagnosed in any patient from either group during the follow-up period.

In the early postoperative phase 9 patients (6 from the selective group) had significant dysphagia, 4 requiring oesophagoscopy and dilatation. Only 1 patient (from the truncal group) had dysphagia at

5 years. The low incidence of heartburn probably indicates a low incidence of hiatus hernia and oesophageal reflux at this stage, perhaps because an attempt was made to narrow the hiatus when it was found to be lax at the primary operation.

Nutritional Changes.—Objective data have been collected in relation to weight changes and haematological and biochemical measurements.

At the 5-year follow-up 37 of the selective group and 32 of the truncal group had gained weight, the mean gain being 4·5 kg. in the selective group and 4 kg. in the truncal group, which is not a significant difference and is very similar to the changes found at the end of the first year (*Table VII*).

Haematological surveys at the end of 5 years were carried out on 73 patients (*Table VIII*). The selective group had a mean haemoglobin level of 14·8 g. per cent, and in the truncal group the corresponding figure was 14·6 g. per cent. There was no patient with a haemoglobin level below 12·0 g. in either group and only 3 patients in each group had a level under 13·0 g. Owing to technical problems we were unable to obtain measurements of vitamin B_{12} in a sufficient number of patients, but the mean corpuscular volume has been studied as an index of incipient macrocytic anaemia. On the auto-analyser a figure up to 99 cu.μ is accepted as normal. Readings between 100 and 106 cu.μ were found in 2 patients in each group.

To investigate the possibility that skeletal problems might ultimately arise in either group the serum-calcium and alkaline-phosphatase levels were studied (*Table IX*). There was no case of hypocalcaemia in either group and there was no significant difference between the selective and truncal vagotomy groups in the mean levels of calcium, which were 9·4 and 9·0 mg. per cent respectively. Raised alkaline-phosphatase levels could have indicated increased skeletal activity, but we did not differentiate between bony and hepatic alkaline phosphatase in this study. Higher levels were found after truncal vagotomy and 4 of this group, compared with 2 of the selective patients, had levels above 15 K.A. units. None of these patients was jaundiced; none was adolescent and none was known to have Paget's or other sketalel disease.

Other biochemical levels, including glucose, uric acid, cholesterol, albumin, and transaminases, were routinely checked by the auto-analyser, but the results revealed nothing worthy of recording here.

DISCUSSION

There can be no dispute about the need for objective data in the assessment of selective vagotomy. The obvious yardstick must be a truncal vagotomy and it is essential in any trial that the drainage procedure is standardized, as pyloroplasty and gastro-enterostomy may give very different results. For example, Goligher, Pulvertaft, Irvin, Johnston, Walker, Hall, Willson-Pepper, and Matheson (1972) found an incidence of recurrent ulcer after truncal vagotomy and pyloroplasty about twice as great as that after truncal vagotomy and gastrojejunostomy. On p. 949 of this Journal the results of a trial of selective vagotomy and pyloroplasty versus selective vagotomy and gastrojejunostomy conducted on similar lines to this present trial are reported.

In planning this study we had to decide whether to limit the study to the practice of one surgeon and his team or to involve a whole hospital in order to collect more cases more quickly. We opted for the former as we felt that uniformity of technique was more important than larger numbers. It was important to ensure, as far as possible, that the extra-gastric fibres really were preserved in the selective vagotomy patients, though one can never be absolutely sure of this preservation. Failure to preserve fibres could be the cause of some anomalous published findings. Uniformity of follow-up assessment was also of obvious importance. All the early follow-ups were conducted by A. M. C.; at 5 years each patient has been seen by A. H. G. L. or E. F.A.S. and graded by agreement between them.

It is difficult to achieve 100 per cent follow-up and obviously impossible when 3 patients die from causes which are presumably unrelated, though one might speculate that both the duodenal ulcer and the bronchial carcinoma were related to smoking in 2 of them. A lost-to-follow-up rate of only 2 per cent in Northern Ireland today is surprising. If each of these 6 patients had retained their earlier grading the overall pattern of results would not have been altered. Since our reported first-year follow-up the failure rate (Visick grades 3 and 4) of 13 per cent has fallen to only 8·5 per cent owing to the better control of, or acceptance of, dumping, diarrhoea, and other side-effects. At the same time failures due to recurrence have increased. Fawcett, Johnston, and Duthie (1969) found that about three-quarters of all their recurrent ulcers appeared within the first year, and this was true of 3 of our suspected and proven recurrent ulcers. Two further suspected recurrences, 1 from each group, have subsequently presented after the 5-year follow-up assessment, and we may yet see more cases in later years. The 5-year recurrence rate of 2 per cent after selective vagotomy is quite acceptable, though 9 per cent after truncal vagotomy is too high by our standards. It may of course be that the recurrence rate is linked to the pyloroplasty, and gastrojejunostomy would have given a lower recurrence rate. This was the experience of Goligher and others (1972), whose suspected and proven ulcer recurrence rate 5–8 years after operation was 14 per cent after truncal vagotomy and pyloroplasty compared with 8·4 per cent after truncal vagotomy and gastrojejunostomy.

The apparent lower incidence of recurrence after selective vagotomy may well be linked to the better denervation indicated by insulin tests carried out 10 days after operation. The validity of these early tests has been questioned, but in our experience the 10-day status has been maintained in 80 per cent of patients (Kennedy, 1973). There is no clear-cut reason why denervation should be better after selective vagotomy, unless it is that this operation demands more care from the surgeon. If a lower incidence of recurrent ulcer, suspected from this trial, is confirmed it would constitute a major reason for preferring selective vagotomy for routine use.

Though the cause of episodic diarrhoea after vagotomy has never been fully elucidated, it has been shown by McKelvey (1970) to be related to rapid uncontrolled gastric emptying. The incidence of diarrhoea has been disputed, varying between 2 per cent (Elliott-Smith, Painter, and Porter, 1961) and 38 per cent (Harkins, Stavney, Griffith, Savage, Kato, and Nyhus, 1963), but definitions vary and the actual incidence of troublesome diarrhoea after truncal vagotomy is probably about 5 per cent (Barnes and Cox, 1969). Virtually all the published figures point to a lower incidence of episodic diarrhoea after selective vagotomy than after truncal vagotomy, whether the drainage procedure has been pyloroplasty, gastrojejunostomy, or antrectomy (Elliott-Smith and others, 1961; Harkins and others, 1963; Burge, 1964; Sawyers and others, 1968; Hendry and Abdulla, 1969; Grassi, 1970; Kronborg and others, 1970). We believe that our trial is the only published one which had been fully controlled, double blind, and with uniformity of the drainage procedure, and we have also found significantly more diarrhoea after 2 years and again after 5 years in the truncal group. The reason for this is not clear. The overall increase in bowel frequency seen equally in both groups was independent of diarrhoea and was not a disability; indeed many patients were delighted to find that their long-standing constipation had been relieved.

Dumping has become less severe with the passage of time and there were no cases of disabling dumping at the 5-year follow-up. One patient with severe dumping at the third year was subsequently lost to follow-up, and others appear to have mastered this problem by simple dietetic adjustment. Why dumping remains as a minor problem in 13 patients after selective vagotomy compared with only 5 after truncal vagotomy we cannot explain, though this difference does not reach statistical significance. An excess of mild dumping after selective vagotomy was also reported by Sawyers and others (1968). Of the miscellaneous symptoms, the commonest was flatulence, but this was seldom a problem. It might seem reasonable to postulate that the preservation of vagal afferents from the upper small bowel could be contributory. Nausea and vomiting were not sufficiently often seen in either group to constitute a problem. Looking at these symptoms together, it seems that selective vagotomy is favoured, but the adverse figures with regard to dumping offset these minor symptoms. The clinical grading table shows more qualified successes (grade 2) and fewer unqualified successes (grade 1) in the selective group.

Gain of weight after operation is a widely used parameter of success, but we have not found any correlation between weight change and Visick grading. Often improvement in Visick grading is associated with some loss in weight and vice versa. Many preoperative patients are overweight as they drink a great deal of milk to control ulcer symptoms. Relief of dyspepsia allows them to omit milk and thus lose weight after a successful operation. Pain from recurrent ulcer may lead to a return to milk and a further gain of weight.

Calcium and alkaline-phosphatase measurements appear to favour selective vagotomy marginally, but the striking finding is the absence of anaemia in each group. Unfortunately we do not know how many patients had been on iron therapy. These figures are in marked contrast to those of Wheldon, Venables, and Johnston (1970), who found a very high incidence of anaemia, hypocalcaemia, and weight-loss 15 years after truncal vagotomy and gastrojejunostomy. Although the blood-calcium levels were all normal the small number of raised alkaline-phosphatase levels give just a hint that metabolic bone disease may become a problem in later years.

The evidence of this trial with regard to diarrhoea, coupled with the low incidence of recurrent ulcer and the smaller incidence of all other symptoms, with the exception of dumping, leads us to advocate selective rather than truncal vagotomy in cases where a drainage procedure is required. Dumping and other symptoms may well be a product of pyloroplasty rather than of either type of vagotomy.

The operation of the future may well prove to be proximal gastric (highly selective) vagotomy and we are one of several teams currently assessing this procedure. To do this properly a control operation is required and selective vagotomy, with standardized drainage, is ideally suited to this purpose.

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PYLOROPLASTY VERSUS GASTROJEJUNOSTOMY

RESULTS OF A DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL

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SUMMARY

A double-blind, randomized, controlled trial of Finney pyloroplasty and gastrojejunostomy, each with selective vagotomy, is reported. There were no operative deaths but 5 patients have subsequently died or have been lost to follow-up, leaving 94 patients, with a mean follow-up time of 3¼ years. There has been 1 proven recurrence after gastrojejunostomy and 2 after pyloroplasty, with 1 further suspected recurrence in each group. The clinical grading marginally favoured gastrojejunostomy. There was no significant difference in the incidence of bilious vomiting, dumping, diarrhoea, or other disturbances, but there was a significantly greater increase in bowel frequency after pyloroplasty. Weight changes were similar, and there was no gross anaemia or calcium deficiency in either group. Gastrojejunostomy is reversible and pyloroplasty is not, and therefore we recommend gastrojejunostomy as the drainage procedure of choice when drainage is necessary after vagotomy.

TRUNCAL vagotomy with pyloroplasty is the operation most commonly used in Britain today in the treatment of chronic duodenal ulcer (Alexander-Williams, 1973). The present study was designed to test the widely held belief that pyloroplasty is superior to gastrojejunostomy when a drainage procedure is required to supplement vagotomy. Pyloroplasty, by causing less distortion of the normal anatomy, has the greater aesthetic appeal. It is recommended by Burge (1964), Wise and Ballinger (1969), and Wastell (1972), who regard it as a more physiological operation. In reviewing the two types of drainage in association with truncal vagotomy, Goligher and Pulvertaft (1969) formed the impression that gastroenterostomy gave better overall results, but the cases reviewed were not entirely comparable. In a recently published controlled trial carried out in Glasgow pyloroplasty was compared with gastrojejunostomy in patients having a truncal vagotomy. The only significant difference found at a mean follow-up of 4 years was a higher incidence of bilious vomiting after gastrojejunostomy (Kennedy, MacKay, Bedi, and Kay, 1973).

PATIENTS AND PROCEDURE

During the years 1968 and 1969 patients under the care of one surgical team coming to elective operation for chronic duodenal ulcer were eligible for admission to this trial. Fifty were treated by selective vagotomy and pyloroplasty, and 50 by selective vagotomy and gastrojejunostomy. The pyloroplasty was of a modified Finney type (*Fig.* 1) similar to that described by Wastell (1972), with an opening between 6 and 10 cm. in length which was closed in such a way as to approximate the antrum to the duodenum. Gastrojejunostomy was retrocolic and juxtapyloric with the stoma as close as possible to the duodenojejunal flexure. The stoma was normally 5 cm. in length with a range of 4–8 cm. In every case a double-lumen gastrostomy tube (Burns and Menzies, 1966) was used, thus eliminating nasogastric intubation and intravenous feeding. One limb of this tube was sutured to the gastric mucosa 1–2 cm. proximal to the anastomotic line.

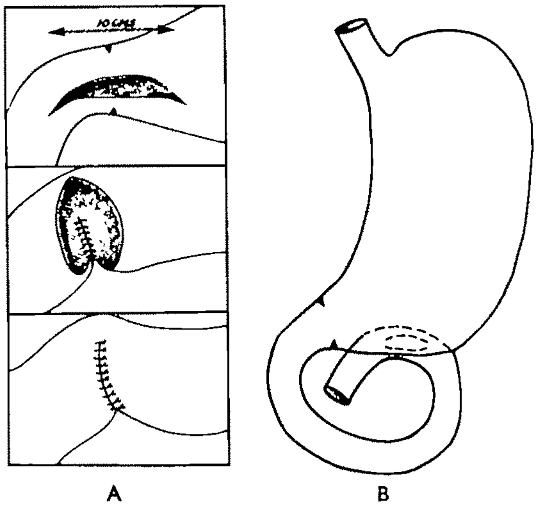

FIG. 1.—A, Pyloroplasty was a modified Finney type. B, Gastrojejunostomy was as close as possible to the pylorus and also to the duodenojejunal flexure.

No patient was accepted for this trial until the abdomen had been opened, the diagnosis confirmed, and the feasibility of selective vagotomy and of either type of drainage procedure established. Any patient with other significant gastro-intestinal disease, for example, gastric ulcer, gall-stones, or pancreatitis, was automatically excluded from the trial. Patients having emergency operations and those who were for any reason unlikely to be readily available for follow-up were excluded. Once a patient was accepted into the trial the drainage procedure to be used was decided by a nurse drawing a card from a box. On or about the tenth postoperative day the majority of patients had an insulin test meal, but in older patients and those with a history of coronary artery disease this test was omitted.

Annual follow-up was conducted by a physician with no knowledge of which drainage procedure had been used. Particular attention was paid to clinical well-being, evidence of recurrence, diarrhoea, dumping, and bile vomiting. Measurement of weight, haemoglobin, and biochemical data were recorded. Each patient was given an overall clinical grading using a modification of the Visick system:—

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1. No symptoms: a perfect result.
2. Mild symptoms: not troublesome.
3. More severe symptoms: some degree of disability.
4. Severe symptoms: disabling side-effects, recurrent ulcer, or reoperation.

In assessing episodic diarrhoea and dumping, mild symptoms were graded +, and moderate and severe symptoms + +.

Table I.—DETAILS OF FOLLOW-UP AT 2–5 YEARS

TYPE OF DRAINAGE PROCEDURE	TOTAL AT ENTRY	DIED*	LOST	INTERVIEWED	QUESTIONNAIRE	AVAILABLE FOR STUDY	MEAN FOLLOW-UP TIME (yr.)
Gastrojejunostomy	50	1	1	37	11	48	3·6
Pyloroplasty	50	2	2	43	3	46	3·5
Total	100	3	3	80	14	94	3·55

* Two further deaths occurred in the fourth year

Table II.—CLINICAL STATUS

TYPE OF DRAINAGE PROCEDURE	NO. OF CASES	VISICK GRADING				RECURRENT ULCERATION		
		1	2	3	4	Suspected	Proven	Total
Gastrojejunostomy	48	26	18	1	3	1	1	2
Pyloroplasty	46	24	16	3	3	1	2	3

For Visick grading, $P = 1·00$ For recurrent ulceration, $P = 0·8043$

Table III.—DUMPING

TYPE OF DRAINAGE PROCEDURE	NO. OF CASES	DUMPING		
		+	++	Total
Gastrojejunostomy	48	10	2	12
Pyloroplasty	46	14	4	18

$P = 0·1851$.

The two groups were comparable so far as age and sex were concerned. In the gastrojejunostomy group the mean age was 46·1 years and there were 10 women; in the pyloroplasty group the mean age was 45·8 years and there were 11 women. Ninety-five of the operations were performed by either T. K. or G. W. J. and the remainder by assistants under our direct supervision. Insulin tests on or about the tenth day were performed in 44 gastrojejunostomy patients, 4 giving a positive result by Hollander's criteria; of 42 tests in the pyloroplasty group, 3 were positive.

All 100 patients who entered the trial survived the operation and left hospital, but 5 have subsequently died, 3 during the first 2 years and 2 during the fourth year. The cause of death was not known in every case but none was thought to be directly related to the operation. Three further cases have been lost to follow-up, leaving 48 patients in the gastrojejunostomy group and 46 in the pyloroplasty group available for study. The duration of follow-up was from 2 to 5 years, with a mean of 3·6 years in the gastrojejunostomy group and 3·5 years in the pyloroplasty group (*Table I*). In 11 of the gastrojejunostomy group and 3 of the pyloroplasty group we had to rely on a postal questionnaire as the patients were not available for further interview at 3–5 years.

RESULTS

Clinical Grading.—Each patient was seen initially by A. M. C. and later by either A. H. G. L. or E. F. A. S., who gave him or her a Visick grading according to our modified scheme. Even in the instances where a postal questionnaire was used the majority of patients had had a previous personal interview. Grading was decided by the physicians in consultation. The results (*Table II*) seem to favour gastrojejunostomy marginally; there were more successes (grades 1 and 2) amongst the gastrojejunostomy cases and more failures (grades 3 and 4) amongst the pyloroplasty cases, but the difference did not reach statistical significance. The main cause of failure was suspected or proven recurrence, but 1 case in each group achieved a grade 4 rating because of reoperation for malfunction of the pyloroplasty or gastrojejunostomy respectively; in neither patient was there any operative evidence of recurrence.

Recurrent Ulcer.—In the gastrojejunostomy group there was 1 suspected and 1 proven recurrent ulcer compared with 1 suspected and 2 proven recurrences in the pyloroplasty group (*Table II*), giving an overall probable recurrence rate at 3½ years of 5·1 per cent.

Dumping.—In this series dumping is defined as a feeling of epigastric fullness or discomfort, of weakness, with sweating and palpitations, and often the need to lie down, coming on within half to three-quarters of an hour after a meal, however small.

These symptoms were often not complained of spontaneously but only revealed by close questioning and were seldom a significant nuisance to the patient. There was more dumping after pyloroplasty, but the result was not statistically significant (*Table III*). The occurrence of 6 moderate or severe cases in the whole series was disquieting.

Bowel Habit.—Episodic diarrhoea, which is intermittent, watery, urgent, and sometimes with incontinence, can be a real disability even with only two episodes per attack, since fear of incontinence may dominate the patient's reactions. There were more mild cases amongst the gastrojejunostomy group (*Table IV*), but only 1 moderate/severe (+ +) case in this group compared with 2 in the pyloroplasty group. In 1 of the latter patients severe diarrhoea was attributed to malfunction of the pyloroplasty. At a second operation gastrojejunostomy was added but improvement was only slight.

The frequency of defaecation before and after operation, excluding episodes of diarrhoea, was also studied. There was an increase in the number of motions in each group; the mean increase of 3·1 motions per patient per week in the pyloroplasty group was significantly greater than the mean increase of 1·1 motions in the gastrojejunostomy group (*Table IV*).

Table IV.—ALTERATION IN BOWEL HABIT

TYPE OF DRAINAGE PROCEDURE	NO. OF CASES	EPISODIC DIARRHOEA		INCREASED FREQUENCY OF DEFAECATION (No. per wk.)
		+	++	
Gastrojejunostomy	48	4	1	1·1
Pyloroplasty	46	1	2	3·1

For episodic diarrhoea, $P = 0·7147$. For increased frequency of defaecation, $0·05 > P > 0·02$.

Table VI.—WEIGHT AND BLOOD CHANGES

TYPE OF DRAINAGE PROCEDURE	INCREASE IN WEIGHT (kg.)	MEAN HAEMOGLOBIN (g. per cent)	MEAN CALCIUM (mg. per cent)	MEAN ALKALINE PHOSPHATASE (K.A. units)
Gastrojejunostomy	2 1	14·01	9 4	10·8
Pyloroplasty	1·6	14·05	9·7	9 4

Bilious Vomiting.—Since this symptom has been particularly associated with the operation of gastrojejunostomy, it was looked for very carefully but no difference was found between the two groups (*Table V*). However, there was 1 patient in the gastrojejunostomy group in whom the bile regurgitation and vomiting, with associated gastritis and oesophagitis, were sufficiently severe to require reoperation with closure of the gastrojejunostomy. In 2 patients in each group vomiting of food also occurred from time to time, but this was not considered to be an important problem.

Miscellaneous Symptoms.—Nausea, heartburn, flatulence, and dysphagia (*Table V*) occurred in small numbers in each group, and there was no apparent difference in incidence. It was difficult to categorize these minor symptoms as there was considerable overlap; for example, patients with bile vomiting often complained also of nausea or heartburn.

In other prospective studies of vagotomy that we have conducted, flatulence as an isolated symptom, not associated with dumping or other symptoms, occurred sufficiently often to attract attention. Like Goligher and Pulvertaft (1969) we noted a higher incidence with pyloroplasty.

Evidence of the development of gall-stones was sought in this study, and 2 patients from the gastrojejunostomy group came to cholecystectomy at 2 and 3 years after vagotomy respectively. We cannot be absolutely certain that these patients had no stones at the time of vagotomy, but it is unlikely as the gall-bladder was carefully inspected and palpated in every case.

Nutrition.—There was an overall tendency to gain weight in both groups, the mean gain being 2·1 kg. in the gastrojejunostomy group and 1·6 kg. in the pyloroplasty group (*Table VI*). This is not a significant difference. Haemoglobin levels were available for 41 pyloroplasty patients and 34 gastrojejunostomy patients. Blood and biochemical results could not be obtained from the patients answering postal questionnaires and some patients who were interviewed in their own homes. No difference was found in the haemoglobin levels, a mean of over 14·0 g. being perfectly satisfactory. There were, however, mild degrees of anaemia (between 11·0 and 12·0 g.) in 2 gastrojejunostomy patients and 3 pyloroplasty patients. The same 75 patients had measurements of mean corpuscular volume but no gross macrocytosis was discovered.

Table V.—UPPER GASTRO-INTESTINAL COMPLAINTS

TYPE OF DRAINAGE PROCEDURE	NO. OF CASES	VOMITING BILE	VOMITING FOOD	FLATULENCE	NAUSEA	HEARTBURN	DYSPHAGIA
Gastrojejunostomy	48	5	2	5	9	2	2
Pyloroplasty	46	4	2	9	8	4	0

Serum-calcium levels were also recorded, a slightly higher mean level being found in the pyloroplasty group. No patient had hypercalcaemia but 1 patient in the gastrojejunostomy group had a level of 8·4 mg. per cent, the only one in either group to fall below our lower limit of normal. Alkaline-phosphatase levels were marginally higher in the gastrojejunostomy group and could perhaps have been related to the slightly lower calcium levels (*Table VI*).

DISCUSSION

If a comparison is to be made between pyloroplasty and gastrojejunostomy it is important that each procedure should be fully standardized and that in each case the same type of vagotomy should be used. Of the many variants of pyloroplasty, we chose a modification of the Finney procedure as this is easy to perform and applicable in practically every case, even with severe duodenal stenosis, the only variation being in the length of the initial pyloroduodenal incision. The gastrojejunostomy was also standardized, the objects being to drain the antrum and to leave as short an afferent loop as possible in the hope that bile stasis and regurgitation would thus be minimized. In order to achieve maximal uniformity we limited the trial to a single surgical team.

This trial must obviously be compared with the much larger trial reported by Kennedy and others

(1973) from Glasgow, in which 83 per cent of 404 patients operated on by no less than 45 different surgeons were reviewed. Our numbers are much smaller but in planning this trial we decided to sacrifice numbers for uniformity, and we felt that there were too many questions to be answered by a prospective controlled trial for us to spend more than about 2 years collecting the patients for any one trial. Perhaps because of the smaller numbers involved we have managed to reduce our 'lost' patients to only 3 per cent.

The completeness of our follow-up by interview has been somewhat disappointing, as personal interview conducted on a blind basis is undoubtedly the only entirely satisfactory way of assessing results where so many symptoms are subjective and where there are so few objective measurements. However, in the socio-political climate in which our patients live it was difficult to persuade those without significant symptoms to make hospital visits. Because of this, many patients had to be interviewed in their own homes and in 14 instances we have been forced to rely on postal questionnaires for the 3–5-year follow-up, although most of these patients had been interviewed at an earlier review. Nevertheless, we feel that the data presented here on 94 patients in this trial are valid and comparable.

The incidence of all side-effects is remarkably similar, though the gastrojejunostomy group emerges with a slightly better Visick grading and most symptoms are a little more frequent in the pyloroplasty group. Dumping is slightly more common after pyloroplasty, where a 9 per cent incidence of moderate or severe symptoms was worrying. Evidence from a previous trial suggests that dumping may be more common after selective vagotomy than it is after the truncal operation (*see* p. 944 of this Journal). Sawyers, Scott, Edwards, Shull, and Law (1968) had a similar experience. We have also noted that the incidence and severity of dumping had decreased markedly by the fifth postoperative year, probably as a result of the patients learning to avoid provocative foods and drinks.

The incidence of mild and moderate episodic diarrhoea in the two groups is not enough to cause comment. Kennedy and others (1973) found no difference in the incidence of diarrhoea in their trial. The significantly greater increase of bowel frequency in the pyloroplasty group is interesting, but there is no obvious explanation. It was not necessarily a disadvantage, many patients being delighted by the relief of long-standing constipation.

Bilious vomiting is the one symptom which has been firmly attributed to gastrojejunostomy, but we found no difference in the incidence in our two groups. The only severe case came from the gastrojejunostomy group and a second operation was performed with closure of the gastrojejunostomy. The reversibility of gastrojejunostomy is considered to be a strong point in its favour; we do not believe that it is possible to restore the pylorus after a pyloroplasty. The Glasgow trial showed a significantly higher incidence of bilious vomiting after gastrojejunostomy, but it may be important that the gastrojejunostomy used differed from ours in two important respects. First, in the Glasgow series the anastomosis was made at the most dependent part of the stomach, whereas ours was much closer to the pylorus; secondly, the afferent jejunal loop in our series was very much shorter. In addition, the pyloroplasty used in the Glasgow trial was of the Heineke-Mikulicz type.

Recurrent ulcer might be expected more commonly after pyloroplasty judging by the experience of Goligher, Pulvertaft, Irvin, Johnston, Walker, Hall, Willson-Pepper, and Matheson (1972), who had almost twice as many suspected and proven recurrences after pyloroplasty and truncal vagotomy as after gastrojejunostomy and truncal vagotomy. The 5 recurrences (suspected and proven) in the present series do not show a difference between the groups. More recurrences may appear in the future, though Fawcett, Johnston, and Duthie (1969) found that 75 per cent of recurrences after vagotomy and drainage appeared within the first year.

There is no pattern in the frequency of miscellaneous symptoms favouring either operation. Many of these minor symptoms occur in association with more troublesome symptoms, such as bile vomiting or diarrhoea. The only one which often occurs alone is flatulence and this was a little more frequent after pyloroplasty.

When objective measurements are considered, it seems that weight-gain was not significantly different in the two groups, but it must be recognized that gain of weight is not a good measure of clinical success. In an unpublished study we have found a negative correlation between weight-gain and improvement of Visick grading. There was no difference in the haemoglobin levels, and the striking feature was the absence of severe anaemia and the small incidence of trivial anaemia in the two groups. Wheldon, Venables, and Johnston (1970) reported a high incidence of anaemia 15 years after truncal vagotomy and gastrojejunostomy. Wastell's findings reported in 1969 were similar, with less anaemia after pyloroplasty. This particular point must obviously be re-examined at a later follow-up. There was no evidence of impending macrocytic anaemia, but this may yet become a problem after longer follow-up. Metabolic bone disease has not been a common reported problem after vagotomy and drainage, and we have found no evidence of it though it could also appear in later years.

At 3½-year follow-up there is very little to choose between gastrojejunostomy and pyloroplasty. The former has a marginally better Visick status, possibly a lower rate of recurrent ulcer, less dumping, less increase of bowel frequency, less flatulence, and more weight-gain, but the only one of these differences which is significant is the change of bowel habit. Pyloroplasty, on the other hand, is favoured by marginally less episodic diarrhoea, slightly less bilious vomiting and dysphagia, and a higher level of serum calcium. The overall balance of advantages appears to lie with gastrojejunostomy. When the reversibility of the primary operation is considered the choice becomes easier. Pyloroplasty is irreversible and surgeons are learning to appreciate the importance of conserving this beautiful mechanism. Gastrojejunostomy, however, is readily closed. In 4 cases outside this trial we have closed the stoma, even with truncal vagotomy, and have had no emptying problems. Although the early vagotomies without drainage failed as a group, it is important to remember that at least half of them remained well in the long term. In another study (*see* p. 944 of this Journal) we found that selective vagotomy was superior to truncal vagotomy when each was combined with pyloroplasty. From the results of this trial, using selective vagotomy as the standard procedure, we must conclude that gastrojejunostomy is a better drainage procedure than pyloroplasty.

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DRILL BIOPSY OF THE BREAST—A CRITICAL ANALYSIS*

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SUMMARY

In a study of drill biopsy carried out in 106 patients with breast lesions, comparing the accuracy of diagnosis with that of clinical examination and excision biopsy, reliability declined as stromal reaction in the tumour increased. Accordingly, a negative result is meaningless. Tumour size did not appear to be an important factor. The significance of these results is briefly discussed.

DEFINITIVE treatment of breast lesions rests upon accurate histological diagnosis, and excision biopsy under a general anaesthetic is universally accepted for this purpose.

In such an easily accessible organ it is not surprising, however, that out-patient procedures, such as needle and drill biopsy under local anaesthetic, with potential advantage to both patient and surgeon, have been described. Drill biopsy, although requiring more specialized equipment, is preferable in that it provides a 'core' of tissue showing architectural features of the tumour as well as the cytology, which alone is shown by needle aspiration.

Kirschner (1935) first described a method of drill biopsy in various tissues using a cylindrical cutting needle and dental drill. Ellis advocated the method again in 1947, and in 1960 Deeley described the use of a high-speed pneumatic drill. Subsequently several workers have discussed its use in biopsy of many tissues, notably lymph-glands (Paine, 1969), tumours of the breast (Burn, 1971), lung, pleura (Steel, 1972), and bone (Deeley, 1972).

In an attempt to evaluate the diagnostic accuracy of drill biopsy it was compared with conventional excision biopsy. Throughout the series frozen-section techniques were used to provide an immediate diagnosis; paraffin sections provided a check on histological accuracy in both drill and excision biopsies.

MATERIAL AND METHODS

One hundred and six consecutive patients with breast lesions presenting between January and November, 1972, were examined and a clinical diagnosis was made. The size of the lesion and other relevant features were noted in the usual way.

Under general anaesthesia the tumour was stabilized gently between finger and thumb and a small skin incision was made over it with the point of a knife. A cylindrical hollow needle, 2 mm. in diameter, was fitted to the pneumatic drill with the air pressure above 60 lb. per in.^{2}. The speed of the drill was about 20,000 revolutions per minute and was to some extent adjustable by pressure on the trigger. It was introduced down into the tumour, which was then drilled through. Gentle negative pressure was applied to the needle with a syringe full of saline after dismantling the drill. The contained core of tissue was then either sucked into the syringe or expelled directly on to a saline swab. Excision biopsy of the lesion was carried out in the usual manner and both specimens were submitted for frozen-section examination.

In most patients two drill biopsies were performed through the same incision.

RESULTS

The pathology of the lesions examined is detailed in *Table I*. Included in the carcinoma group were 1 mucoid, 1 squamous, and 1 intraduct carcinoma. There were 2 medullary and 1 male breast carcinoma.

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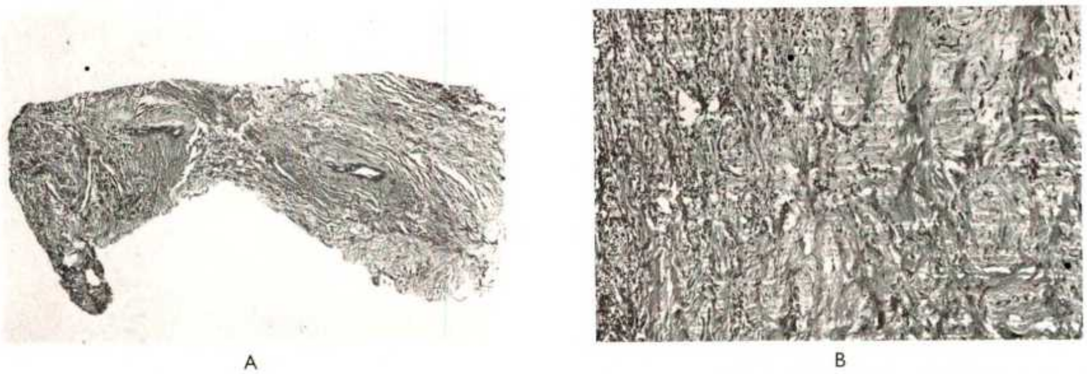
* Presented to the Royal Society of Medicine, 21 Feb., 1973.

Carcinomas.—The diagnostic accuracy of clinical examination, drill biopsy, and frozen-section excision biopsy is compared in *Table II*. Drill biopsy is the least accurate, but excision biopsy and clinical examination both missed carcinomas. Those missed clinically were all 2·5 cm. or less in size. The false negative occurring with excision biopsy was discovered because of continuing clinical suspicion. The patient was readmitted for further biopsy and subsequent mastectomy 6 weeks later.



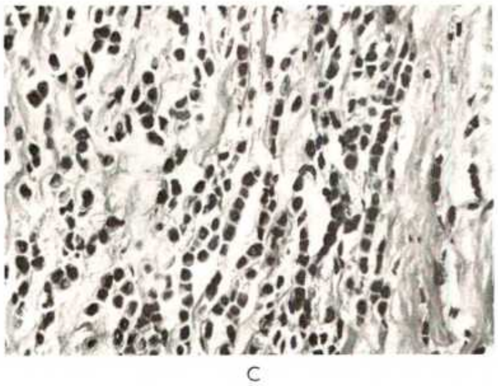


FIG. 1.—A, Drill biopsy showing ducts and dense fibrous tissue. A few cells of doubtful histogenesis are included but there is no valid evidence of tumour growth. H. and E. (× 56.) B, Excision biopsy from the same lesion. The tumour shows marked stromal reaction; only on the left of the field is there overt infiltration by carcinoma. It is obvious that a sample obtained by drill biopsy can readily prove uninformative. H. and E. (× 60.) C, High-power examination shows clearly the neoplastic nature of the infiltrate in the left field of B. H. and E. (× 266.)

Table I.—PATHOLOGY OF ALL THE LESIONS EXAMINED BY DRILL BIOPSY OF THE BREAST (106 PATIENTS)

Pathology	*No. of Cases*
Carcinoma	40
Fibro-adenosis	45
Solitary cyst	11
Fibro-adenoma	4
Fat necrosis	3
Cystosarcoma phylloides	1
Acute mastitis of pregnancy	1
Florid papilloma	1

Benign Lesions.—The three methods of diagnosis are again compared in *Table III* in respect of benign pathology. In 14 cases in the drill-biopsy group the histology, although benign, was not representative of the lesion subsequently excised; this group included 11 solitary cysts which were aspirated, but only fragmentary tissue for histology was obtained: 2 of these cysts were misinterpreted as carcinoma clinically.

The case of cystosarcoma phylloides could have been misinterpreted as malignant on the drill-biopsy specimen; this was thought to be true also of a biopsy of fibro-adenosis with marked epitheliosis.

The doubtful false positive on excision biopsy was a florid papilloma, diagnosed as an early intraduct carcinoma, but not confirmed on paraffin section.

Table II.—ACCURACY OF DIAGNOSTIC METHODS IN CARCINOMA OF THE BREAST (40 PATIENTS)

Diagnostic Method	*Correct Diagnosis*	*False Negative*
Clinical	37	3
Drill biopsy	30	10
Excision biopsy	39	1

Table III.—ACCURACY OF DIAGNOSTIC METHODS IN BENIGN BREAST LESIONS (66 PATIENTS)

Diagnostic Method	*Correct Diagnosis*	*False Positive*
Clinical	64	2
Drill biopsy	64	2 doubtful
Excision biopsy	65	1 doubtful

Table IV.—ACCURACY OF DRILL BIOPSY IN RELATION TO TUMOUR SIZE IN CARCINOMA OF THE BREAST (40 PATIENTS)

	TUMOUR SIZE		
	2 cm. or less	2·5–5 cm.	6 cm. or more
No. of carcinomas	15	17	8
False negatives	4	3	3

Tumour Size.—Comparing tumour size and accuracy of drill biopsy (*Table IV*), this series does not suggest any direct relationship. Early in the series the impression was gained that false negatives were more frequent among the smaller tumours, and this is the experience of others (Burn, 1971).

Stromal Reaction.—In an attempt to investigate the cause of inaccuracy further the tumours were classified according to the stromal reaction which they evoked histologically (*Table V*). It is appreciated that stromal reaction may vary greatly from field to field in any one tumour; nevertheless, it is a semi-quantitative characteristic of breast carcinoma which has broad general validity.

Tumours with marked stromal reaction are associated with a greater number of false-negative results on drill biopsy. It is likely that the core from a drill biopsy in this group will have a high proportion of stromal elements to tumour cells, the latter being often insufficient to give a definitive diagnosis by any method (*Fig.* 1). Some such biopsies were reported as suspicious but not diagnostic. Trauma is a further contributory factor to inaccuracy, sometimes preventing definitive diagnosis (*Fig.* 2). *Fig.* 3 illustrates a tumour having minimal stromal reaction, and a diagnostic drill biopsy was consequently obtained.

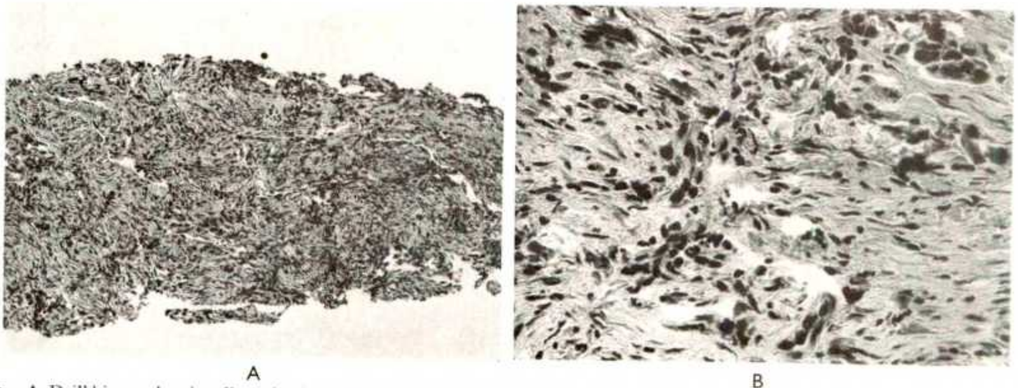


FIG. 2.—A, Drill biopsy showing distortion by trauma, producing a pseudofasciculation and suggesting a connective-tissue lesion. H. and E. (× 66.) B, High-power examination is more suggestive of an infiltration but its precise nature remains in doubt. H. and E. (× 266.)

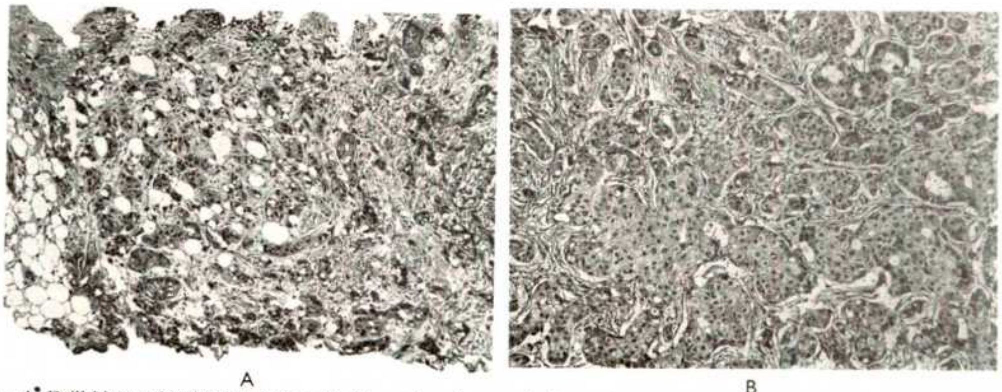


FIG. 3.—A, Drill biopsy showing infiltration of adipose tissue by anaplastic carcinoma. H. and E. (× 60.) B, Excision biopsy from the same lesion. The minimal stromal reaction assures an informative drill biopsy and a definitive diagnosis. H. and E. (× 60.)

Table V.—ACCURACY OF DRILL BIOPSY IN RELATION TO STROMAL REACTION IN CARCINOMA OF THE BREAST (40 PATIENTS)

Stromal Reaction	*Correct Diagnosis*	*False Negatives*
Nil	5	1
Mild	14	0
Moderate	10	2
Marked	11	7

The overall accuracy is expressed as a percentage in *Table VI*. The clinical accuracy compares favourably with that of other series (Gravelle, 1969, 88·1 per cent; Strax, Venet, Shapiro, Gross, and Venet, 1971, 77 per cent). The accuracy of excision biopsy in this series also compares favourably with that of Sparkman (1962, 97·7 per cent). Drill biopsy in the present series was not as accurate as the 95 per cent rate of Burn (1971) and the 90 per cent of Ellis (1947), but compares well with the 70 per cent of Paine (1969); in our series, however, frozen-section methods were used to give an immediate answer.

Table VI.—OVERALL ACCURACY OF DRILL BIOPSY OF THE BREAST (106 PATIENTS)

DIAGNOSTIC METHOD	CORRECT DIAGNOSIS	
	No.	Percentage
Clinical	101	95
Drill biopsy	92	84
Excision biopsy	104	98

DISCUSSION

Drill biopsy combined with frozen section may give an immediate definitive diagnosis of carcinoma and can be used as an out-patient procedure. The clinician can then discuss the diagnosis with the patient and her subsequent treatment with added confidence. In addition, the urgency of the situation can be judged more accurately for admission purposes and subsequent investigations planned more effectively. For example, bone scans with radionuclides are often used as an adjunct to clinical tumour staging to determine whether curative or palliative therapy is indicated, and histological proof is desirable in patients in their reproductive years. Unnecessary referral to radiotherapy departments might also be avoided; the surgeon could proceed to mastectomy without further biopsy, thus minimizing contamination of the operative field.

Potential disadvantages of the method may be local seeding of the tumour from the biopsy track and this has been reported with needle biopsy (Godwin, 1956); to date it has not been found in drill biopsy (Steel and Winstanley, 1967). The danger of contributing to further metastases has also been investigated by Burn, Deeley, and Malakar (1968) using the Walker 256 tumour in rats; no increased evidence of metastasis was found in rats submitted to drill biopsy.

The accuracy of our series is disappointing, especially compared with needle-aspiration cytology which is claimed by Webb (1970) to be 97·3 per cent accurate. With the latter method experience has been shown to improve the results (Adair, 1949), but it is difficult to believe that this would be true of drill biopsy if the findings relating to stromal reaction are significant—about 25 per cent of carcinomas will have marked stromal reaction and the proportion of stromal tissue to tumour elements will remain high. Under these circumstances chance is likely to play a greater part than skill in providing the correct diagnosis. Sampling error can therefore be very great and a negative result is quite meaningless.

It is worth noting that a wide experience of biopsies of similar size and nature, e.g., bronchial biopsies, has demonstrated that there are no special difficulties of interpretation peculiar to the frozen-section method.

It is concluded from this study that while drill biopsy with frozen section has many potential advantages it is of insufficient accuracy to supersede excision biopsy. The biological nature of the tumour (rather than its size or the skill of the surgeon) may be the reason for the difficulties encountered.

Acknowledgements.—Patients in this series were under the care of Mr. T. J. McNair and Mr. J. W. W. Thomson, and we are grateful to them for their encouragement and advice. We would also like to thank Mr. Ian Burn for introducing us to the technique.

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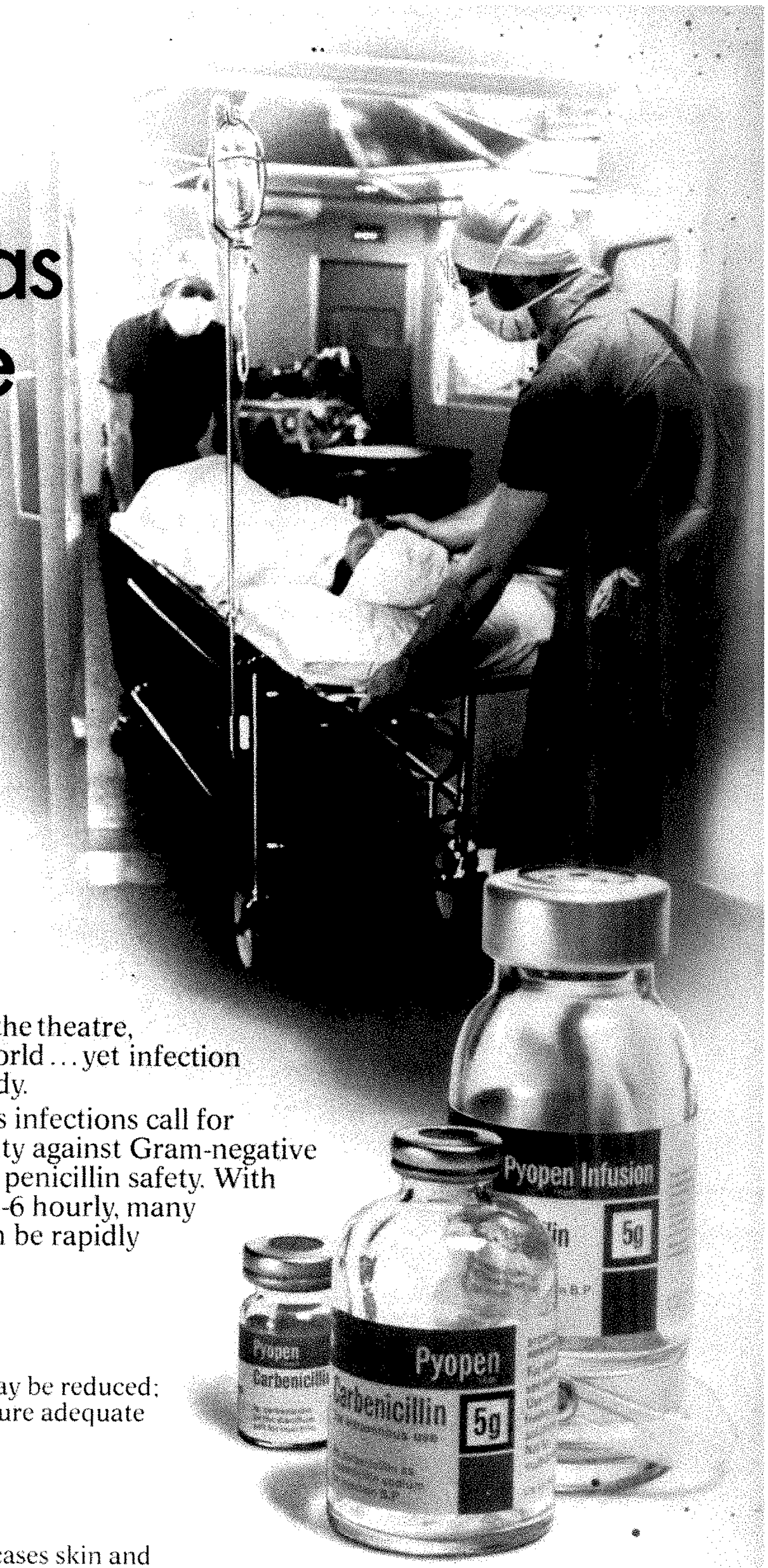

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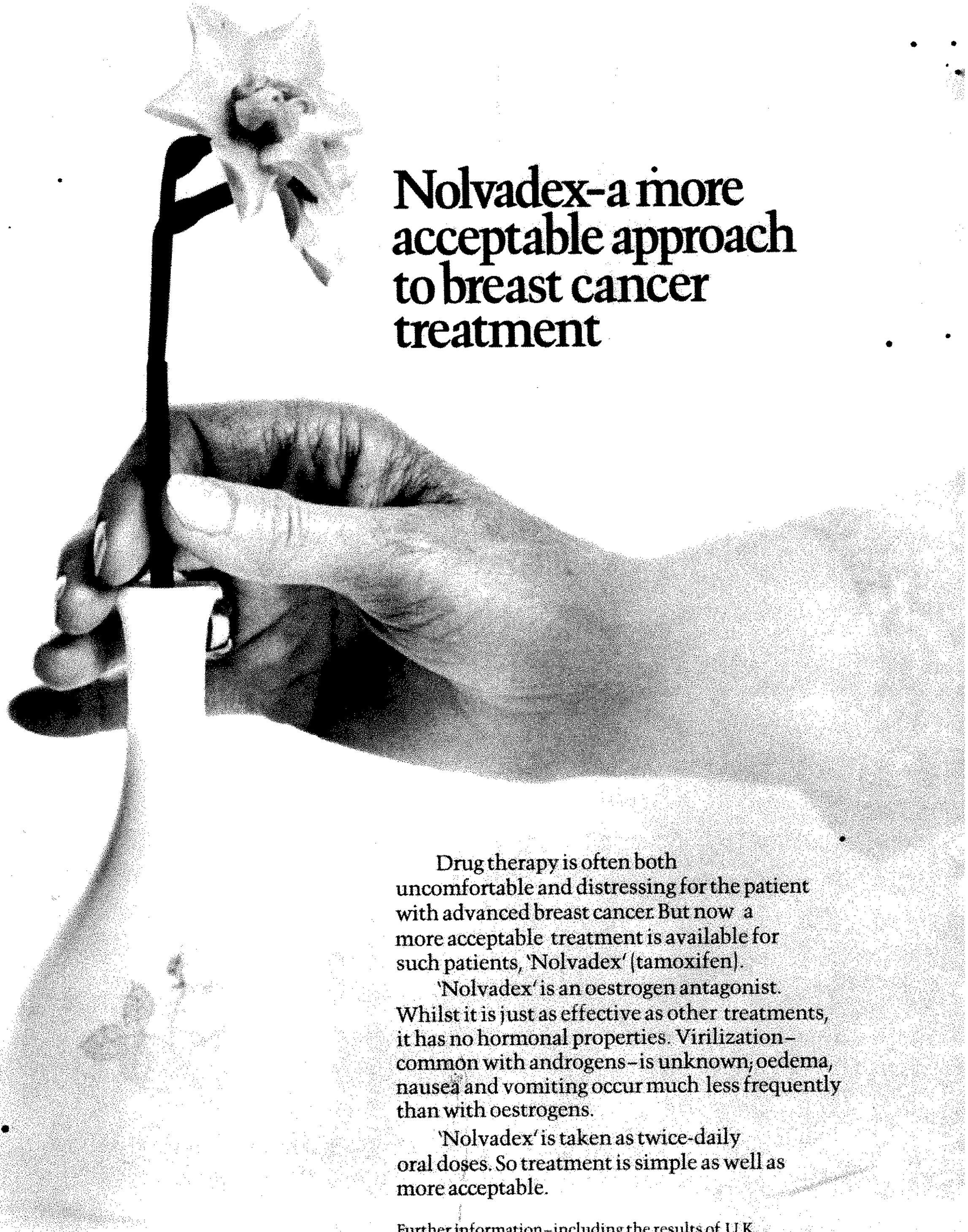

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2 *British Medical Journal* (1973), **1**, 13.

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THE PROBLEM OF LOCAL RECURRENCE FOLLOWING CONSERVATIVE SURGERY FOR CARCINOMA OF THE BREAST

By M. E. BAILEY, K. RATNAVEL, and A. P. WYATT
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SUMMARY

Follow-up of patients after local excision of carcinoma of the breast indicated that there was a high incidence of local recurrence and that this could be a difficult problem to manage. A retrospective study was performed comparing 50 patients who had undergone local excision and radiotherapy with 50 patients following simple mastectomy and radiotherapy. Local recurrence occurred in 16 per cent of the local excision group compared with 2 per cent in the simple mastectomy group.

MATERIALS AND METHODS

Forty-six patients with clinical stage I and 4 patients with clinical stage II carcinoma of the breast underwent local excision of the tumour and postoperative radiotherapy (group 1) between the years 1960 and 1969. These were compared with 50 patients treated during the same period by simple mastectomy and radiotherapy (group 2). They were matched for age, time of operation, and clinical stage of the carcinoma. The follow-up varied from 18 months to 18 years. All the patients were interviewed and examined and any local or systemic recurrence was recorded. Local recurrence was defined as that occurring in the treated area of the chest wall (Haagensen, Cooley, Miller, and others, 1969) and included any recurrence in the residual breast tissue.

Table I.—Results of Local Excision and Radiotherapy compared with Those of Simple Mastectomy and Radiotherapy for Carcinoma of the Breast

Type of Recurrence	Local Excision and Radiotherapy (50 patients)		Simple Mastectomy and Radiotherapy (50 patients)	
	No.	Per cent	No.	Per cent
Local	8	16	1	2
Distant	16	32	12	24
Combined local and distant	3	6	1	2
Local but no distant	5	10	0	
Overall mortality	14	28	9	18

RESULTS

The mean age of the patients in the local excision group was 56·3 years and in the simple mastectomy group 55·9 years, the greatest age difference being 6 years. On average the local excisions were performed 22·5 days later than the mastectomies. The mean length of follow-up was 5·2 years.

Recurrence within the treated area occurred in 8 out of 50 patients (16 per cent) treated by local excision and radiotherapy, and in 1 out of 50 patients (2 per cent) treated by simple mastectomy and radiotherapy; 16 patients in the first group (32 per cent) and 12 in the second group (24 per cent) developed distant metastases (*Table I*). The number of patients with both local and distant recurrences in group 1 was 3 (60 per cent) and in group 2 was 1 (2 per cent). Therefore there were 5 patients (10 per cent) in group 1 who had local recurrence without evidence of systemic recurrence. The overall mortality in group 1 was 14 out of 50 (28 per cent) and in group 2 was 9 out of 50 (18 per cent).

DISCUSSION

This study is a retrospective one and suffers from all the limitations and disadvantages of any such study. However, much has been written concerning the type and extent of treatments for carcinoma of the breast in terms of survival rates (McWhirter, 1955; Peters, 1967; Haagensen and Cooley, 1969; Handley and Thackray, 1969; Kaae and Johansen, 1969; Miller, 1969), but less emphasis has previously been given to local recurrence following conservative surgery (Mustakallio, 1954; Porritt, 1964; Crile, 1965; Crile and Hoerr, 1971; Taylor, Baker, Fortt, and Hermon-Taylor, 1971; Atkins, Hayward, Klugman, and Wayte, 1972).

Mustakallio (1954) reported 127 patients with stage I lesions 'no bigger than a hen's egg' treated by local excision and radiotherapy. The local recurrence rate was not stated but 3 patients did subsequently require radical mastectomy for this. He also stated that if local recurrence was present distant metastases were 'simultaneously or almost simultaneously to be found'. In 10 per cent of our patients this was not the case. Mustakallio found that 'it also appeared that local metastases could be controlled or cured with roentgen therapy'.

Porritt (1964) reported 85 per cent 5-year survival 'in early cases' treated by local excision and radiotherapy and a 22 per cent survival 'in late cases' similarly treated. The 10-year survivals were 70 per cent and 30 per cent respectively. These rates compared favourably with those in cases treated by radical mastectomy and radiotherapy but no mention was made of local recurrence following either type of procedure.

Crile (1965) recorded a 65 per cent 5-year survival following local excision and radiotherapy and a local recurrence rate in clinical stage I lesions of 1 in 12 (8·33 per cent). In stage II lesions the local recurrence was 4 out of 8 (50 per cent). No mention was made of their subsequent management.

Crile and Hoerr (1971) reported a 5-year survival rate of 67 per cent in 55 patients treated by local excision, 40 of whom were clinically stage I and 15 stage II; 34 patients were alive without evidence of growth, and 3 were alive with recurrent carcinoma. This compares with a 68 per cent 5-year survival in all operable patients (i.e. 317 out of 465 patients) treated in the same period either by simple mastectomy or modified radical mastectomy with or without radiotherapy. The local recurrence rate in the two groups was 11 per cent after local excision and 8 per cent after mastectomy. There were no recurrent tumours in the breast tissue. Crile states that 'most of the time' the incidence of locally recurrent tumours was controlled satisfactorily by irradiation.

Taylor and others (1971) found a local recurrence rate of 14 out of 77 patients (18 per cent) following sector mastectomy and postoperative radiotherapy; 11 within the first 5 years and 1 after 15 years. They could find no distinctive clinical or pathological features to predict the likelihood or otherwise of local recurrence in any individual case in the series, there being no difference in mean age at diagnosis or size of tumour, but the proportion of stage II lesions (50 per cent), histological grade 3 (14 per cent), and absence of lymphocytic reaction (54 per cent) was higher in the recurrence group.

Atkins and others (1972) described 45 out of 182 patients developing local recurrence following wide excision ('extended tylectomy') and postoperative radiotherapy, compared with 13 out of 188 following radical mastectomy and radiotherapy. From their figures it appears that 26 out of 45 patients in the first group underwent further surgery. It is also worth noting that 31 out of 182 patients who had had extended tylectomies had local recurrence without simultaneous widespread dissemination.

In the series reported here the local excision varied from wide removal of the tumour to segmental excision of the part of the breast containing it. No axillary dissection or node biopsy was performed. All the local recurrences except 1 were in clinical stage I cases, which is contrary to most other series. There was a much higher percentage of local recurrence in the local excision and radiotherapy group compared with the simple mastectomy and radiotherapy group (16 per cent compared with 2 per cent).

Ten per cent of the patients in group 1 had local recurrence without any evidence of distant metastases. In 3 of these patients the local recurrence was extensive by the time of diagnosis, with local cutaneous growth, infection, and, in 1 case, fungation. These presented considerable difficulty in local management since further direct operation was not possible and response to further radiotherapy was poor. Hormonal ablation similarly was ineffective.

Local recurrence may be diagnosed late in such circumstances because of failure of patients to attend for regular follow-up or because of difficulty in differentiation between recurrent growth and post-operative or radiotherapy effects (Williams, Murley, and Curwen, 1953).

It is suggested that there is considerable evidence that the local recurrence rate is higher in patients who have conservative surgery for carcinoma of the breast compared with those who have a more radical operation, and that this can present difficulty in management in a patient who may otherwise be clinically free from disease.

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THE EFFECT OF INCREASED OXYGEN IN PROLONGED ACUTE LIMB ISCHAEMIA

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SUMMARY

Prolonged acute hindlimb ischaemia was produced in anaesthetized ventilated dogs. During ischaemia, oxygen extraction and consumption rose initially but later consumption fell towards normal in the least severely ischaemic limbs; a progressive fall to below normal occurred in the most severely ischaemic limbs. Hyperbaric oxygen (2 ATA) did not influence blood-flow or metabolic exchange in either of these groups; in the remaining 40 per cent of the animals blood-flow fell significantly but oxygenation of the perfused areas of the limbs appeared to improve.

HYPERBARIC oxygenation has been used extensively in the treatment of various ischaemic conditions. The method, however, has not realized the initial clinical expectation. One of several possible explanations for this disappointing observation may be the vasoconstrictor effect of hyperoxia which has been described both in normal subjects (Bird and Telfer, 1966) and in patients with peripheral vascular disease (Schraibman and Ledingham, 1969a). Further physiological studies of the relationship between arterial oxygen tension and peripheral ischaemia seem justified.

In a previous experimental study (Stalker, McEwan, and Ledingham, 1973) the authors described the changes in limb blood-flow and oxygen consumption in dogs subjected to a brief period of ischaemia, and showed that the administration of oxygen at 2 ATA was associated with an increase in oxygen availability to the ischaemic limb and in the oxygen tension of the effluent venous blood; no consistent change in oxygen consumption occurred with hyperoxia. The present study reports the effects of more prolonged limb ischaemia on blood-flow and oxygen consumption and the different patterns of response to hyperbaric oxygen during the period of sustained ischaemia.

MATERIALS AND METHODS

Studies were performed on 12 mongrel dogs (weight range, 22–30 kg.) within one of the large compressed air chambers at the Western Infirmary, Glasgow. Anaesthesia was induced with sodium thiopentone (20 mg. per kg.) and maintained with trichlorethylene. Intermittent suxamethonium chloride was given as required to prevent reflex movement. The dogs were intubated and intermittent positive-pressure ventilation was established using a Palmer pump, the stroke volume of which was adjusted to maintain an arterial carbon dioxide tension (Paco$_2$) between 35 and 45 mm. Hg. The inspired oxygen concentration was measured with a paramagnetic oxygen analyser (Servomex DCL 101 Mk II). A catheter inserted in the brachial artery was advanced to lie in the mid-aorta (proximal to the site of subsequent arterial ligation). Arterial blood samples were withdrawn from this site and pressure recordings made using an ink-jet recorder (Elema Schönander Mingograph 81). Limb skin and mid-oesophageal temperatures were recorded on an Ellab TE3 Universal Thermocouple and the latter temperature was maintained constant within ± 1° C.

The canine limb is well supplied with collateral arterial channels. The lower limb vessels were exposed, therefore, at the root of the aorta and ischaemia was produced by ligating the external, internal, and circumflex iliac arteries as well as the median sacral artery. A T-tube was inserted at the level of the groin into the femoral vein and heparin was administered by the intravenous route in a dose of 100 mg. per kg. Blood-flow was measured by first clamping the proximal limb of the T-tube and thereafter collecting the effluent venous blood during exactly 30 or 60 seconds. Blood removed in this fashion was retransfused. The bulk of the blood passing out of the limb traversed the T-tube. Venous pressure was recorded before and after each blood-flow measurement. After initial surgery the animal was allowed to settle for a minimum period of 1 hour.

Table I.—DATA (MEAN ± S.E. OF THE MEAN) IN 12 DOGS BEFORE AND AFTER ARTERIAL LIGATION

	PRE-ISCHAEMIA		EARLY ISCHAEMIA (15 min)		LATE ISCHAEMIA (4 hr.)
Limb blood-flow (ml. per min.)	100 ± 7	$P<0{\cdot}001$	31 ± 3		23 ± 4
Pvo$_2$ (mm. Hg)	71 ± 4	$P<0{\cdot}001$	26 ± 2		30 ± 2
Pvco$_2$ (mm. Hg)	42 ± 2	$P<0{\cdot}001$	60 ± 3	$P<0{\cdot}001$	113 ± 13
O$_2$ availability (ml. per min.)	25·9 ± 2·1	$P<0{\cdot}001$	7·8 ± 0·8		5·6 ± 0·8
O$_2$ extraction (per cent)	6 ± 2	$P<0{\cdot}001$	59 ± 4		65 ± 5
O$_2$ consumption (ml. per min.)	1·1 ± 0·6	$P<0{\cdot}001$	4·7 ± 0·6		3·7 ± 0·6
Excess lactate (mmol per litre)		$P<0{\cdot}001$	1·4 ± 0·2	$P<0{\cdot}005$	6·1 ± 1·2

Mid-aortic and femoral venous blood samples were withdrawn for measurements of oxygen and carbon dioxide tension and *p*H using a triple electrode system (Radiometer Micro Electrode Unit with *p*H-meter 27 and Gas Monitor). Correction for the difference in oxygen-tension measurement between gas and blood was made using tonometered blood (McDowall, Ledingham, and Tindal, 1968). Further correction of the blood-gases and *p*H was made for any temperature difference between the electrode recirculation system and the animal's mid-oesophageal temperature (Radiometer Blood Gas Calculator Type B.G.C.1). Arterial and venous blood was removed for lactate and pyruvate estimations using the method of Boehringer and Sons. Haemoglobin (Hb) and packed-cell volume (P.C.V.) were measured at intervals throughout the experiment. The following data were derived:—

1. *Blood-oxygen content* (ml. per 100 ml.) = Hb (g.) × 1·34 × (O_2 saturation/100) + Po_2 (mm. Hg) × 0·0031 (Bunsen coefficient).

2. *Limb oxygen consumption* (ml. per min.) =

$$\frac{\text{Femoral vein flow (ml. per min.)} \times \text{femoral arteriovenous oxygen content difference (ml. per 100 ml.)}}{100}.$$

3. *Limb oxygen availability* (ml. per min.) =

$$\frac{\text{Femoral vein flow (ml. per min.)} \times \text{arterial oxygen content (ml. per 100 ml.)}}{100}.$$

4. *Limb oxygen extraction* (per cent) =

$$\frac{\text{Femoral arteriovenous oxygen content difference (ml. per 100 ml.)} \times 100}{\text{Arterial oxygen content (ml. per 100 ml.)}}.$$

5. *Excess lactate of the ischaemic limb*, according to the formula:—

$$(L_n - L_0) - (P_n - P_0)(L_0/P_0),$$

where L_0 and P_0 are the initial venous lactate and pyruvate values and L_n and P_n are the subsequent venous lactate and pyruvate values.

After the period of stabilization baseline measurements were recorded and the limb was rendered ischaemic as previously indicated. The initial period of study was performed at normal atmospheric pressure with the inspired gas mixture adjusted to maintain the arterial oxygen tension (Pao_2) between 95 and 105 mm. Hg; this period lasted at least 3 hours. The subsequent stage of each experiment was conducted at 2 ATA with oxygen as the inspired gas (Pao_2, ca. 1100 mm. Hg); this period lasted at least 1½ hours. Previous experiments established that pressure *per se* did not influence blood-flow and metabolism (Stalker and others, 1973).

RESULTS

The data in all 12 dogs before and up to 4 hours after arterial ligation are shown in *Table I*. Arterial ligation was associated with a fall in limb blood-flow on the affected side and a rise in oxygen extraction and oxygen consumption ($\dot{V}O_2$). The femoral venous oxygen tension (Pvo_2) fell by 45 mm. Hg and femoral venous carbon dioxide tension ($Pvco_2$) rose by 18 mm. Hg and continued to rise until at 4 hours the value was 113 ± 13 mm. Hg (mean ± standard error of the mean). Excess lactate showed a similar progressive rise and oxygen availability a progressive fall.

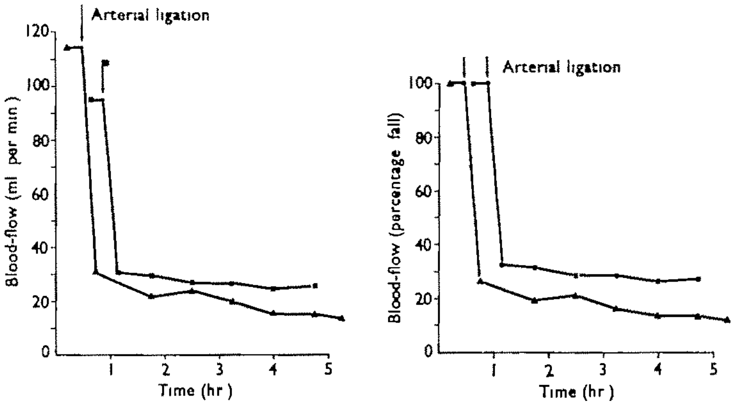
Analysis of the data of the individual dogs demonstrated that sustained arterial ligation resulted in a progressive fall in limb blood-flow in 3 of the dogs while the flow remained stationary in the other 9 (*Fig.* 1). In the 3 animals with a progressive fall in limb blood-flow the latter did not improve on release of the arterial ligatures, and skin temperature and excess lactate were also unaltered. These features along with marked muscle rigidity suggested that the limbs were dying (*Fig.* 2). In contrast, animals with a stable blood-flow exhibited a brisk reactive hyperaemia after release of the ligatures with an associated rise in skin temperature and fall in excess lactate, i.e., the limbs appeared to be surviving (*Fig.* 2).

Subsequent analysis of the experimental data is based on the observed variation in haemodynamic and metabolic response to hyperoxia during sustained ischaemia. Hyperbaric oxygen did not influence blood-flow in the 3 limbs which were judged to be dying (group A) or in 4 of the surviving limbs (group B—non-reactors); in the other 5 surviving limbs (group C—reactors) hyperoxia was associated with a further significant fall in blood-flow in the ischaemic limb ($P < 0·01$).

In all three groups of dogs ligation of the hind-limb arteries produced a substantial fall in blood-flow with parallel changes in oxygen availability (*Fig.* 3). Immediately after ligation blood-flow in the non-reactors exceeded that in the reactors by 9 per cent, but immediately prior to the period of hyperoxia the flows in both groups were comparable and exceeded flow in the dying limbs by 15 per cent. Oxygen extraction in all three groups (*Fig.* 4) rose initially by 53–59 per cent and, in general, the more severe the initial ischaemia the more marked were the changes in extraction. Thereafter, oxygen extraction tended to fall in the 5 animals of group B (non-reactors) and continued to rise in the other two groups, reaching 80 per cent 4½ hours after ligation in the dying limbs (group A). Oxygen consumption in all three groups rose fivefold after ligation and then fell in the animals with the dying limbs and in the surviving non-reactors. The fall in the latter group occurred immediately, but after the third hour flattened out at a level over twice normal. In the dying limbs the fall was delayed but once started became progressive. Oxygen consumption in the surviving reactor limbs did not fall throughout the 3½-hour period of ligation.

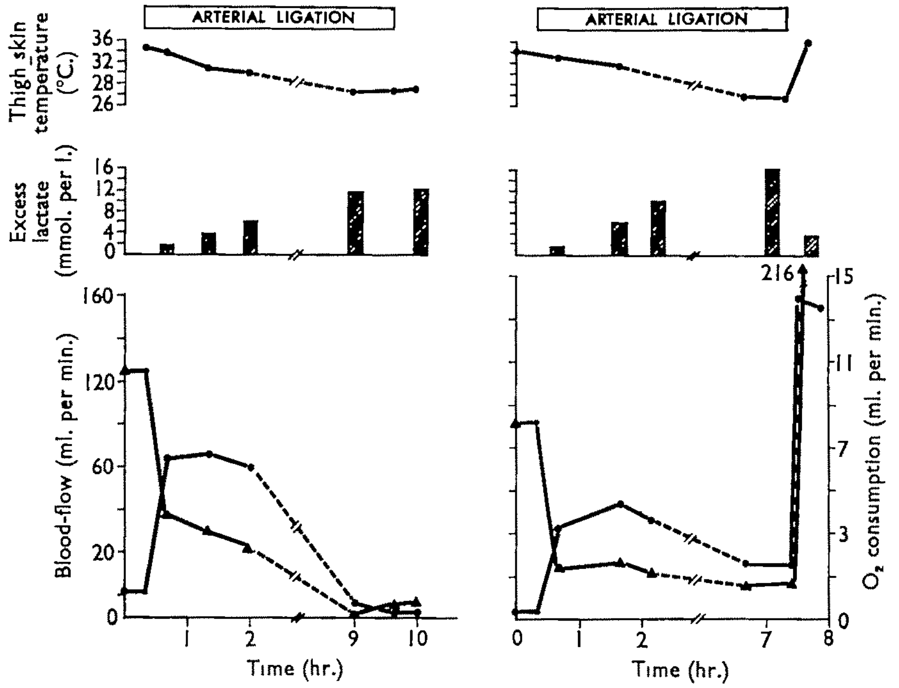
Pvo_2 fell to values between 20 and 30 mm. Hg in all three groups (*Fig.* 5), but just prior to the administration of hyperbaric oxygen the value in the surviving non-reactor limbs exceeded that of the other two groups by 10 mm. Hg. $Pvco_2$, having risen initially, plateaued at around 70 mm. Hg in the surviving non-reactor limbs and continued to rise in the other two groups to values of between 140 and 180 mm. Hg. The surviving non-reactor limbs were strikingly different from the other two groups in respect of excess lactate (*Fig.* 6), the level in the former levelling off at below 3 mmol per litre and rising progressively in the latter to between 7 and 11 mmol per litre.

The administration of oxygen at 2 ATA produced only slight transient falls in blood-flow in the dying and surviving non-reactor limbs (*Fig.* 3). In these same groups there was a transient fall in oxygen extraction and a rise in Pv_{O_2} (*Figs.* 4, 5), but the pattern of change in Pv_{CO_2} and in excess lactate was not altered (*Figs.* 5, 6). Oxygen consumption continued to fall in the dying limbs but appeared to rise slightly in the surviving non-reactor limbs. In the surviving reactor limbs, i.e., those demonstrating a significant reduction in blood-flow and oxygen availability ($P < 0{\cdot}01$), there was a sustained fall in oxygen extraction and consumption (*Fig.* 4). Pv_{O_2} and Pv_{CO_2} both rose initially and then levelled off, while excess lactate plateaued immediately and even began to fall.



A B

FIG 1.—Blood-flow (A) and percentage change in blood-flow (B); flow fell progressively in 3 animals (▲) and remained unchanged in 9 (■).



A B

FIG. 2.—Examples of 'dying' (A) and 'surviving' (B) limbs; a period of hyperoxia (not depicted) occurred in both animals, after which the arterial ligatures were released. ▲, Blood-flow. ●, Oxygen consumption.

DISCUSSION

The initial degree of ischaemia induced by arterial ligation in this study was comparable to that reported in the earlier investigation of acute limb ischaemia (Stalker and others, 1973). The curious finding of a disproportionately large increase in oxygen extraction was also confirmed. Thus oxygen consumption, as derived from the product of blood-flow and arterio-venous oxygen content difference, was substantially elevated, although in the majority of animals the initial very high values began to decrease after 1–2 hours of ischaemia and in the severely ischaemic limbs fell below normal after 6–7 hours.

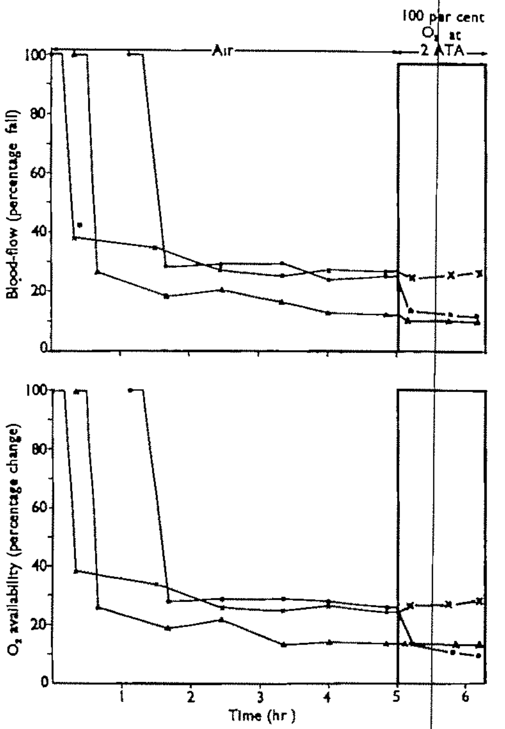


Fig. 3.—Percentage changes in blood-flow and oxygen availability in the three groups: group A, dying (▲); group B, non-reactors (×); group C, reactors (●). In the reactor group oxygen availability was significantly reduced during hyperoxia. The difference between the three groups in duration of ischaemia was calculated in a retrospective fashion from the onset of hyperoxia.

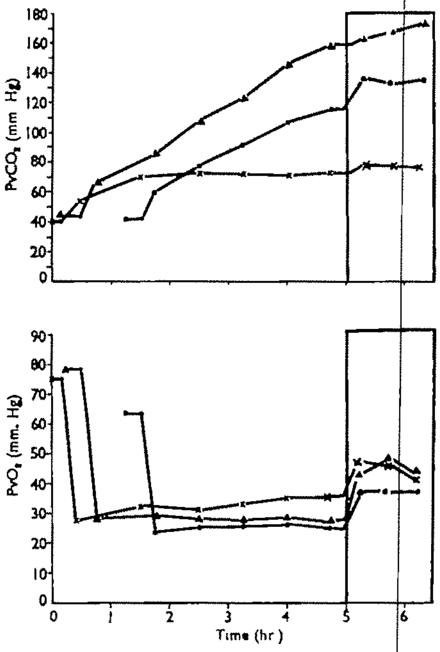


Fig. 5.—Venous P_{CO_2} and P_{O_2} values in the three groups. All groups showed a rise in P_{vO_2} during hyperoxia. P_{vCO_2} rose initially in all animals but flattened out in the non-reactors. Symbols as in *Fig.* 3.

During the course of the present study further steps were taken to eliminate the possibility of an error in experimental technique to explain the oxygen consumption data.

1. Oxygen Content Measurement.—The derived method of measurement of oxygen content was previously validated by comparison with the direct method of Van Slyke. Recently a further comparison between the derived method and a new direct method (Valeri, Zaroulis, Marchionni, and

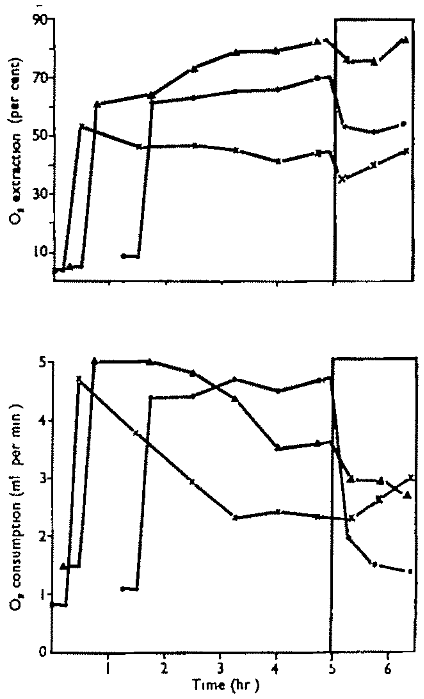


Fig. 4.—Oxygen extraction and consumption in the three groups. The greater the degree of initial ischaemia the higher was the extraction. The post-ligation rise in oxygen consumption was sustained only in the reactor group, to fall dramatically during hyperoxia. Symbols as in *Fig.* 3.

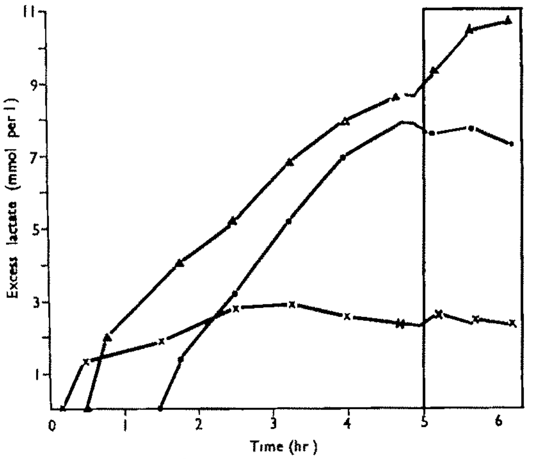


Fig. 6.—Excess lactate in the three groups. Again the non-reactor group differed strikingly from the other two groups Symbols as in *Fig.* 3.

Patti, 1972) has been made on 45 paired samples of blood. The results indicate, over a wide range of oxygen content values, a very close relationship between the two methods ($y=1·017x-0·431$; $r=0·993$).

2. **Temperature Correction.**—The temperature of the ischaemic limb fell progressively with sustained ischaemia. The possibility existed that an error in the calculation of oxygen content might have occurred as a result of the animal's mid-oesophageal temperature being used in the calculation. A systematic examination in 8 dogs, however, indicated that this factor could be excluded as a possible source of error.

3. **Arterial Sampling Site.**—The normal site for arterial sampling was the mid-aorta. Arterial blood reaching the ischaemic limb passed through tortuous collateral channels and it was considered that some loss of oxygen might have occurred between the mid-aorta and the distal collateral arteries as they entered the limb. Using the mid-aortic blood for measurement of arterial oxygen content thus might have given a falsely high value for the arteriovenous oxygen content difference. Blood samples were taken, therefore, from several arterial sites within the ischaemic limb. No consistent difference in oxygen content between these and samples taken from the mid-aorta was discovered.

From these further methodological studies it can be accepted that the changes in oxygen extraction and consumption recorded were accurate and that before the oxygen consumption of an ischaemic limb fell below normal in the process of dying there was a phase of increased metabolic activity. Since there was a simultaneous progressive increase in excess lactate in the venous effluent it must be assumed that some tissues of the limb were undergoing anaerobic metabolism at the same time as other tissues had increased aerobic metabolism. The less severe the ischaemic insult the less obvious were these various effects, as seen in the surviving non-reactor limbs. The measurements of venous carbon dioxide tension and excess lactate were considerably more valuable in distinguishing between different groups of animals than the absolute measurement of blood-flow. The combined effects of the disturbances in the respiratory and non-respiratory components of acid–base balance resulted in a difference in venous *p*H of from 0·13 to 0·38 unit between non-reactor surviving limbs immediately prior to hyperoxia and the other two groups (means of 7·22 and 7·09/6·84 units respectively).

The effect of hyperbaric oxygen administration in experimental limb ischaemia seemed to take three principal courses. In the limbs in which the ischaemic insult was most severe there was little if any effect other than an increase of 15–20 mm. Hg in venous oxygen tension, which can, therefore, be taken to be of little value as an indicator of improved tissue oxygenation. The same general comments may be made of the limbs in which the ischaemic insult was least severe, i.e., the surviving non-reactor limbs, in which the metabolic disturbances were minimal. Blood-flow in the remaining 40 per cent of the animals, i.e., the surviving reactor limbs, was at a critical level since, although the absolute flow reduction was not distinguishable from that of the other surviving limbs, the metabolic changes were comparable to those in the dying limbs. The changes in this group during hyperoxia suggest that some areas ceased to receive any blood supply, which would account for the reduced total effluent blood-flow. The remaining areas, however, would appear to have been better oxygenated, as suggested by the levelling off of the venous carbon dioxide tension and reduction in excess lactate formation.

If these conclusions are correct it would be important in future studies to determine which tissues cease to receive a blood-supply and which are better oxygenated. Thereafter, pharmacological methods of altering the distribution of ischaemic blood-flow could be investigated, as previously described in chronic peripheral ischaemia in patients undergoing hyperbaric oxygenation (Schraibman and Ledingham, 1969b). Of considerable practical interest was the observation that the venous oxygen tension gave no clue as to the variation in tissue oxygen exchange occurring in the different groups of ischaemic limbs. Of much greater value were the measurements of venous carbon dioxide tension, excess lactate, and *p*H.

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COMPARISON OF TWO ELECTROLYTE SOLUTIONS FOR SHORT PERFUSION AND HYPOTHERMIC STORAGE IN EXPERIMENTAL RENAL PRESERVATION

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SUMMARY

In recent years the need for preserving kidneys has become of great importance because of the development of renal transplantation. The most effective and practical method yet described to preserve kidneys outside the body appears to be immersion in a cooled solution combined with initial perfusion. The aim of the present study was to compare two perfusates routinely used in this procedure: Collins solution and Perfudex. A total of 22 kidneys was removed and stored with one of these perfusates and then autotransplanted.

Renal function was monitored by radio-isotope measurements: $^{197}HgCl_2$ uptake and radio-hippuran renography. An assessment of the histological evidence of renal damage was made on preserved kidneys 3 months after transplantation.

As judged by the results of these investigations the most satisfactory preservation of kidneys was obtained with the Collins solution. The use of this perfusate allows a storage time of 24 hours without decreased function or morphological changes in the kidneys. Other investigators have also confirmed the efficacy of the Collins solution and have provided further evidence for its superiority over conventional perfusates for kidney preservation. The current use of the Collins solution, as now recommended by the *France Transplant Association*, makes the future of clinical kidney transplantation more hopeful.

THE recent development of kidney transplantation has stimulated increased investigation into the problem of renal preservation. Kidney storage is required to allow time for tissue typing and for the preparation of the recipient.

Belzer, Ashby, and Dunphy (1967) and Woods (1971) have been able to preserve dog kidneys successfully for 3, 5, and 7 days with continuous perfusion systems. However, such a complex, bulky, and expensive method cannot provide a suitable solution in clinical transplantation and therefore a more practical method is desirable. It is generally agreed that good preservation of kidneys can also be achieved by hypothermic storage only if the organs have been initially perfused with a cooled electrolyte solution. This procedure is uncomplicated and does not require constant monitoring by a technician. Its efficacy seems chiefly to depend on the perfusate composition, but there is no agreement about the solution to be used. In the present report two conventional perfusates are compared: an electrolyte solution (C_3), described by Collins, Bravo-Shugarman, and Terasaki (1969), the ionic composition of which is similar to that of intracellular fluid, and a dextran-containing plasma substitute (Perfudex) routinely used in Scandinavia (Franksson, Collste, Lundgren, Magnusson, and Wehle, 1967; Brunius, Fritjofsson, and Gelin, 1969).

MATERIALS AND METHODS

Twenty-two dog kidneys were preserved for 24 hours with the Collins solution or with Perfudex and were then reimplanted into their hosts. In fact, much longer periods of kidney preservation could have been undertaken with such a method but preservation for 24 hours seems to provide enough time for pre-transplant studies and for preparing the recipients. *Table I* lists the composition of the solutions used in this procedure; solution C_3 was identical to that described by Collins and others (1969) except for the reduction of magnesium sulphate in order to prevent the turbidity which results from its addition. Heparin was added to Perfudex in the same proportions as to C_3.

Table I.—CONSTITUENT OF THE TWO MODIFIED SOLUTIONS USED IN THE PRESENT STUDY

Constituent	*Perfudex*	*Solution C_3*
NaCl (g. per l.)	8	—
$Na_2HPO_4.2H_2O$ (g. per l.)	0 06	—
$NaHCO_3$ (g. per l.)	—	0·84
KCl (g. per l.)	0·40	1·12
KH_2PO_4 (g. per l.)	0·06	2·05
$K_2HPO_4.3H_2O$ (g. per l.)	—	9·70
$MgSO_4.7H_2O$ (g. per l.)	0·20	3 69
Glucose or dextrose (g. per l.)	1·00	25·00
Dextran 40 (g. per l.)	0·5	—
Heparin (I.U.)	5 000	5·000
Procaine (g. per l.)	—	1
Papaverine (g. per l.)	—	0 015

Preservation and Autotransplantation Procedures.—The left kidney was removed through a flank incision and immediately perfused for about 5 minutes, with the storage solution cooled to 4° C., from a height of 100 cm. through a catheter introduced into the renal artery. The kidney was then stored for 24 hours before reimplantation.

Group 1: *Collins.*—Eight kidneys flushed with perfusate C_3 were immersed in this solution cooled to 4° C. as described by Collins and others (1969).

Group 2: *Perfudex.*—Nine kidneys perfused with Perfudex were wrapped in a gauze compress moistened in this solution and kept at a temperature of 4° C.

Group 3: *Modified Perfudex.*—Five kidneys which were also perfused with Perfudex were stored by simple immersion in this solution in the manner described for group 1.

Group 4: *Control*.—Two kidneys were immediately reimplanted without preservation.

Reimplantation was carried out through a midline incision. The kidney was revascularized by the anastomoses of the renal vein end to side with the iliac vein and of the renal artery end to end with the external iliac artery. The ureter was anastomosed to the bladder.

Assessment of Renal Function after Transplantation.—Two radio-isotope measurements were used for assessing the transplant's functional status.

Renal $^{197}HgCl_2$ *Uptake*.—Because of the affinity of the mercury atom for tubular cells the injection of $^{197}HgCl_2$ provides a way of studying the kidney's viability by scanning of the renal surface. The renal

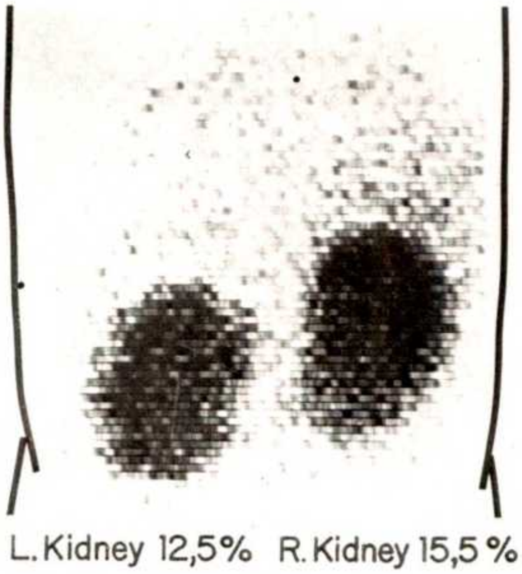

FIG. 1.—Normal $^{197}HgCl_2$ renal uptake before preservation.

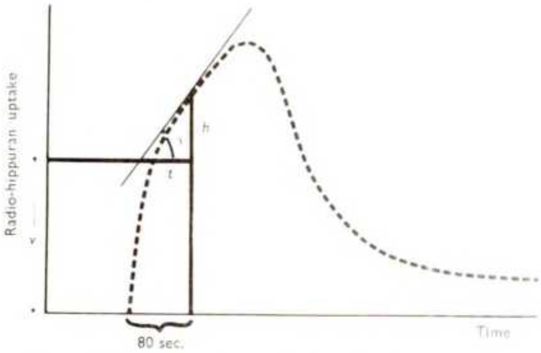

FIG. 2.—Normal radio-hippuran renogram illustrating determination of the slope of the secretory phase and calculation of the index of radio-hippuran uptake.

$i = tg\,\alpha/\tau$.

GRADE OF CHANGES	GROUP "COLLINS"								GROUP "PERFUDEX"									GR. "MODIFIED PERFUDEX"				
	C_2	C_{10}	C_{11}	C_{19}	C_{22}	C_{27}	C_{28}	C_{29}	C_4	C_7	C_8	C_{12}	C_{16}	C_{20}	C_{21}	C_{25}	C_{26}	P_1	P_2	P_3	P_4	P_5
slight	■	■	■		■	■	■	■			■	■					■	■		■		
moderate				■					■					■								
severe										■			■		■	■			■		■	■

FIG. 3.—Histological changes of transplanted kidneys.

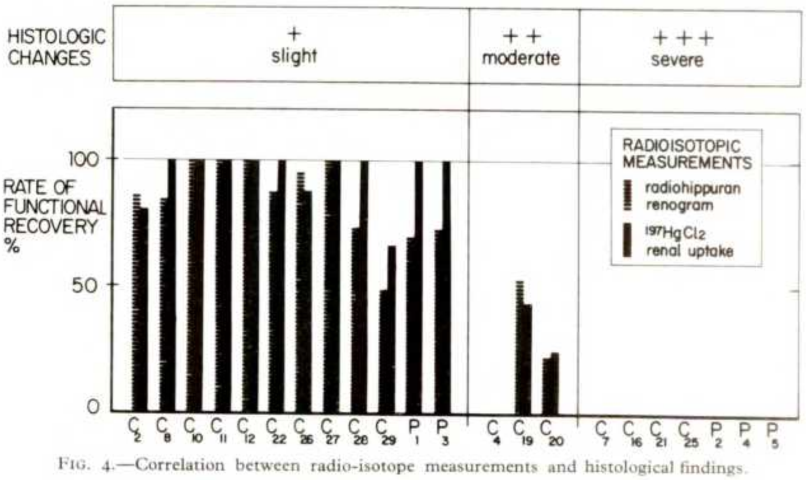

FIG. 4.—Correlation between radio-isotope measurements and histological findings.

scintigram affords an impression of size and form of the kidney and so enables the viability of the renal parenchyma to be affirmed. However, this scan does not give evaluation of renal function. Raynaud, Desgrez, and Kellershohn (1969) showed that a quantitative measurement can be made of such a scintigraph for obtaining information on renal function; this is the measurement of the fixation rate of $^{197}HgCl_2$.

This measurement was performed 1 day before preservation and then 1, 3, 6, and 10 weeks after transplantation. $^{197}HgCl_2$ in a dose of 500 μc. was injected intravenously. The percentages of this dose taken up by the transplanted kidney and by the contralateral kidney were determined after subtracting the background radiation on the third day after mercury injection. Usually 15 ± 5 per cent of the injected $^{197}HgCl_2$ is fixed in each kidney (*Fig.* 1).

Radio-hippuran Renogram.—This test was performed at the same time as $^{197}HgCl_2$ scintigraphy. ^{131}I-labelled ortho-iodohippurate (hippuran) was given as a single intravenous dose of 5 μc. for each study. Radioactivity was determined by placing over each kidney a sodium iodide crystal scintillation probe connected to a ratemeter and a rectilinear recorder. The normal renogram exhibits three segments: the vascular segment, the secretory segment, and the excretory segment. The first is a rapid rise of radioactivity on the tracing which may be ascribed to the radio-hippuran reaching the kidney's vessels. A second phase then occurs in which radioactivity rises more slowly. This is due to differential concentration of the material by the kidney and is assumed to be evidence of active tubular transport of the ortho-iodohippurate (Collins and Richard, 1965). The third segment, in which the radioactivity decreases, relates to the excretion of the secreted radioactive material. In fact, the three phases are not exactly in succession since the process of excretion begins during the second phase.

Following the work of Collins and Richard (1965) and in the belief that any rise in concentration of radioactivity during the second phase was evidence of extraction by functioning proximal tubular epithelium, it has been assumed that the slope of the secretory segment is of value in the study of renal function. This slope is dependent on the concentration of the hippuran reaching the intravascular space in the area 'seen' by the probe. This implies that the measurement of this slope is only reliable in the assessment of renal function if the height of the vascular segment is considered. Therefore, we have defined an index (i) of radio-hippuran uptake which has been determined 80 seconds after the beginning of the test, because at this time the process of secretion is not yet competing with that of excretion.

$$i = tg\,\alpha/v,$$

where $tg\,\alpha$ is the slope of the secretory segment at 80 seconds, and v is the radioactivity detected at the end of the vascular segment.

$$tg\,\alpha = h/t,$$

where h is the increase in radioactivity detected between the end of the vascular segment and 80 seconds, and t is the time of the determination of the index (80 seconds).

$$i = \frac{h/t}{v} = \frac{h/v}{t} = \frac{\text{concentration}}{\text{time}}.$$

Thus, this index must be considered as active concentration per minute. *Fig.* 2 illustrates this.

Histological examination of the transplanted kidneys was performed 3 months after transplantation.

RESULTS

Radio-isotope Measurements.—The measurements recorded 10 weeks after transplantation were compared with those obtained preoperatively. Thus, for each transplanted kidney (T.K.) a rate of functional recovery at the tenth week was calculated from the following formula (*Table II*),

$$R_1 \text{ (per cent)} = \frac{\text{T.K. index of radio-hippuran uptake at 10 weeks}}{\text{T.K. index of radio-hippuran uptake before transplantation}}$$

For each dog the rate of $^{197}HgCl_2$ fixation of the transplanted kidney was compared with that of the contralateral kidney (R.K.) before preservation and at 10 weeks after transplantation (*Table III*).

$$R_2 \text{ (per cent)} = \frac{\text{At 10 weeks (T.K. rate of } ^{197}HgCl_2 \text{ fixation)/(R.K. rate of } ^{197}HgCl_2 \text{ fixation)}}{\text{Before transplantation (T.K. rate of } ^{197}HgCl_2 \text{ fixation)/(R.K. rate of } ^{197}HgCl_2 \text{ fixation)}}$$

Most kidneys (6 out of 8) preserved with the Collins solution showed good recovery of function: $R_1 > 70$ per cent; $R_2 > 70$ per cent. In contrast, of the 14 kidneys perfused with Perfudex, 9 failed to function: $R_1 < 30$ per cent; $R_2 < 30$ per cent. No clear-cut difference was noted between groups 2 and 3; the bad results of these groups appeared to be due to the composition of Perfudex and were not affected by the storage technique of either immersion or wrapping in a compress.

Histological Examination.—The histological changes observed on the transplanted kidneys were graded blindly for comparative purposes as slight (+), moderate (+ +), or severe (+ + +).

Slight changes: These consisted of interstitial oedema and congestion in a few glomeruli. Some of the tubules were lined by regenerating flattened epithelium.

Moderate changes: Extravasation of red blood-cells was noted in the interstitium. The glomerular cells showed hydropic degeneration and large amounts of proteinaceous material were found in the tubules.

Severe changes: Interstitial fibrosis was observed with vacuolation in the glomerular tufts and cellular necrosis in the tubules.

In *Fig.* 3 the transplanted kidneys have been divided into three groups according to this grading. The most severe changes were found in the kidneys preserved with Perfudex, while those perfused by the Collins solution showed minimal changes. Thus the histological examination confirmed the results obtained by radio-isotopic measurement as to the efficacy of solution C$_3$ compared with Perfudex as a perfusate for hypothermic kidney preservation.

DISCUSSION

Renal autotransplantation appears to be the most practical procedure for assessing the efficacy of a preservation technique without adding immunological problems (Dunphy and Jacob, 1960). Although many studies have been done on the important problem of how to recognize kidneys which have suffered damage during preservation all the tests so far described, such as histological examination (Fisher, Copeland, and Fisher, 1967), oxygen consumption determination (Lannon, Tukaram, Olivier, MacKinnon, and Dossetor, 1967), surface *p*H measurements (Alexander, Dmochowski, Murray, and Couch, 1970), and the tetrazolium test (Terazaki, Martin, and Smith, 1967), often do not provide enough information to judge whether a preserved kidney is suitable for transplantation. Moreover, contralateral nephrectomy was not performed in our experimental procedure because it has several disadvantages. Since stored kidneys always demonstrate some degree of reduced function simultaneous removal of the opposite kidney provides too severe a test. By contrast, when contralateral nephrectomy is performed later, the function of the stored kidney cannot be assessed by conventional methods for several weeks. The radio-isotopic measurements used in the present study have enabled us to assess the function of both the transplanted and the remaining kidneys. The correlations observed between these results and the histological examination have been aimed chiefly at establishing the value of the quantitative tests of renal function (*Fig.* 4). Thus in only 2 cases (dogs C$_4$ and C$_{29}$) was there no correlation between the findings.

The value of the radio-isotopic investigations in assessing renal function has been confirmed by numerous reports. Sharpe, King, Hume, Lee, and Kauffman (1966), Burke and Halko (1967), and Magnusson, Collste, Franksson, and Lundgren (1967) showed that ^{131}I hippuran renography has its greatest value when performed serially in the follow-up studies of renal grafts. Raynaud and others (1969) drew attention to the good agreement between measurement of the rate of ^{197}HgCl$_2$ fixation and other renal-function tests, especially creatinine and PAH clearance. This measurement was also thought by Cendron, Raynaud, and Desgrez (1970) to be extremely valuable for making separate records of the renal function in dogs in view of the multiple sources of error in separate catheterization.

Our observations are similar to the results obtained by other groups working in this field. Collste, Bjorken, Collste, and Groth (1970) and Collins, Hartley, and Clunie (1971) conducted experimental series of kidney preservation in which direct comparison was made between the C$_3$ solution and a dextran-containing plasma substitute, and they confirmed the greater efficacy of the C$_3$ solution. Successful renal preservation for 48 hours has been obtained by these authors and by Wen Pen Liu, Humphries, Russel, Stoddard, and Moretz (1971) after brief perfusion and hypothermic storage using the Collins solution. On the other hand, Brunius and others (1969), who obtained the best results with

Table II.—INDEX OF RADIO-HIPPURAN TAKEN UP BY TRANSPLANTED KIDNEYS (T.K.)

INDEX (per cent)	CONTROL GROUP		COLLINS GROUP								PERFUDEX GROUP									MODIFIED PERFUDEX GROUP				
Dog	T$_1$	T$_2$	C$_2$	C$_{10}$	C$_{11}$	C$_{19}$	C$_{22}$	C$_{27}$	C$_{28}$	C$_{29}$	C$_4$	C$_7$	C$_8$	C$_{12}$	C$_{18}$	C$_{20}$	C$_{21}$	C$_{25}$	C$_{26}$	P$_1$	P$_2$	P$_3$	P$_4$	P$_5$
Before transplantation	0·76	0·82	0·82	0·65	0·80	1·04	0·68	0·90	1·02	0·98	0·60	0·82	0·95	0·76	0·98	0·62	1·09	1·20	0·99	0·71	0·52	1·04	0·90	0·95
At 10 weeks	0·78	0·75	0·70	0·80	0·82	0·56	0·39	0·97	0·73	0·48	0·00	0·00	0·80	0·85	0·00	0·14	0·00	0·00	0·94	0·95	0·20	0·05	0·00	0·00
R_1	100	91	85	100	100	53	87	100	73	49	0	0	84	100	0	22	0	0	95	70	0	73	0	0

Table III.—RATE OF ^{197}HgCl$_2$ UPTAKE OF TRANSPLANTED KIDNEYS (T.K.) AND CONTRALATERAL KIDNEYS (R.K.)

INDEX (per cent)	CONTROL GROUP		COLLINS GROUP								PERFUDEX GROUP									MODIFIED PERFUDEX GROUP				
Dog	T$_1$	T$_2$	C$_2$	C$_{10}$	C$_{11}$	C$_{19}$	C$_{22}$	C$_{27}$	C$_{28}$	C$_{29}$	C$_4$	C$_7$	C$_8$	C$_{12}$	C$_{18}$	C$_{20}$	C$_{21}$	C$_{25}$	C$_{26}$	P$_1$	P$_2$	P$_3$	P$_4$	P$_5$
R.K. before transplantation	13·3	10·5	14·0	16·3	11·1	19·5	26·0	11·4	17·6	11·5	8·5	16·2	16·0	17·3	11·3	20·7	19·1	18·0	11·3	14·9	14·8	15·1	17·1	19·7
T.K. before transplantation	10·5	10·8	14·0	12·9	8·7	17·8	20·6	10·2	12·0	11·5	7·9	9·9	10·4	12·0	9·6	12·3	14·7	8·5	8·8	10·1	15·5	12·7	12·0	22·4
R.K. at 10 weeks	12·4	12·0	9·6	14·6	20·8	14·9	13·3	12·3	14·5	23·0	27·5	26·4	14·5	16·9	8·3	21·5	12·5	26·4	16·3	13·8	11·7	14·5	17·6	21·1
T.K. at 10 weeks	10·2	11·9	7·7	13·8	21·5	6·0	16·6	12·3	12·4	15·0	0·0	1·0	9·6	12·2	0·0	3·2	0·50	1·4	8·8	10·9	0·5	11·1	0·0	0·0
R_2	99	88	80	100	100	43	100	100	100	66	0	0	100	100	0	24		0	88	100	0	100	0	0

Perfudex, did not report successful kidney preservation in excess of 24 hours.

The reasons for the more beneficial effects of intracellular electrolyte solutions are well known because of the present knowledge of tissue injury occurring during hypothermic storage. When used for long periods of preservation cooling can induce severe renal damage.

Vascular Thrombosis.—This results from the activation of cold agglutinins (Lofstrom and Zederfeldt, 1967) and from the increase in the blood viscosity (Levy, 1959). In fact, the development of flow obstructions can be avoided by brief perfusion before storage (Cleveland, Lee, Prout, and Hume, 1964). Perfudex, which contains low molecular weight dextran 40, seems to give rise to an effective wash-out of red cells because of its viscosity-lowering and non-aggregating effect (Hitchcock, Kiser, Telander, and Peterson, 1964). The efficiency of dextran 40 in clearing the kidney of formed blood elements has been demonstrated by Kerstein, Bergentz, and Lewis (1970). The Collins solution in addition to its similarity to intra-cellular ionic composition also has some ability to effect a wash-out of the capillary bed: the lack of a sodium–potassium gradient because of the presence of C_3 in the capillary lumen causes the membrane potential of the vascular smooth muscle to be low. The resulting passive vasodilatation would improve the wash-out of red cells (Langer, 1968). However, it would appear that C_3 is significantly less effective in clearing the kidney than Perfudex, but this effect is obviously not essential prior to renal preservation.

Cellular Ionic Disturbances.—Hypothermia lowers the renal metabolic rate so that the energy requirements are less than normal. It also reduces the active membrane transport mechanisms. Therefore the renal cells gain water and sodium and lose magnesium and potassium when the kidney is stored in the cold (Ennerson, 1966; Keeler, Swinney, Taylor, and Uldall, 1966). These ionic shifts resulting from diffusion down concentration gradients cause cellular damage. There is evidence that preservation of cellular architecture can only be ensured by perfusates close to intracellular ionic composition which are able to reduce the entry of sodium into the cell and the loss of potassium. Wallach, Cahill, Rogan, and Jones (1962) and Kamiyama, Webb, and Ecker (1970) have speculated on the mechanism of the protection offered by the high concentration of magnesium in the Collins solution. They contended that it was due to a 'stabilizing' effect on the lysosomal membrane. Indeed, during preservation kidneys always suffer some degree of ischaemia, which if severe can cause lysosomal membrane rupture, release of acid hydrolases, and intracellular digestion (Groenwald, Weber, Van der Walt, Greeff, and Van Zyl, 1971). Finally, the hyperosmolarity of the Collins solution reduces cellular swelling. This also is a factor of importance.

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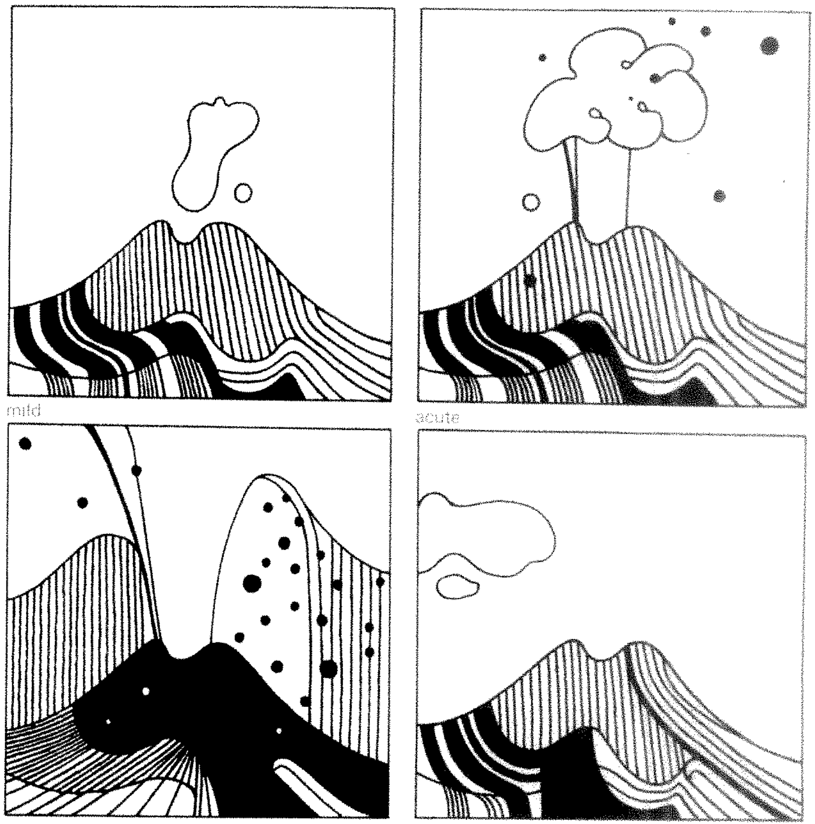

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REGENERATION OF PARIETAL AND VISCERAL PERITONEUM IN THE IMMATURE ANIMAL: A LIGHT AND ELECTRON MICROSCOPICAL STUDY

By A. T. Raftery

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Summary

1. The healing of visceral and parietal peritoneum has been investigated in the immature animal by both light and electron microscopy.

2. Healing has been found to occur more rapidly in the immature animal when compared with the adult animal. Parietal peritoneum was covered by a new mesothelium in 7 days, while the liver was covered in 5 days.

3. The new mesothelium developed from subperitoneal perivascular connective-tissue cells but it was not possible to determine whether these were primitive mesenchymal cells or fibroblasts.

4. The findings are discussed in relation to the pathogenesis of peritoneal adhesions.

The healing of peritoneum in the immature animal is of interest in view of the fact that intestinal obstruction due to peritoneal adhesions is more common following abdominal surgery in early life (Devens, 1963; Replogle, Johnson, and Gross, 1966), especially in the neonatal period. The greater incidence and severity of adhesions in the infant compared with the adult may reflect a difference in the nature of healing of peritoneum. Ellis, Harrison, and Hugh (1965) have shown that peritoneal regeneration occurred more rapidly in the immature rat than in mature ones, but flattening of the surface layer of cells, as seen in paraffin sections cut perpendicular to the wound surface, was used as a criterion for assessing complete mesothelial regeneration. This has been shown to be an inadequate method of assessment and the need for Häutchen preparations in which the surface cells are viewed *en face* has been stressed (Eskeland, 1966; Raftery, 1973a). The present investigation was undertaken to determine, by both light and electron microscopy, the nature of peritoneal regeneration in the immature animal and to compare the findings with those for the adult animal (Raftery, 1973a, c).

MATERIALS AND METHODS

A total of 92 male Sprague-Dawley rats weighing 50–60 g. was used in this investigation. The rats were anaesthetized with ether and the abdominal cavity was opened through a midline incision 3 cm. long. The operative technique was clean but not strictly aseptic. Wounds approximately 1 mm. deep and either 0·5 × 0·5 cm. or 1 × 1 cm. were made in the liver capsule by a tangential cut with a scalpel blade. A wound was also made on each side of the midline in the parietal peritoneum, that on the left side being 2 × 2 cm. and that on the right side 1 × 1 cm. The peritoneum, together with the underlying layer of muscle, was removed within this area. The abdominal incision was closed in two layers, catgut sutures being placed through the musculoperitoneal layer and silk sutures through the skin. Animals were killed by exsanguination under ether anaesthesia at 12 hours, 24 hours, and at daily intervals up to 8 days after operation. At least 3 animals were examined at each stage.

The liver was removed, rinsed briefly in 5 per cent glucose, immersed in 0·25 per cent silver nitrate for 30 seconds, rinsed again in 5 per cent glucose, and then fixed in 10 per cent formol–saline for 8–12 hours. The wounds in the parietal peritoneum were removed together with a wide margin of adjacent peritoneum, pinned flat on cork, and treated in the same manner as the liver. Häutchen preparations of the wounds were subsequently made as described by Eskeland (1966) and stained with haematoxylin. In other animals the wounds were excised, fixed in formol–sublimate or Bouin's fluid, dehydrated, and embedded in paraffin wax. Serial sections were cut perpendicular to the wound surface at 6 µm. These sections were stained with haematoxylin and eosin and by either the picro-Gomori method or Ledrum's stain (Humason, 1962) for fibrin and collagen.

Specimens of parietal peritoneum and liver were also fixed in 2·5 per cent glutaraldehyde in 0·1 *M* cacodylate buffer, post-fixed in 1 per cent osmium tetroxide in 0·1 *M* phosphate buffer, dehydrated in graded solutions of ethanol, passed through epoxypropane, and embedded in Araldite. Sections 1 µm. thick were cut on an LKB Ultrotome III, stained with methylene blue–Azure II (Richardson, Jarett, and Finke, 1960), and examined by light microscopy. Such sections were cut from specimens obtained from different areas of the wound surface. When appropriate areas were found, thin sections were cut, mounted on uncoated grids, and either stained with lead citrate alone (Reynolds, 1963) or double stained with uranyl acetate (Stempack and Ward, 1964) and lead citrate, prior to examination in an AEI type EM6B electron microscope.

In order to label the peritoneal macrophages some animals were given an intraperitoneal injection of 1 ml. of a 0·2 per cent suspension of polystyrene spheres (0·79 µm. diameter Dow–Latex; Serva, Feinbiochemica, Heidelberg) in 0·9 per cent saline at the time of operation. Specimens from these animals were processed for Häutchen preparations in order to check if the inflammatory reaction caused by the polystyrene spheres had any effect on the nature of healing. Some specimens were processed for electron microscopy as described above. Some normal animals were given an intraperitoneal injection of 1 ml. of a 0·2 per cent suspension of polystyrene spheres in order to check that normal mesothelial cells and subperitoneal fibroblasts did not ingest polystyrene spheres. Specimens of parietal and visceral peritoneum from these animals were fixed in 2·5 per cent glutaraldehyde, processed as described above, and examined by electron microscopy.

RESULTS

1. Macroscopic.—Adhesions to the wounds were found in 16 animals and in all but one of these the liver was adherent to part of the wound in the parietal peritoneum. The one exception was an adhesion between the omentum and parietal peritoneum.

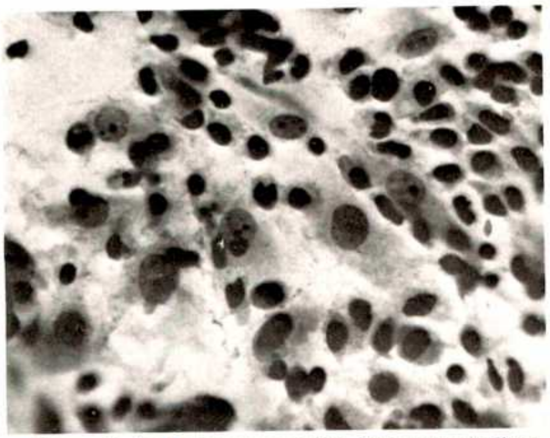

FIG. 1.—Parietal peritoneum at 2 days. Two types of cell are seen on the wound surface: one resembling a monocyte, the other a large cell with an indistinct boundary, prominent nucleoli, and pronounced cytoplasmic basophilia resembling a fibroblast. Häutchen. (× 450.)

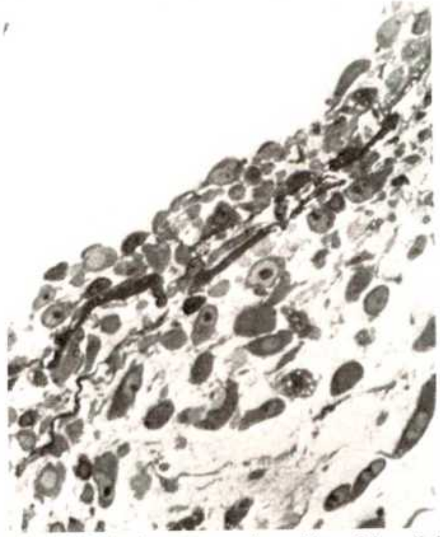

FIG. 2.—Parietal peritoneum at 2 days. Most of the cells in the deeper parts of the wound resemble fibroblasts. Similar cells are also seen in the more superficial parts of the wound. 1 μm. Araldite section, methylene blue–Azure II (MB–AII). (× 220.)

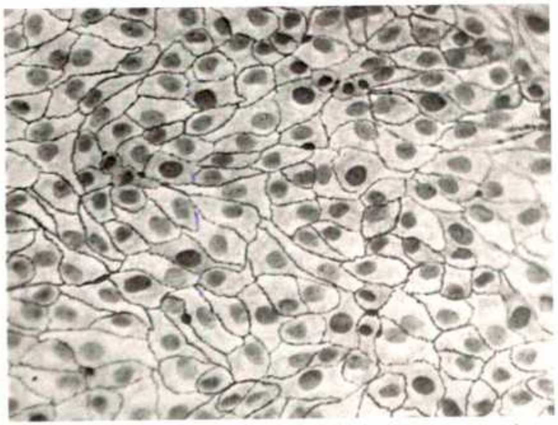

FIG. 3.—Parietal peritoneum at 7 days. Note the complete healing of the mesothelial layer; occasional mitotic figures are seen on the wound surface. Häutchen. (× 280.)

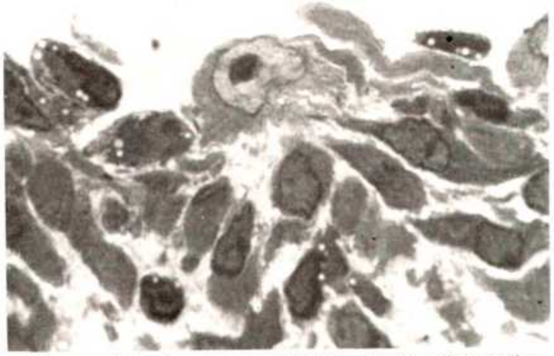

FIG. 4.—Parietal peritoneum at 4 days. A large cell possessing a prominent nucleolus and resembling a fibroblast is seen on the wound surface. Note that, in contrast to the macrophages, it contains no polystyrene spheres. 1 μm. Araldite section, MB–AII. (× 900.)

During the first 24 hours the wounds were uneven and haemorrhagic, but by 2 days they were paler, and by 3 days they were usually smooth and glistening. At 5 days it was difficult to distinguish the wound from the normal surrounding parietal peritoneum. The wounds in the liver capsule appeared as greyish-white puckered areas and were easily visible at 8 days.

2. Light Microscopy.—

Control Animals.—Following intraperitoneal injection of polystyrene spheres into normal animals none was seen in mesothelial cells or subperitoneal fibroblasts.

Intraperitoneal injection of polystyrene spheres did not have any discernible effect on the time or nature of peritoneal healing.

a. Parietal Peritoneum.—The cellular changes which occurred on the wound surface, in its base, and in the adjacent peritoneum were similar to those reported for the adult animal (Raftery, 1973a) but occurred more rapidly in the immature animal. Thus, by 2 days after operation the initial acute inflammatory response had subsided and two well-defined types of cell were seen on the wound surface (*Fig.* 1): one was a small round cell with a dark staining, eccentric, kidney-shaped nucleus which was identified as a cell of the monocyte/macrophage type, and the other was a large cell with an ill-defined boundary, having a large, round, or oval nucleus, containing one or more prominent nucleoli and with pronounced cytoplasmic basophilia. The latter resembled fibroblasts. The above changes were not seen until 3 days in the adult animal. In sections cut perpendicular to the wound surface marked fibroblastic proliferation was seen in the base of the wound at 2 days (*Fig.* 2), and only occasional macrophages were seen. The number of monocyte-like cells on the wound surface gradually decreased and at 5 days only the fibroblast-like cells remained. These cells came into contact with one another as shown by complete silver lines in Häutchen preparations, and reconstituted the new mesothelium. Healing was completed by 7 days (*Fig.* 3) compared with 8 days in the adult animal.

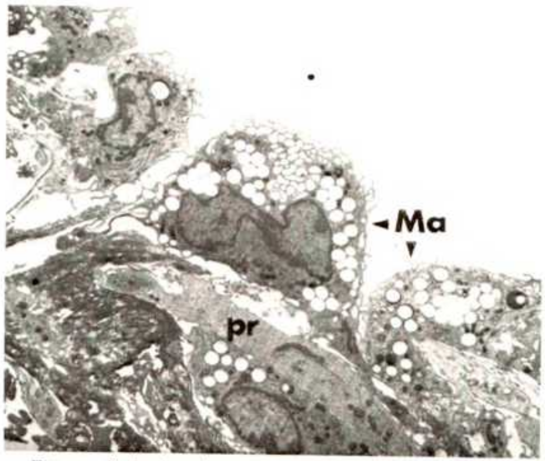

FIG. 5.—Parietal peritoneum at 2 days. Macrophages (**Ma**) containing polystyrene spheres rest on a fibrin base. A process (**pr**) of a primitive mesenchymal cell extends towards the wound surface. Uranyl acetate (UA) + lead citrate (LC). (× 2000.)

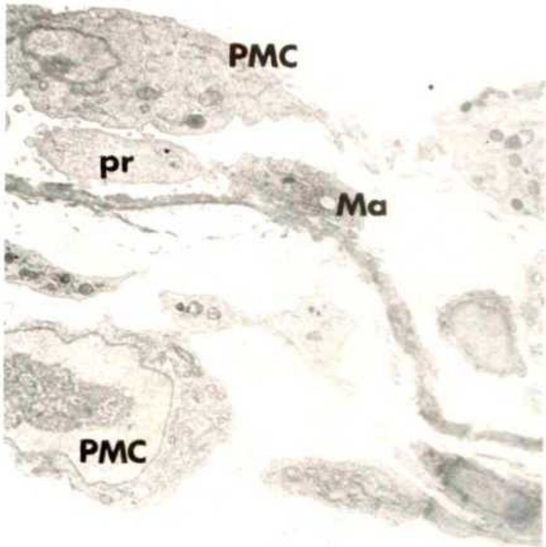

FIG. 6.—Parietal peritoneum at 2 days. Primitive mesenchymal cells (**PMC**) are seen on the wound surface and in the base of the wound. A process (**pr**) of a primitive mesenchymal cell and part of a macrophage (**Ma**) containing a polystyrene sphere are also seen. LC. (× 3000.)

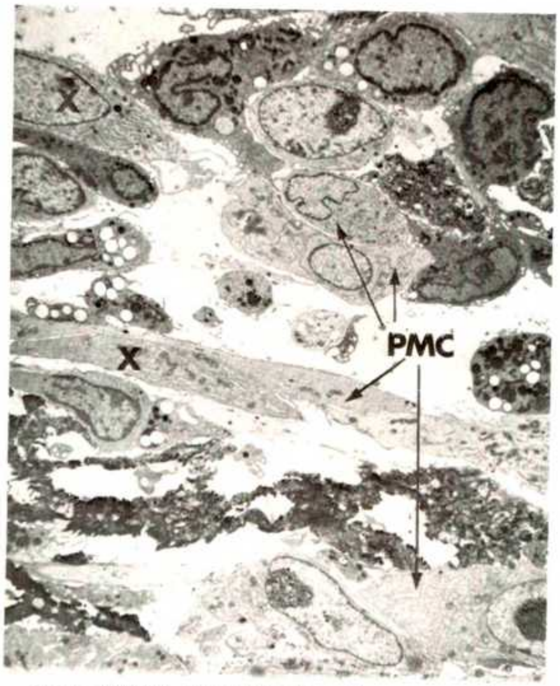

FIG. 7.—Parietal peritoneum at 2 days. Numerous macrophages and primitive mesenchymal cells (**PMC**) are seen in the base of the wound. Some cells (**X**) have some characteristics common to both primitive mesenchymal cells and fibroblasts and probably represent intermediate forms between the two. Polystyrene spheres are seen only in macrophages. UA + LC. (× 2000.)

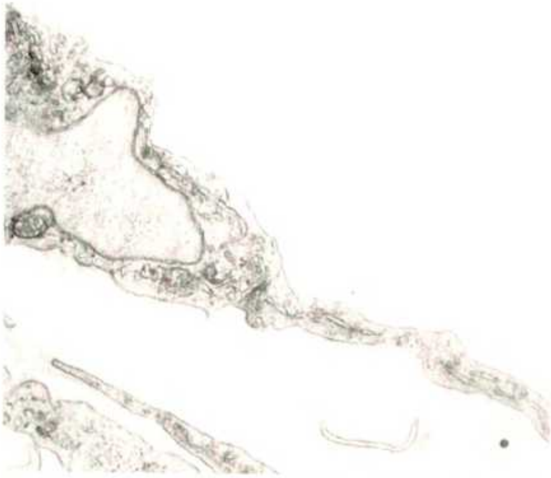

FIG. 8.—Parietal peritoneum at 2 days. A long process of a primitive mesenchymal cell extends along the wound surface. LC. (× 7500.)

Throughout the course of healing polystyrene spheres were seen only in cells of the monocyte/macrophage type (*Fig.* 4) and never in fibroblasts or mesothelial cells. There was no difference in the time or nature of healing between small and large wounds.

b. Liver.—Healing of wounds in the liver capsule closely resembled the healing of parietal peritoneum for the most part. Again healing of the wound occurred more rapidly than in the adult animal and a complete layer of mesothelium had covered the wound by 5 days compared with 7 days in the adult animal. There was no difference in the time or nature of healing between small and large wounds.

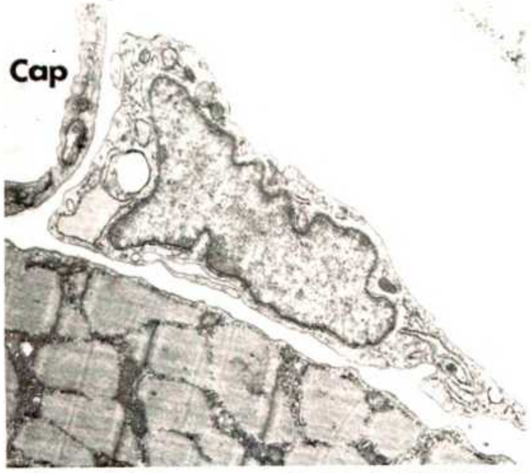

FIG. 9.—Parietal peritoneum at 2 days. A perivascular connective-tissue cell is seen adjacent to a capillary (**Cap**). This cell closely resembles a primitive mesenchymal cell. LC. (× 7500.)

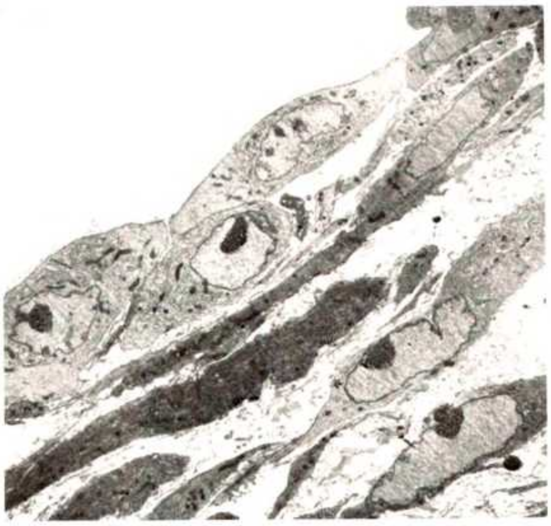

FIG. 11.—Parietal peritoneum at 5 days. The surface cells closely resemble the underlying fibroblasts in nuclear and cytoplasmic characteristics. UA + LC. (× 2750.)

3. Electron Microscopy.—The findings for parietal peritoneum and liver will be described together and where any variation occurred this will be pointed out at the relevant stage.

12 *Hours*.—Numerous cells were seen entangled within fibrin strands. Polymorphs predominated but macrophages and a few eosinophils and mast cells were also seen. Polystyrene spheres were seen in polymorphs and macrophages. No detached mesothelial cells were seen on the wound surface.

24 *Hours*.—The majority of cells on the wound surface were macrophages resting on a fibrin base. No cells which could be identified as detached mesothelial cells were seen on the wound surface.

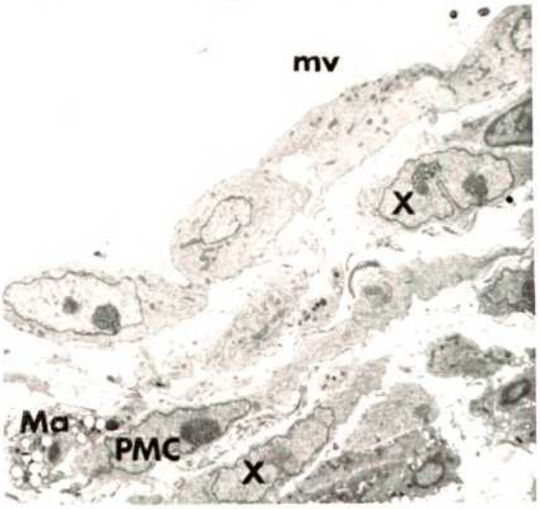

FIG. 10.—Parietal peritoneum at 3 days. The surface cells possess microvilli (**mv**) and have nuclear and several cytoplasmic characteristics in common with primitive mesenchymal cells (**PMC**) and proliferating fibroblasts. Some cells (**X**) appear intermediate in form between primitive mesenchymal cells and proliferating fibroblasts. Note that polystyrene spheres are seen only in macrophages (**Ma**). LC. (× 1750.)

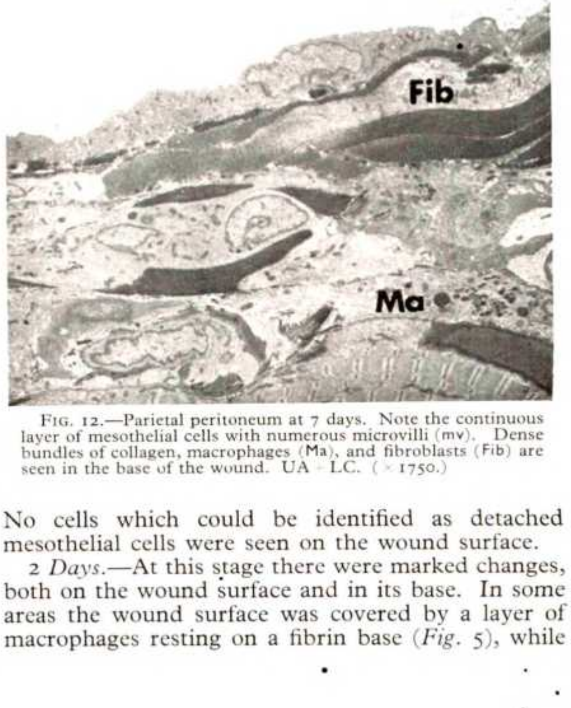

FIG. 12.—Parietal peritoneum at 7 days. Note the continuous layer of mesothelial cells with numerous microvilli (**mv**). Dense bundles of collagen, macrophages (**Ma**), and fibroblasts (**Fib**) are seen in the base of the wound. UA + LC. (× 1750.)

2 *Days*.—At this stage there were marked changes, both on the wound surface and in its base. In some areas the wound surface was covered by a layer of macrophages resting on a fibrin base (*Fig.* 5), while

in others, primitive mesenchymal cells were seen (*Fig.* 6). Even in areas where macrophages predominated on the wound surface, numerous primitive mesenchymal cells were seen in the base of the wound (*Fig.* 7). Many of the latter possessed long processes which extended towards the wound surface (*Fig.* 5). These processes contained chiefly aggregates of ribosomes and few other organelles. In areas where primitive mesenchymal cells were present on the wound surface long processes often extended from them along the wound surface (*Fig.* 8). There was a close similarity in nuclear and cytoplasmic characteristics between primitive mesenchymal cells on the wound surface (*Fig.* 8) and perivascular connective-tissue cells in the base of the wound (*Fig.* 9). No detached mesothelial cells could be identified on the wound surface at this stage. Polystyrene spheres were seen only in macrophages and never in primitive mesenchymal cells.

3 *Days* (*Fig.* 10).—At this stage very few macrophages remained on the wound surface. The majority of cells seen on the wound surface resembled the proliferating fibroblasts or primitive mesenchymal cells in the base of the wound in nuclear and cytoplasmic characteristics except that adjacent cells were often joined by tight junctions. In many cases it was not possible to draw a sharp distinction between primitive mesenchymal cells and fibroblasts and many cells appeared intermediate in form between the two. Small amounts of collagen were now seen in the base of the wound. Macrophages were the only cells to contain polystyrene spheres.

4 *Days.*—The appearances were similar to those at 3 days.

5 *Days.*—At this stage there were differences between the wounds in the parietal peritoneum and the liver. The cells on the surface of the wounds in the parietal peritoneum were of uniform appearance and, apart from microvilli and tight junctions, closely resembled proliferating fibroblasts in the base of the wound in both nuclear and cytoplasmic characteristics (*Fig.* 11). However, tight junctions were not always seen between cells on the wound surface. In the case of the liver there was a continuous layer of mesothelial cells on the wound surface and either tight junctions or desmosomes were seen between adjacent cells. A basement membrane was seen beneath some mesothelial cells covering the liver at this stage but frequent breaks were observed in it. No basement membrane was observed beneath mesothelial cells covering the wound in the parietal peritoneum.

6 *Days.*—The appearances at 6 days did not differ from those at 5 days in the case of both the liver and the parietal peritoneum.

7 *Days* (*Fig.* 12).—A continuous layer of mesothelial cells was seen on the surface of both the liver and the parietal peritoneum. A basement membrane was seen beneath the mesothelial cells in most areas but gaps in it were still visible. Dense bundles of collagen were seen in the base of the wound together with fibroblasts and macrophages. No polystyrene spheres were seen in mesothelial cells although some were still present in macrophages.

8 *Days.*—The appearances were similar to those at 7 days except that a continuous basement membrane was now seen beneath the mesothelial cells.

DISCUSSION

This study of peritoneal wound healing in the immature animal has in part confirmed the findings of Ellis and others (1965) that peritoneal healing is more rapid in the immature animal. The earlier authors noted a flattened layer of cells on the wound surface at 3 days as well as numerous elongated fibroblasts in the base of the wound. The present study has shown that, while cells on the surface of the wound in the parietal peritoneum were mainly flattened by 3 days, complete mesothelial regeneration did not occur until 7 days, as shown by Häutchen preparations, compared with 8 days in the adult animal. In the case of the visceral peritoneum covering the liver healing was complete by 5 days, compared with 7 days in the adult animal (Raftery, 1973a).

Previous investigations have led to the conclusions that the new mesothelium arises by three possible mechanisms:—

1. Transformation of peritoneal macrophages.
2. Metaplasia of subperitoneal connective-tissue cells.
3. Seeding of mesothelial cells from the adjacent normal peritoneum.

It has been shown (Raftery, 1973a, c) that there is no evidence to support the theory that seeding of mesothelial cells from adjacent surfaces makes a significant contribution to peritoneal healing, although a few mesothelial cells are present in the peritoneal fluid of operated animals (Raftery, 1973b). Also no evidence was found to support the theory that peritoneal macrophages are transformed into mesothelial cells either directly or via fibroblasts. It was concluded that the new mesothelium arose from subperitoneal perivascular connective-tissue cells but it was not possible to determine whether these were primitive mesenchymal cells or fibroblasts (Raftery, 1973c). Undifferentiated primitive mesenchymal cells are considered to be present in the perivascular connective tissue and to have the potentiality of becoming transformed into other types of cells (Maximow, 1927).

The ultrastructural study of peritoneal regeneration in the immature animal did not provide any evidence to support the theory that macrophages were transformed into fibroblasts or mesothelial cells. If the latter were true it is likely that at some stage polystyrene spheres would be seen in fibroblasts and mesothelial cells. At a time when macrophages were filled with polystyrene spheres none was seen in fibroblasts or mesothelial cells. It is concluded that in the immature animal, as in the adult animal, mesothelial cells do not arise by transformation of peritoneal macrophages. No detached mesothelial cells were seen on the wound surface in the early stages of healing and it is therefore concluded that the new mesothelium does not arise by seeding of mesothelial cells from the adjacent peritoneum. The results of the light microscopical study suggested that the new mesothelium arose by metaplasia of subperitoneal fibroblasts. However, correlation of the results obtained by light and electron microscopy indicated that many of the cells which were designated as fibroblasts on the basis of light microscopy represented a spectrum of cells ranging from primitive mesenchymal cells to mature fibroblasts. The results suggest that the new mesothelium arises in the immature animal in the same manner as it does in the adult animal, namely from the subperitoneal perivascular connective-tissue cells, but it has not been possible to determine whether these are primitive mesenchymal cells or fibroblasts. Proliferation of primitive mesenchymal cells and the appearance of fibroblasts and collagen occur more rapidly in the immature animal. It is suggested that because proliferation of primitive mesenchymal cells and the appearance of fibroblasts occur more rapidly mesothelial regeneration is correspondingly more rapid.

The healing of the visceral peritoneum covering the liver is faster than the healing of the peritoneum of the abdominal wall. This finding is similar to that in the adult animal. The most likely explanation for this finding is that the liver provides a fairly firm substrate for healing while the peritoneum of the anterior abdominal wall is subject to distension.

Adhesions occurred more commonly in the immature animal than in the adult animal. Thus, while in adult animals adhesions were seen in only 6 out of 100 animals and involved adhesion between the liver and the midline laparotomy wound (Raftery, 1973a), in the immature ones adhesions occurred in 16 out of 92 animals and involved adherence between the liver wound and part of the wound in the parietal peritoneum. It has been reported (Howes and Harvey, 1932) that fibroplasia occurs earlier in the immature animal, and in the present study a more rapid proliferation of fibroblasts and appearance of collagen have been observed compared with the adult animal. This may have a bearing on the greater incidence of adhesions in the immature animal. The wounds made in the immature animal were the same size as those made in the adult animal (Raftery, 1973a) and it is possible that the relatively large size of the wound in the immature animals resulted in ischaemia in the base of the wound and adhesions arose as the result of ischaemia, as suggested by Ellis (1962).

How can the concept of mesothelial regeneration from subperitoneal perivascular connective-tissue cells be related to the pathogenesis of peritoneal adhesions? Ellis (1971) stated in his review of the causes of peritoneal adhesions that it has been accepted in the past that absorption of a fibrinous exudate depended on the presence of an intact mesothelium. If this remained intact, it was argued, fibrin disappeared. If it was destroyed persistent fibrous adhesions would develop. It has been shown (Robbins, Brunschwig, and Foote, 1949; Trimpi and Bacon, 1952; Williams, 1955; Ellis, 1962), however, that large peritoneal defects would heal without adhesion formation in the majority of cases, but when an attempt was made to appose the edges of the wounds by sutures, adhesions were formed to the wound (Thomas and Rhoads, 1950; Ellis, 1962; Hubbard, Khan, Carag, Albites, and Hricko, 1967). On the basis of his studies Ellis (1962) concluded that it was not the peritoneal defect itself that was a stimulus to adhesion formation but the presence of ischaemic tissue which probably resulted from pulling the wound edges together under tension with sutures. Hartwell (1955) wrote:—

> 'the characteristics of serosal cells being what they are, it is only logical to believe that they prevent adhesions by combining their fibrinolytic power with their epithelial-like function of extending themselves as a solid sheet of cells to cover any raw surface. This gives them the ability to come between any two apposed musculo-fibrous surfaces which are stuck together only by fibrin, which has not been organised by the growth of granulation tissue or laying down of collagen. Adhesions are composed of collagen fibres. If fibroplasia occurs between two surfaces before motion or before serosal cells grow in to separate them a permanent adhesion will be formed. If serosal covering of one or both of the apposed denuded surfaces be rapid and permanent no adhesions will form.'

At the time that this statement was written there was no evidence to support the claim that serosal cells had fibrinolytic power, but recently Myhre-Jensen, Larsen, and Astrup (1969) have demonstrated fibrinolytic activity in peritoneal mesothelium. Also, the statement regarding the epithelial-like function of serosal cells in extending themselves as a solid sheet to cover any raw surface is erroneous (Ellis and others, 1965; Eskeland, 1966; Raftery, 1973a). Ellis (1962) attributed adhesion formation to ischaemia but does not appear to have considered closely the effect of ischaemia on the mesothelial cells. They would probably undergo necrosis, but firm evidence on this point is lacking. A possible relationship exists between the theory of Ellis and the findings of the present investigation showing that mesothelial cells arise from perivascular cells, be they mesenchymal cells or fibroblasts. Ischaemia could result from either inadequate proliferation of vessels in the base of the wound or, if adequate proliferation of vessels did occur, an inadequate blood-flow in these vessels. In either case it is conceivable that the perivascular connective-tissue cells may not proliferate owing to ischaemia, and mesothelial cells would not appear, or appear more slowly, in the area of ischaemia. The absence of definitive mesothelial cells, with associated fibrinolytic activity, could lead to adhesion formation due to fibroplasia before definitive mesothelial cells grow between the two apposed surfaces. While this is largely conjectural it would suggest that an investigation of the fibrinolytic activity of regenerating mesothelium is required.

The present study has shown that regeneration of peritoneum occurs more rapidly in the immature animal. It has shown also that the new mesothelium arises from subperitoneal connective-tissue cells, but it has not been possible to determine whether these are primitive mesenchymal cells or fibroblasts.

Acknowledgements.—I wish to thank Professor R. L. Holmes for his helpful criticism, Messrs. R. K. Adkin and R. H. Nettleton for technical assistance, Mr. P. McPhie for preparation of the specimens for electron microscopy, and Mrs. Sandra Brougham for typing the manuscript.

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PINWORM INFESTATION OF THE APPENDIX

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SUMMARY

Eight cases of pinworm infestation of the appendix presenting with symptoms simulating acute appendicitis are reported from a study of 293 appendicectomy operations performed at University College Hospital, London, in the past 2 years.

In each case a diagnosis of appendicitis was made on clinical grounds but in 6 patients the appendix was normal histologically.

Symptoms mimicking appendicitis but caused by *Enterobius vermicularis* infestation merit recognition as a disease process and treatment to eradicate the worm must not be overlooked.

THE vermiform appendix is an anatomical blind loop of the gastro-intestinal tract within which it is possible for pathogenic organisms to become established, later to manifest their presence in disease. Among the pathogens which may behave in this way are schistosome ova (Turner, 1909; Abdel Shafi, 1940; Elwi and El Tiraei, 1955), *Entamoeba histolytica* (Manson-Bahr, 1946), and *Enterobius vermicularis* (Duran-Jorda, 1957; Coutelen, Deblock, Biguet, and Capron, 1958; Richmond and Guthrie, 1964).

Eggs transferred from an infected patient on the fingers or on towels and linen are ingested and hatch in the gastro-intestinal tract. Mature pinworms inhabit the caecum and appendix and the male worms perish in the bowel. Gravid females, however, migrate to the anus and appear on the perianal skin. where they die liberating their eggs. This process, especially at night, causes intolerable itching and inevitably in time contamination of fingers and fomites. Usually infestation of one member of a family will result in the infestation of the remainder.

Appendicitis caused by obstruction of the appendix by a bolus of worms is recognized, but symptoms simulating appendicitis in the absence of obstruction or secondary infection have not often been reported.

MATERIALS AND METHODS

Surgical specimens removed at operation for appendicitis performed either as an emergency procedure or electively after a mass had settled were studied. Appendices removed in the course of other surgical procedures were excluded. The specimens were fixed by immersion in formol–saline and set in paraffin wax. Microtome sections were cut and stained with haematoxylin and eosin. In the 2 years of this study 293 appendicectomies were performed.

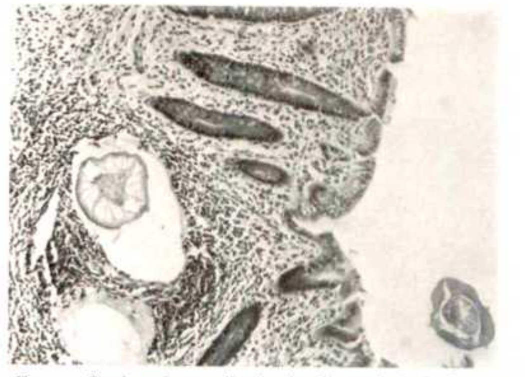

FIG. 1.—Section of appendix showing *E. vermicularis* pinworms in the lumen and embedded in the mucosa, without evidence of active inflammation. (× 138.)

RESULTS

Two hundred and seventeen specimens showed the histological changes of acute bacterial inflammation, 68 specimens were normal, and 8 specimens contained pinworms. Six of the 8 specimens containing pinworms showed no evidence of inflammation despite the presence of the worms and the preoperative clinical picture of appendicitis. Even if the worms lie within the mucosa there may be no active inflammation (*Fig.* 1). *Table I* summarizes the findings in the patients in whom worms were found in the appendix.

DISCUSSION

Symptoms which closely mimic those of appendicitis may be found in association with pinworm infestation (Gross, 1953). Nausea and vomiting, abdominal pain, and tenderness in the right iliac fossa may cause the clinician to decide that appendicectomy is the proper course of action and in a proportion of such patients the appendix will contain pinworms.

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The incidence of infestation is thought to vary according to the environment and to the prevailing standards of hygiene. Figures as high as 57·5 per cent have been reported for children in northern France (Coutelen and others, 1958), and 10·8 per cent for patients in Egypt (Soliman, 1966). In this country specimens from Manchester Children's Hospital showed infestation in 52 of 691 patients, giving an incidence of 7·1 per cent (Duran-Jorda, 1957). In our study we have found an incidence of 2·7 per cent, and it is of interest to note that only in the 2 cases where the patient was over 21 years of age was there evidence of acute inflammation. Usually the worms live in the appendix without causing damage, but eventually they may erode through the mucosa as in the present *Case* 5. Bacterial contamination could arise via this route and it is possible that prolonged infestation is related to the development of inflammatory change.

Table I.—SUMMARY OF THE FINDINGS IN THE PRESENT SERIES

CASE	AGE (yr.)	CLINICAL PRESENTATION	OPERATIVE FINDINGS	HISTOLOGY
1	6	Colicky abdominal pain for 3 days which had localized in the lower abdomen. Anorexia but no vomiting. Temp., 37·7° C. Tenderness and guarding in the right iliac fossa	Normal appendix	Pinworm in the lumen, but no inflammatory changes in the wall
2	7	Central abdominal pain for 2 days which had shifted to the right iliac fossa. She had not vomited, but was generally feeling unwell. Temp., 38° C. Tenderness in the right iliac fossa with gaurding and slight rebound tenderness	Normal appendix	Mild inflammatory changes of the mucosal layer and large lymphoid follicles with hyperplastic germinal centres in the submucosal layer. The appendicular lumen contained adult pinworm
3	12	24-hour history of right iliac fossa pain associated with nausea and vomiting. Temp., 37° C. Tenderness in the right iliac fossa but no guarding or rebound tenderness	Normal appendix	Essentially a normal appendix containing a worm
4	12	4-hour history of pain in the right iliac fossa, anorexia, and nausea. Temp., 38·3° C. Tenderness and guarding in the right iliac fossa	Normal appendix	Segments of pinworms in the lumen with a focal granulamatous eosinophilic reaction at one point in the mucosa
5	17	48-hour history of central colicky abdominal pain which shifted into the right iliac fossa associated with vomiting but no diarrhoea or urinary symptoms. Temp., 37·1° C. Tenderness in the right iliac fossa but no guarding or rigidity	Normal appendix	Atrophic appendix showing adult pinworms inside the lumen and one worm in the mucosal layer of the appendix but no active inflammation (*Fig.* 1)
6	19	Central abdominal pain for 12 hours which settled in the right iliac fossa, associated with nausea and vomiting. Temp., 38·3° C. Tenderness with rebound in the right iliac fossa	Normal appendix	Pinworms in the lumen but no local inflammation
7	25	Had an attack of acute appendicitis which settled on conservative treatment but continued to have episodes of right iliac fossa pain lasting a few hours. Elective appendicectomy	Large swollen appendix with evidence of previous infection	Rather early acute appendicitis affecting all coats; lumen contained disintegrating worms
8	69	Admitted with acute sickness, vomiting, and abdominal pain of 2 days' duration. Temp., 37·7° C, with tenderness and rebound in lower abdomen	Purulent free fluid and gangrenous perforated appendix	Acute on subacute peritonitis with pieces of partly calcified worms in serosa

Preoperative investigation is unhelpful in this condition since the eggs are not passed in the stools and eosinophilia is an uncommon finding (Tolstedt, 1968). Often the diagnosis is made only at histological examination. Postoperatively the patients are still infested with pinworms and we strongly recommend that the patients should be given a suitable antihelminthic and that all other members of their family should also be treated.

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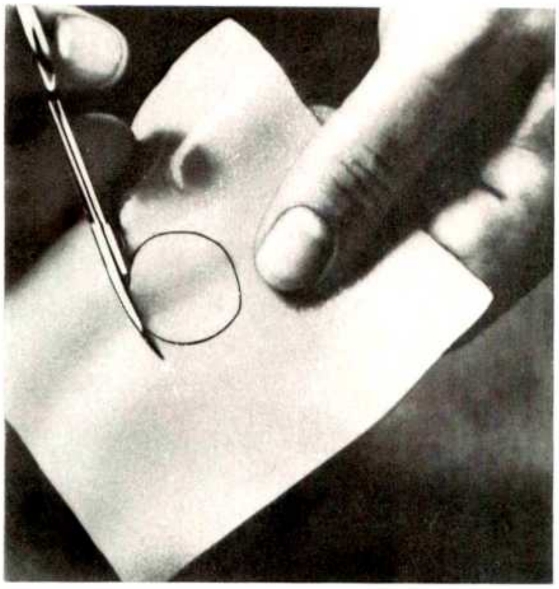

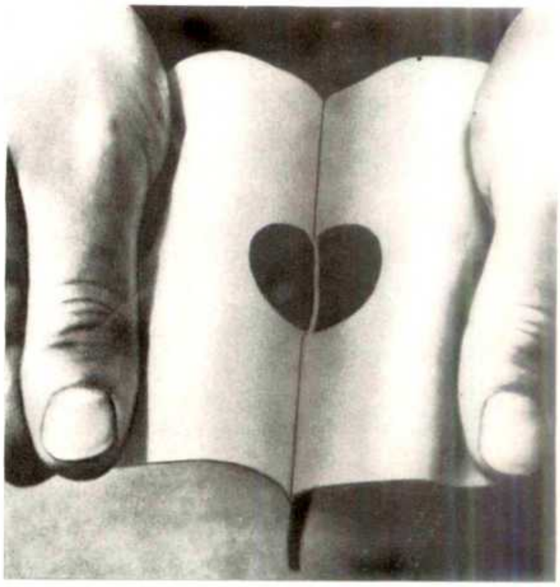

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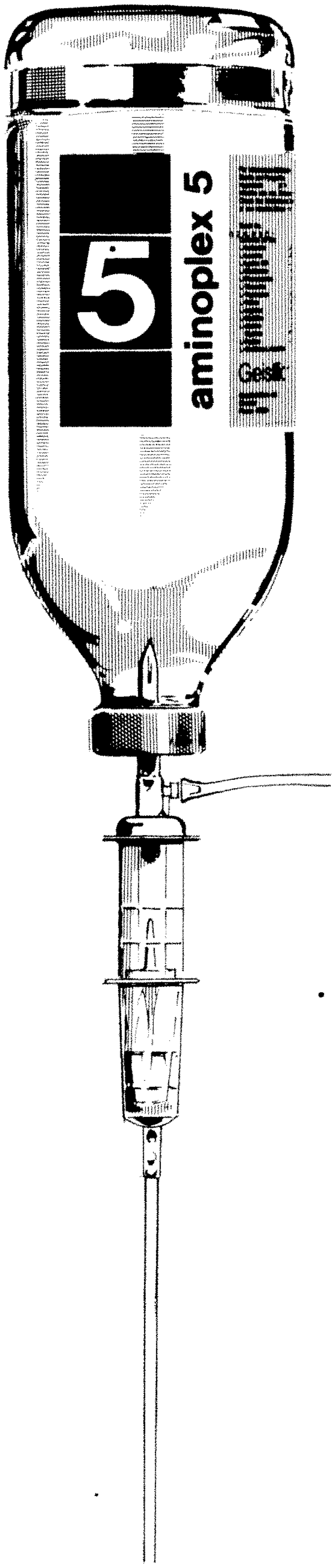

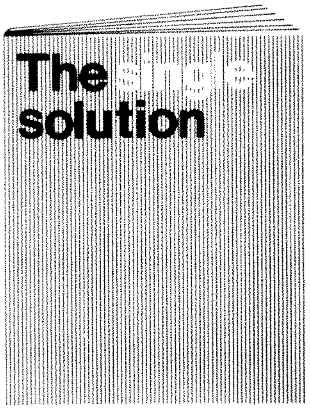

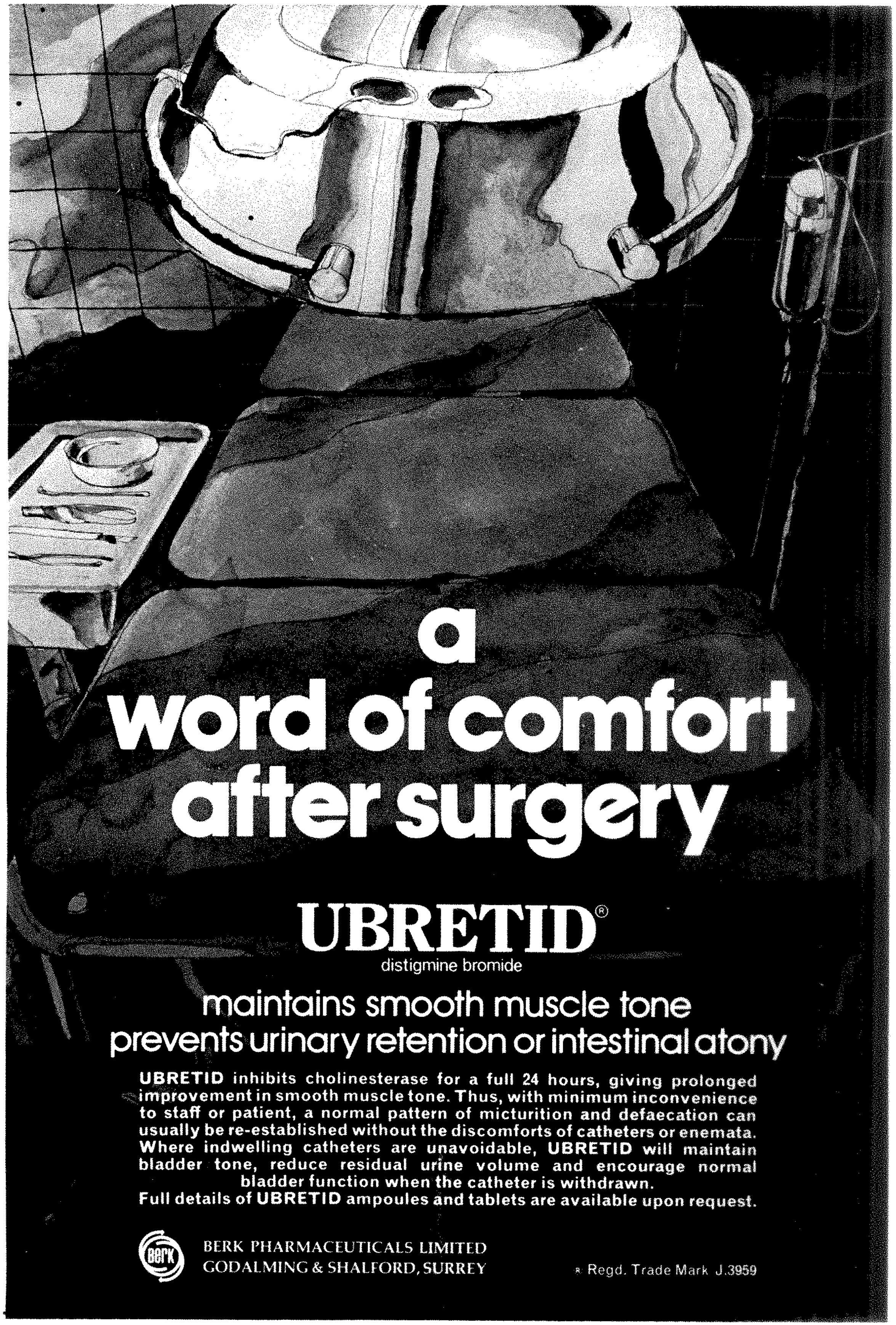

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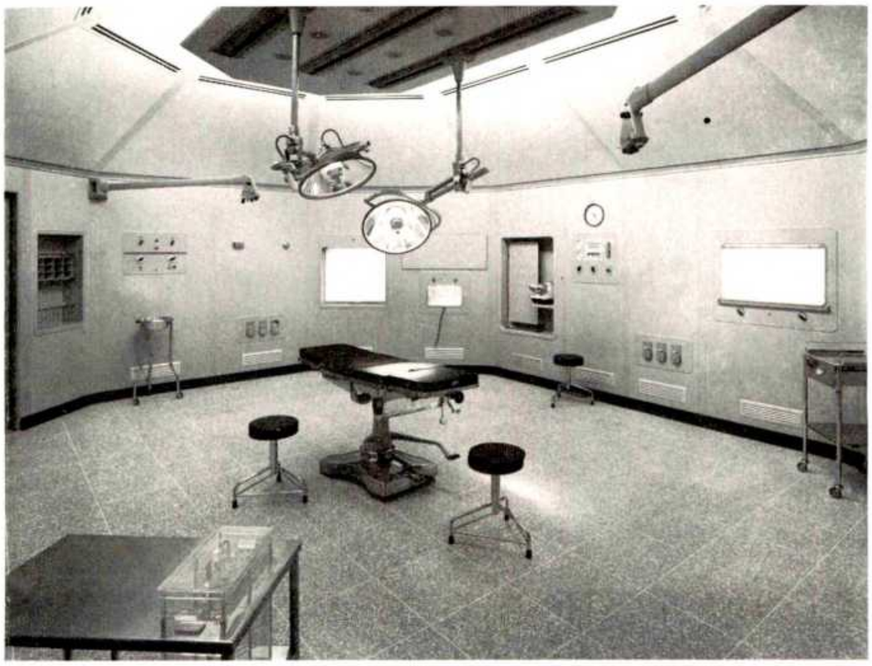

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SHORT NOTES OF RARE OR OBSCURE CASES

HUMAN TOXOCARIASIS (VISCERAL LARVA MIGRANS) CAUSING AN ABSCESS OF THE RECTUS SHEATH IN AN INFANT

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HAMMERSMITH HOSPITAL, LONDON

SUMMARY

A patient is described with an abscess of the rectus sheath associated with the clinical features and operative findings of toxocariasis (visceral larva migrans).

Few cases of this condition are ever submitted to laparotomy, and the complication of rectus sheath abscess has not previously been reported. A brief review of the literature is given in order to outline the salient features of the condition.

HUMAN toxocariasis is rare, it being mainly a disease of cats and dogs. In 1964 Woodruff and Thacker found that 20 per cent of dogs and 22·7 per cent of cats in the home counties had *Toxocara canis* ova in their stools. However, 6 years later there were only 2·5 per cent infected dogs in the same area, probably as a result of deworming (Woodruff, 1970). Thus, the present main source of infection is the cat and the puppy prior to deworming.

The first report by Zuelzer and Apt (1949) of human visceral lesions with eosinophilia, and the finding of larvae in the liver by Mercer, Lund, Bloomfield, and Caldwell (1950) and Beaver, Synder, Carrera, Dent, and Lafferty (1952), led to many patients being diagnosed by exclusion and inference rather than by biopsy and histology. However, larvae and the classic eosinophilic infiltration and surrounding cell damage have been demonstrated on several occasions (Behrer, 1951; Beaver and others, 1952; Nichols, 1956; Ashton, 1960).

It is generally regarded as a benign condition which is protracted in its course, but the first lethal case describing granulomata in the lungs, heart, liver, and kidneys was reported by Brill, Churg, and Beaver (1953), and other deaths have been recorded by Moore (1962) and Schoenfield, Ghitric, and Rosen (1964).

Toxocara infestation appears to affect predominantly the age-group 1–5 years, and because it is acquired by puppies in utero it is more usual for human infestation to originate from the puppy than from the older dog. Beaver and others (1952) gave 3 clear case reports of young children, all of whom were submitted to laparotomy. In 2 of these cases the liver was seen to contain numerous whitish plaques which were biopsied; in both cases microscopy showed massive eosinophilic cell infiltration with some plasma and epithelioid cells, with necrosis of hepatic parenchymal cells. In only 1 case were larvae of *Toxocara canis* isolated. Woodruff, Ashton, and Stott (1961) emphasized the difficulty of finding larvae, and reported that only after cutting 100 sections was the larva found from the toxocaral lesion in the eye of a 5-year-old boy. Woodruff (1970) also emphasized the value of the *Toxocara* skin test and the fluorescein antibody test. The incidence of positive reactions in apparently healthy persons is 2 per cent, but the test remains positive for many years and therefore if it is positive it may not indicate present active infection. Indeed, isolation of larvae from either biopsy material or the patient's faeces is exceedingly uncommon, so that in many reported cases the diagnosis is presumptive (Shrand, 1964; Huntley, Costas, and Lyerly, 1965).

While in most cases laparotomy may not be deemed justified to clarify the diagnosis, in cases of obscure but intense eosinophilia liver biopsy may be of value and, in fact, produced evidence of larvae in 4 out of 10 patients in a series published by Snyder (1961). Toxocariasis in the human may reasonably be regarded as the correct diagnosis if the appearance of the liver biopsy is as described by Beaver and others (1952) in a patient with eosinophilia of over 30 per cent in the peripheral blood, especially in a child aged 1–5 years who plays with a dog or cat or is known to eat dirt (pica) from that animal's play area. It is rare for the pathologist to find the larvae in tissue sections because the larvae die in the tissues without reaching adult form.

The patient reported here is unusual because he had an abscess within the rectus sheath which appeared to originate from a parasite infection in the left lobe of the liver. His anaemia and eosinophilia which are so common in human toxocariasis favour the diagnosis (Dickson and Woodcock, 1959).

CASE REPORT

A 22-month-old male was admitted on 16 May, 1972, as an emergency. The patient's mother commented that for 1 week he had had abdominal pain and occasional vomiting and in the past few days an upper abdominal swelling had appeared. Apart from frequent coughs and colds he had been otherwise well from birth. The family had a 2-year-old pet dog with which he played but the child had not been seen to eat dirt.

On admission the patient's temperature was 37·5° C. which settled to normal in 24 hours. He was a well-nourished child and was not jaundiced and there were no enlarged lymph-nodes. The spleen was not palpable. The liver was just palpable, firm, and smooth. In the epigastrium to the left of the midline there was a firm tender swelling, 5 × 3·8, cm., which was not mobile on respiration and was not fluctuant.

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The results of the relevant haematological investigations are shown in *Table I*. The erythrocyte-sedimentation rate was 16 mm. in 1 hour, no ova or parasites were found in the stools, and the Casoni test was negative. The immunoglobulins were raised when compared with the normal values for a 22-month old child: IgG 11 g. per litre (normal 3–11 g. per litre), IgA 1·5 g. per litre (normal 0·1–0·8 g. per litre), and IgM 1·2 g. per litre (normal 0·2–1·0 g. per litre). The *Toxocara* skin test was negative. The bone-marrow showed an active cellular marrow in which the myeloid : erythroid ratio was within normal limits; 20 per cent of the total cells were eosinophils, more than half of which were mature, the remainder being eosinophil myelocytes (6 per cent) and promyelocytes (2 per cent).

Table I.—RESULTS OF THE HAEMATOLOGICAL INVESTIGATIONS

DAY OF INVESTIGATION	HAEMOGLOBIN (per cent)	WHITE-BLOOD COUNT	
		Total	Eosinophil (per cent)
1	68	19,600	40
2	65	17,200	44
9	108*	12,400	56
19	92	15,700	28
27	84	21,000	34

* After transfusion.

A skeletal survey and liver scan were normal.

Operation was postponed for 5 days because of a severe cough. At this time his chest radiograph showed inflammatory changes in both lung fields. He received a 5-day course of phenoxymethylpenicillin on the presumptive diagnosis that the lung changes were due to an allergic eosinophilic pneumonitis, although there was no clinical evidence of bronchospasm.

Laparotomy was performed after a blood transfusion. Under the anaesthetic palpation revealed that the epigastric mass had become considerably smaller but was still present.

The abdomen was opened through a left upper paramedian incision. The rectus sheath and the rectus muscle were found to be oedematous. Between the muscle and the posterior rectus sheath there was a small quantity of thin white-yellow pus (which proved sterile on culture, and no acid-fast bacilli were seen). Frozen section of this part of the rectus sheath showed a lymphocyte reaction, with only occasional eosinophils and plasma cells. On opening the peritoneum there was no free fluid but the omentum was adherent with a white-grey nodule in the left lobe of the liver. The liver was of normal size but studded with numerous white-grey nodules between 0·5 and 1·5 cm. in diameter which were solid when incised for biopsy. The spleen was slightly enlarged and there were many enlarged lymph-nodes at the coeliac axis. There were six areas of intussusception involving the small bowel, and while there was one yellow nodule on the peritoneal coat of the small bowel at the site of one of the intussusceptions the bowel wall was not thickened. The intussusceptions were both antegrade and retrograde. The omentum and peritoneum did not contain nodules.

Frozen section of the liver nodules showed 'eosinophilic granuloma' (lymphocyte and intense eosinophil infiltration). The postoperative course was uneventful and the patient was discharged on the tenth day. He was well a few weeks later and the swelling had not recurred.

The histological report stated that the liver showed an intense eosinophilic infiltration equivalent to an eosinophilic abscess. Histiocytes were not seen and no definite parasites could be identified, although some foreign material which was not chitin was present. The material taken from the rectus sheath was more granulomatous in nature and contained only a few eosinophils but showed a well-marked histiocytic reaction, including an occasional small giant cell. Again parasite remnants were not seen. The lymph-glands showed reactive hyperplasia only.

DISCUSSION

There is no record in the literature of eosinophilic granuloma affecting the liver; it usually affects the stomach or bowel and is rarely seen in association with such intense eosinophilia in an otherwise fit child. Eosinophilic granuloma is also a condition of adults. Good reviews of the features of eosinophilic granuloma are given by Ureles, Alschibaja, Lodico, and Stabins (1961) and Salmon and Paulley (1967).

In a series of 57 patients with a tentative diagnosis of 'visceral larva migrans' Huntley and others (1965) showed that in 34 patients (children between 1 and 5 years) with an eosinophilia greater than 30 per cent only 1 gave a positive reaction when sera were tested for the *Toxocara* antigen. In fact, the evidence that they presented to suggest that their patients were suffering from toxocariasis is slight. None of the patients was submitted to laparotomy or liver biopsy. They did find that half the patients possessed precipitating antibodies to blood-group substances A and B and that the total gammaglobulins were significantly elevated in just over half the series (especially the IgM fraction).

An editorial in the *Lancet* (1972) stated that 'the diagnosis is suspected from the clinical features . . . with persistent eosinophilia; only occasionally is it possible or necessary to confirm the diagnosis by biopsy or demonstration of larvae in tissue sections; and the presumptive diagnosis may be assisted by the results of a *Toxocara* skin test'.

In the patient reported here who presented with a sterile abscess of his rectus sheath associated with an intense eosinophilia (peripheral blood and bone-marrow picture) and hepatic lesions (macroscopic and microscopic), the diagnosis of human toxocariasis was made. The difficulties in diagnosis are obvious, for few cases of this condition are submitted to laparotomy, thus enabling direct liver biopsies to be taken as in this patient.

Acknowledgements.—My thanks are due to Professor O. P. Gray and Mr. Hugh Jones, under whose care this patient was admitted, for permission to publish details of the case, and to Professor James Calnan for his help and encouragement.

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PYLORIC STENOSIS: HOLD-UP OF ENTERIC COATED ASPIRIN TABLETS

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SUMMARY

The case is presented of a 68-year-old woman with adult hypertrophic pyloric stenosis who ingested 66 enteric coated 650-mg. aspirin tablets over the course of 11 days immediately prior to her admission to hospital. Most of these tablets remained intact in the hugely dilated obstructed stomach and were recovered at emergency gastrotomy. The mechanism of disintegration of enteric coated tablets and the possible consequences of *en masse* disintegration of these ingested tablets are discussed.

ALTHOUGH reports have occurred of ingested enteric coated tablets being recovered whole in the stool (Pirnie and Staffurth, 1961; Wynn and Landon, 1963) no report has been found in the English literature of intact enteric coated tablets accumulating in a stomach over the course of several days. This report describes a patient in whom the accumulation of tablets reached such a proportion as to constitute a potentially life-threatening state.

CASE REPORT

The patient was an intelligent 68-year-old woman who had been known for 11 years to have rheumatoid arthritis affecting mainly her hands, wrists, and knees. Her arthritic pains had been well controlled with aspirin and she had been accustomed to taking 6 enteric coated aspirin tablets daily for more or less the whole of the 11 years. There had never been recourse for her to commence steroids nor had she ever taken indomethacin or phenylbutazone.

There had been no remote antecedent history of upper-gastro-intestinal discomfort, but 2–3 months before presentation she had developed anorexia and general malaise and in a short period she had lost 6 kg. in weight. One month before presentation she had begun experiencing aching epigastric pain unrelated to meals, epigastric fullness, nausea, bitter regurgitations at night, and foul flatulence, and she had had one large vomit of stale porridgy material 3 days before presentation.

In the belief that the epigastric pain might have been due to her aspirin ingestion the patient had stopped taking the tablets shortly after the onset of the epigastric pain. However, stopping the tablets allowed no improvement in the epigastric pain but merely permitted an exacerbation of rheumatoid joint pain to occur, and so 11 days prior to presentation she had resumed taking 6 enteric coated aspirin tablets each day, but now, however, there was no attendant improvement in the arthritic pain.

At this stage the patient was urgently referred to the Out-patients' Department of Musgrove Park Hospital, Taunton, where the presence of a marked succussion splash and a moderately distended abdomen was noted. The patient was admitted to hospital and an emergency barium-meal examination was performed with remarkable findings (*Figs.* 1, 2).

A large-bore nasogastric tube was passed and a small quantity of thick porridgy material of acid reaction was aspirated. No attempt was made to irrigate the stomach for fear of dissolving the tablets *en masse*.

The serum salicylate level on admission was 2·6 mg. per 100 ml. and the haemoglobin, P.C.V., plasma proteins, and serum electrolytes were all normal. The patient, however, appeared clinically slightly dehydrated and therefore was intravenously rehydrated overnight.

The following day laparotomy was performed. The hugely dilated stomach was opened and the contents were evacuated. From the slurry thus obtained 61 intact enteric coated aspirin tablets and several enteric shells of disintegrated tablets were recovered (*Fig.* 3).

The pylorus was found to be greatly reduced in diameter and would only admit the tip of a haemostat, but there were no signs of active pyloric or duodenal ulceration or of chronic fibrosis or malignancy.

Total vagotomy and posterior gastrojejunostomy were performed from which the patient made an uneventful recovery to be allowed home 18 days after admission.

DISCUSSION

The radiological and clinical findings were consistent with a diagnosis of adult hypertrophic pyloric stenosis. In this condition the resting gastric *p*H is variable and there may be hyperacidity or achlorhydria (Keynes, 1965).

The patient had ingested 66 enteric coated aspirin tablets over an 11-day period immediately prior to admission; 61 of these tablets containing nearly 40 g. of aspirin were recovered intact at gastrotomy. The accepted fatal dose of aspirin for an adult lies between 24 and 30 g. (*Extra Pharmacopoeia*, 1967).

The enteric coating employed in the manufacture of these tablets comprises a layer of cellulose-acetate-phthalate (C.A.P.) and the integrity of the coating is *p*H dependent in aqueous media, being unaffected by digestive enzymes. The critical *p*H for the coating is 6·0; below this *p*H the layer is stable but above this *p*H the coating softens, swells, and disintegrates (Payne, 1966). If, however, there is a flaw in the coating then the contents of the tablet may be released in any aqueous medium independently of pH. Such flaws may occur in manufacture if the coating is not quite entire but all batches are, in fact, meticulously sample-tested before distribution to retailers in order to ensure the highest possible quality of the coating. However, flaws in the form of chips off the coating occur more commonly after distribution and are caused by mechanical trauma such as may be occasioned by agitation of the tablets within a bottle (Medical Department, Eli Lilly & Co. Ltd., 1973).

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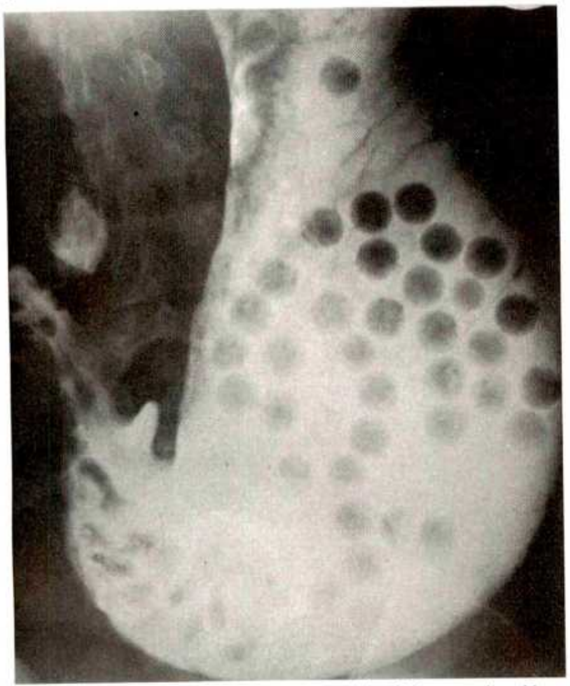

FIG. 1.—Barium-meal film showing the filling defects produced by the ingested aspirin tablets.

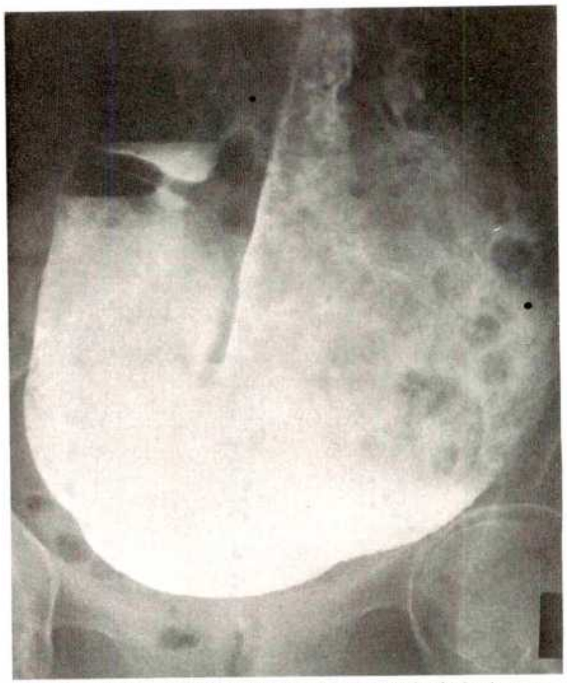

FIG. 2.—Barium-meal film showing the degree of pyloric obstruction, the extent of gastric dilatation, and the filling defects.

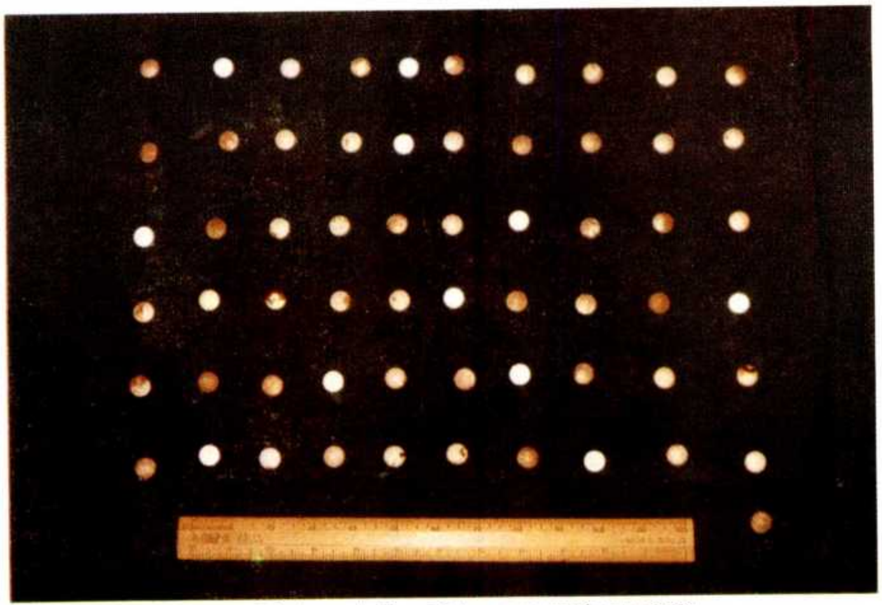

FIG. 3.—The ingested tablets which were recovered at gastrotomy.

The recovered intact ingested tablets in the present case have been subjected by the manufacturers to the B.P. enteric coated tablet disintegration test (*British Pharmacopoeia*, 1968). The tablets have been found to satisfy the B.P. requirements for enteric coated tablets such that they are capable of withstanding an acid environment without disintegration and yet will undergo disintegration subsequently if immersed for half an hour in a buffer solution of *p*H 6·8.

The plasma salicylate level is dose-dependent and 1 g. of enteric coated aspirin can be expected after an absorption delay of 8 hours to give a level of 7–8 mg. per 100 ml. which then falls to near zero after a further 8 hours (Ansell, 1962).

To account for the trace of salicylate found in the sample of plasma taken on admission, at least one of the ingested tablets must have disintegrated within a short period prior to the patient's admission. In fact, remnants of 5 tablets were recovered from her stomach and it would seem likely that each of these 5 tablets possessed a flaw in its C.A.P. coating and underwent disintegration shortly after each was ingested, because had disintegration of the coating been caused by a rise in *p*H of the gastric contents, then all 66 tablets would have been affected equally.

The fact that 61 tablets, which later in the laboratory proved still capable of disintegration after half an hour of immersion in a buffer solution of *p*H 6·8, remained intact in a stomach for up to 11 days indicates that neither did these recovered tablets possess any flaws in their coating nor could the stomach *p*H have risen above the critical *p*H of 6·0 for any significant length of time.

Stafforth in 1953 showed that the stomachs of 8 patients with upper gastro-intestinal disorders could be maintained at an alkaline *p*H for at least half an hour by the administration of a single 8-g. dose of sodium bicarbonate. Sippy in 1915 showed that 'in cases of high grade pyloric obstruction' all free hydrochloric acid can be neutralized by the administration of 6·5 g. (100 grains) of sodium bicarbonate at hourly intervals.

It is very fortunate indeed that the patient of this present report did not seek to relieve her 'indigestion' by taking the hitherto popular household remedy of a teaspoonful or two of sodium bicarbonate. The 6–12 g. of sodium bicarbonate so taken would almost certainly have raised her stomach *p*H high enough for a sufficient length of time to allow most if not all the ingested tablets to disintegrate within a short period perhaps with serious results because aspirin is rapidly absorbed even by gastric mucosa.

Acknowledgements.—My thanks are due to Mr. R. D. Rowlands under whose care the patient was admitted and to Mr. J. B. Grundy of the Medical Department of Eli Lilly & Co. Ltd. for his help in arranging the testing of the tablets.

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CARCINOMA ARISING IN A DUPLICATED COLON

CASE REPORT AND REVIEW OF LITERATURE

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SUMMARY

A case of primary adenocarcinoma arising in a duplication of the right colon is reported. The unusual clinical presentation and management are discussed.

DUPLICATIONS of the gastro-intestinal tract are many and variable, the most common sites being in the oesophagus and ileum. The ascending colon is infrequently involved. Even less frequent is malignant change in these anomalies. This paper reports a case of adenocarcinoma arising in a duplicated right colon.

CASE REPORT

Mrs. A. C., aged 50 years, had been examined regularly by her gynaecologist for fibroids of the uterus. She was well until December, 1972, when she developed lower abdominal pain, which was sharp, non-radiating, and associated with anorexia, nausea, vomiting, and diarrhoea. On physical examination in hospital a large, 5 × 10 × 5 cm., tender and mobile mass was palpable on the right side of the abdomen. The haematocrit was 39 per cent and the white-blood count was 8900 per c.mm. The clinical impression was that of infarcted uterine fibroid or torsion of an ovarian cyst. At surgery a firm perforated caecal mass was noted. Firm mesenteric lymph-nodes were also present. A right hemicolectomy was performed with end-ileostomy and colostomy. Ileocolostomy was performed on the fifteenth postoperative day. Recovery was uneventful except for a wound infection which responded to conservative management.

PATHOLOGY.—The specimen consisted of a resected distal ileum, appendix, caecum, and ascending colon. At the level of the ileocaecal valve but situated posterolaterally there was a round mass measuring 6 × 8 cm. which when opened contained thick brownish material (*Fig.* 1). The cyst wall was flattened over most of its surface except at its attachment to the caecal wall, where a raised irregular surface (2·5 × 3·0 cm.) was noted. On the caecal side the mucosa appeared unremarkable except at the level of the adherent cyst wall, where it was thickened and contained a small (0·4 cm.) opening which when probed entered the cyst cavity (*Fig.* 2). Sections through this area revealed invasive adenocarcinoma (*Fig.* 3). The mesenteric nodes also contained tumour cells. Sections through the smooth cyst wall showed muscle layers and a flattened mucosa, consistent with a duplication. There was also evidence of chronic inflammation and fibrosis.

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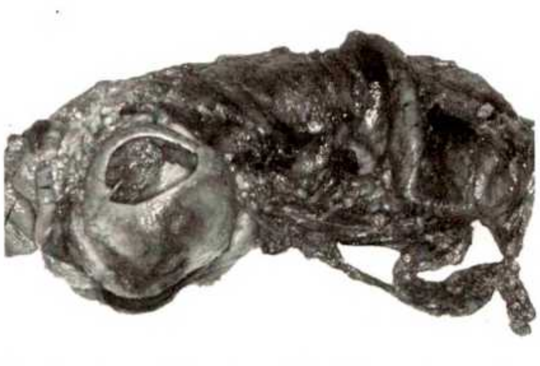

FIG. 1.—Resected specimen demonstrating the duplication adjacent to the posterolateral aspect of the caecum.

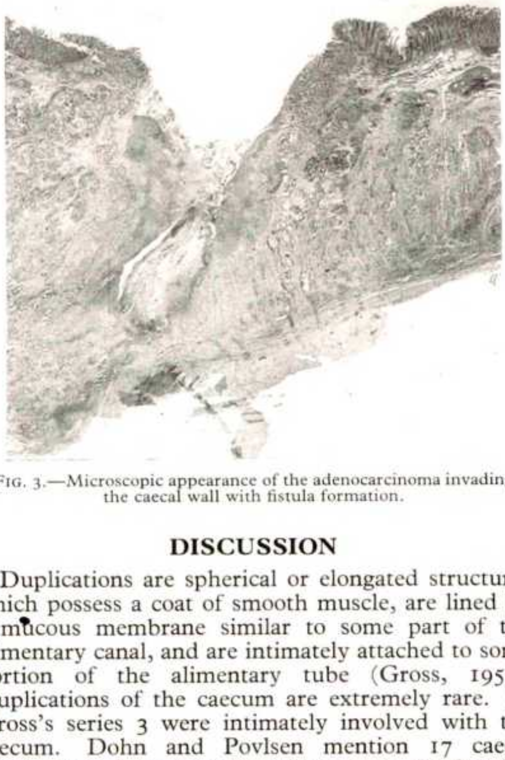

FIG. 3.—Microscopic appearance of the adenocarcinoma invading the caecal wall with fistula formation.

DISCUSSION

Duplications are spherical or elongated structures which possess a coat of smooth muscle, are lined by a mucous membrane similar to some part of the alimentary canal, and are intimately attached to some portion of the alimentary tube (Gross, 1953). Duplications of the caecum are extremely rare. In Gross's series 3 were intimately involved with the caecum. Dohn and Povlsen mention 17 caecal duplications in their review up to 1951. Perforation of a colonic duplication is rare and can present as peritonitis (Reid, 1969). Neoplasia arising in a duplication of the colon has only been reported twice in the English literature. Tamoney and Testa (1967) described a case in a 61-year-old female who presented with nausea and abdominal pain. Barium-enema examination revealed a large filling defect consistent with a tumour of the caecum, and right hemicolectomy and ileotransverse colostomy were performed. Pathological analysis of the specimen demonstrated a duplication of the caecum in which was present an infiltrating adenocarcinoma. Larizadeh and Powell (1965) described the case of a 44-year-old female who developed nausea and abdominal pain. Abdominal examination revealed a 7·5-cm. mass to the right of the umbilicus. Barium-enema examination filled a tract outside the right colon. At laparotomy a mass was found to involve the transverse colon. A right hemicolectomy and ileotransverse colostomy were performed. Pathological analysis revealed a duplication opening into the ileocaecal area of the intestine and running along the lateral aspect of the ascending colon to the hepatic flexure and terminating in a neoplastic mass in the mid-transverse colon. Histological analysis demonstrated a squamous-cell carcinoma.

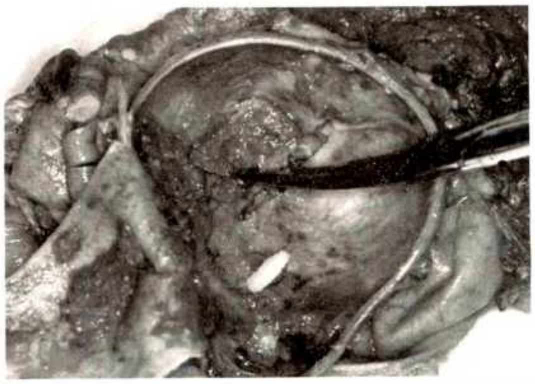

FIG. 2.—Site of perforation of the adenocarcinoma in the duplication.

The present report discusses the third case to be reported in the literature of a carcinoma arising in a duplication of the colon. This patient was asymptomatic until obstruction and perforation developed. It is postulated that the carcinoma arose in the medial wall of the duplication and penetrated into the caecum, resulting in obstruction and perforation. Because of the hazards of performing an intestinal anastomosis in the presence of perforation and obstruction, the distal ileum, caecum, and ascending colon were resected and an ileostomy and colostomy were performed. Two weeks later the ileostomy and colostomy were taken down and ileotransverse colostomy was performed with no adverse sequelae.

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THROMBOSIS OF THE SUBCLAVIAN-AXILLARY ARTERY FOLLOWING RADIOTHERAPY FOR CARCINOMA OF THE BREAST

By G. E. Mavor, A. T. Kasenally, D. R. Harper, and P. W. H. Woodruff.
ABERDEEN ROYAL INFIRMARY

SUMMARY

Two cases of subclavian-axillary-brachial artery occlusion following irradiation damage are reported. Both followed radiotherapy for carcinoma of the breast at intervals of 11 and 26 years respectively.

ARM morbidity following mastectomy, particularly when associated with radiotherapy, is well known and is compounded of many factors including axillary and subclavian vein thrombosis, ablation or destruction of arm lymphatic drainage vessels, and poor incision placements with subsequent scarring. A less well-known cause is serious ischaemia resulting from occlusion of the main artery of the limb.

CASE REPORTS

Case 1.—J. W. M., a woman aged 65 years, was referred to the Vascular Clinic of Aberdeen Royal Infirmary on 11 Jan., 1972, with a 3-month history of right forearm pain and marked cyanosis and numbness of her right hand. Eleven years previously a right mastectomy had been carried out in the treatment of carcinoma of the breast. Surgery had been followed by radiotherapy. Using a 250-kV. Marconi therapy tube at 10 MA., with a triple Thoraeus filter and a focal skin distance of 50 cm., a central dose of 4274 r had been administered to the breast area in two opposing tangential fields, each 15 × 10 cm., over a period of 19 days. The supraclavicular and axillary fields, the anterior one being 25 × 12·5 cm. and the posterior one 15 × 10 cm., had been given a central dose of 3750 r and a maximum dose of 4440 r over the same period of time using a Thoraeus filter. A severe skin reaction had followed radiotherapy but this had settled with time and local ointments. Since the initial therapy there had been no clinical evidence of recurrence or metastases.

Three months prior to her present referral the patient had noted the gradual onset of paraesthesia and an aching pain in her arm when in use. These symptoms were promptly relieved by rest. Her symptoms had gradually become worse and she had also developed numbness, coldness, and cyanosis of the right hand.

On examination relevant findings were related to the right breast area and right arm. There was no evidence of local recurrence or metastases in relation to her previous right breast carcinoma. There was extensive telangiectatic skin changes over the irradiated area (*Fig.* 1). The left arm blood-pressure was 198/104 mm. Hg and the pulse-rate was 84 and regular. The right arm blood-pressure was not recordable. The right arm was markedly wasted. There was no swelling and movements were full. All pulses distal to the subclavian were absent. The haemoglobin was recorded twice and was 16·2 (110 per cent) and 15·2 (104 per cent) g. per 100 ml. The corresponding P.C.V.'s were 55 and 44 per cent. The E.S.R. was 10 mm. fall in the first hour. Serum urea, electrolytes, sugar, and proteins were normal and the serum cholesterol was 276 mg. per cent. A chest radiograph was normal. A right subclavian arteriogram showed segmental occlusion of the upper brachial artery of about 4 cm. in length. The collateral circulation was poor in that there were no large vessels, but distal filling was satisfactory (*Fig.* 2 A).

Treatment consisted of exposure of the axillary and brachial arteries and the insertion of a 14-cm. autogenous vein by-pass graft, consisting of reversed right long saphenous vein. The occluded portion of the brachial artery was fibrotic and cord-like. There was no notable irregularity, plaques, or calcification. No biopsy was taken. There was no evidence of atherosclerosis at the sites of the anastomoses, but the proximal axillary artery was more thick-walled than expected. Soon after surgery the patient regained the right brachial and radial pulses and went on to make a straightforward recovery. Two years after surgery an arteriogram showed the graft to be satisfactory (*Fig.* 2 B), and the patient had no complaints referable to the arm or hand. At follow-up examination the haemoglobin was 15·3 g. per 100 ml. (105 per cent) with a P.C.V. of 46 per cent. Her red-cell mass was within normal limits.

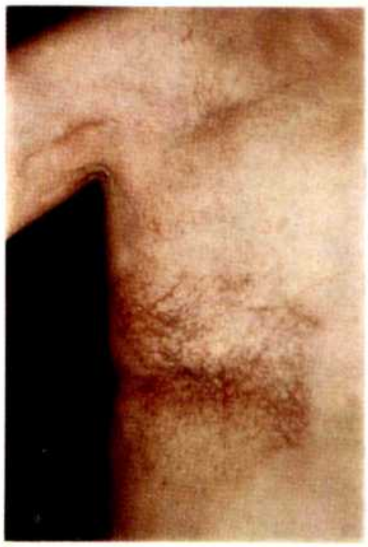

FIG. 1.—*Case* 1. Extensive post-irradiation telangiectatic skin changes. Skin incisions are also visible.

Case 2.—H. D., a woman aged 70 years, was seen on 12 Jan., 1971, with a 6-month history of increasing discomfort in her left arm, hand, and fingers.

The relevant feature of her past medical history was that 26 years previously she had undergone a left radical mastectomy followed by radiotherapy. Using a 250-kV. Marconi therapy tube at 10 MA., with a triple Thoraeus filter and a focal skin distance of 60 cm., a central dose of 3000 r in 12 days had been applied to the breast area in two opposing tangential chest fields, each 20 × 10 cm.

The same dosage had been applied to a similar area of both the supraclavicular and axillary fields. She had had a severe skin reaction but this had subsided with topical treatment. Over the past 26 years, apart from slight swelling and residual weakness in her left arm, she had been in good health. Six months before her present admission she had noticed that her left arm and hand were becoming stiff and painful. Exercise had made these complaints worse and discomfort had prevented her from playing the piano. She had also noticed her left hand and fingers becoming cold and discoloured.

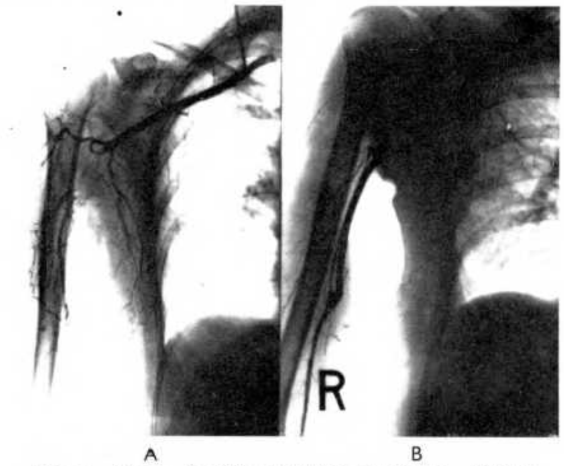

FIG. 2.—*Case* 1. A, Right subclavian arteriogram. There is segmented occlusion of the upper brachial artery. The collateral circulation is poor but distal filling is satisfactory. B, Follow-up right subclavian arteriogram after reconstructive surgery, showing the autogenous vein by-pass.

On examination relevant findings were limited to the left chest and arm. The right arm blood-pressure was 160/90 mm. Hg and the pulse 72 beats per minute and regular. The left arm blood-pressure was not recordable. There was no evidence of heart failure or cardiomegaly. The left radical mastectomy scar reached the left arm. Extensive telangiectatic skin changes were noted over the irradiated area on the left side of the chest. There was no evidence of recurrent carcinoma. There was marked restriction of abduction of the arm, and the arm, hand, and fingers were markedly cold. Coldness and pallor increased with exercise and the fingers showed early ischaemic changes. No subclavian, axillary, brachial, or radial pulse could be located. The haemoglobin was 14·7 g. per 100 ml. (101 per cent), blood-urea 24 mg. per cent, fasting blood-sugar 74 mg. per cent, and serum cholesterol 202 mg. per cent. The electrocardiogram showed minor ischaemic changes with possible subendocardial infarction. A chest radiograph showed fibrosis in the left upper zone with extensive post-irradiation bone damage in the left ribs, clavicle, scapula, and humerus (*Fig.* 3). A skeletal survey showed no metastatic deposits.

Arteriography showed that the left subclavian artery was obstructed immediately distal to the origin of the vertebral artery. Proximal to this the artery showed considerable irregularity and narrowing. No definite collateral circulation was demonstrated and no refilling of the artery occurred (*Fig.* 3). In the absence of evidence of distal reconstitution of the artery treatment was conservative.

DISCUSSION

From experimental and clinical studies it would seem that radiation injury to tissues and organs is in part mediated through damage to the fine vasculature (Rubin and Casarett, 1968). The capillaries, arterioles, and venules are particularly susceptible, and large and medium-sized arteries are damaged primarily through the involvement of the vasa vasorum networks in an irregular though widespread manner. The failing nutrition of the vessel wall leads to serious consequences as regards the integrity of the larger vessel, with sclerosis, atheromatous-like changes, narrowing, aneurysm formation, and occlusion being possible (Smith, 1961; Sams, 1965; Rubin and Casarett, 1968). Furthermore, because of the widespread nature of irradiation damage, it is unlikely that in the presence of narrowing or occlusion of an important artery an adequate collateral circulation can develop. It is surprising that there are so few reports in the literature of irradiation damage to medium and large arteries. Most of these have been cases of early rupture, usually complicated by infection (Marcial-Rojas and Castro, 1962). Pearson (1958) described coronary artery occlusion 6 months after irradiation of the chest for tumour. There are reports of aortic thrombosis (Thomas and Forbus, 1959), subclavian and innominate thrombosis (Heidenberg, Lupowitch, and Tan, 1966), femoral artery thrombosis (Gross, 1969), profunda stenosis (Pouliaf, Giannopoulos, and Frangagis, 1967), and bilateral common iliac artery stenosis (Johnson, Lane, Rains, O'Connell, and Ramsay, 1969), all following irradiation for various conditions. Some of these arterial effects may have been due to perivascular fibrosis. A recent case of femoral artery aneurysm has been described (Ross and Sales, 1972). No report can be found describing subclavian and axillary occlusion following irradiation in the treatment of carcinoma of the breast.

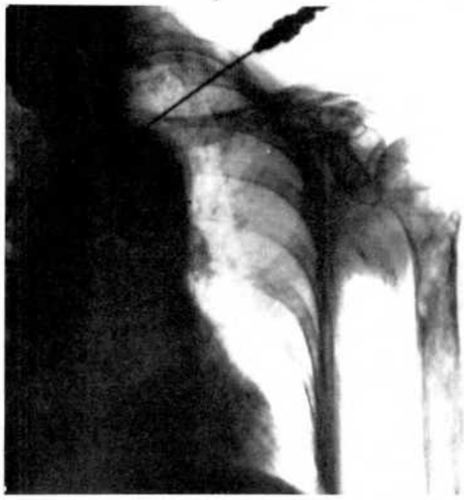

FIG. 3.—*Case* 2. Left subclavian arteriogram and chest radiograph. There is extensive post-irradiation bone damage to the ribs, clavicle, and humerus. The left subclavian artery is obstructed just beyond its origin. No collateral circulation and no distal filling are present.

The aetiology of occlusion in these 2 cases probably lies between traumatic thrombosis, a non-specific arteritis, atherosclerosis with secondary thrombosis, and irradiation damage. The possibility of trauma relates only to *Case* 2 in relation to the radical mastectomy. It is unlikely, however, that axillary artery thrombosis resulting from operative damage would be undetected for so long. The possibility of an arteritis is entirely speculative. If atheromatous, the lesions may be either primary or secondary to irradiation damage. Primary atherosclerosis is uncommon in the axillary-brachial artery. The only evidence of possible atherosclerosis elsewhere in either case is in relation to the coronary arterial system in *Case* 2. At operation in *Case* 1 the occluded segment of the brachial artery was uniformly sclerotic without atheromatous irregularity or calcification.

In both the cases reported here severe local skin reaction occurred and telangiectasis was extensive. In *Case* 2 where extensive bone damage was visible on radiography the X-ray dosage may have been excessive, but this can hardly have occurred in *Case* 1. A feature of both arteriograms is the absence of any reasonably sized collateral channels. Although surgical ligation of some of the available collaterals was probably undertaken in *Case* 2, the inadequacy of the collateral circulation is possibly inherent in the nature of the irradiation damage and no doubt accounts for the extent of the main vessel occlusion in *Case* 2, even though at that stage the occlusion was segmental and limited, and the severe ischaemia in *Case* 1.

It would appear that large and medium artery sclerosis following irradiation is slowly progressive, leading to final thrombosis not only long after the initial insult but at an extremely variable interval. The prognosis, which is related to the extent of the occlusion and the progressive peripheral ischaemia, is not good unless reconstructive arterial surgery is feasible.

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REVIEWS AND NOTICES OF BOOKS

Diagnostic Bronchoscopy. An Introduction. Second edition. By PETER STRADLING, M.D. (Lond.), F.R.C.P., F.R.P.S., Royal Postgraduate Medical School, London. 10 × 7¾ in. Pp. 125+ix, with 166 illustrations. 1973. Edinburgh: Churchill Livingstone. £4.

DR. STRADLING is far too modest in calling this second edition of his book 'an introduction'. The manipulation of the bronchoscope, even by those experienced in its use, carries certain hazards, some minor and some major, such as damage to teeth, temporary interference with the airways to the lung, and severe haemorrhage during the taking of biopsies. This book lays down not only the principles but also the details of how to avoid such problems. Today bronchoscopists, by and large, employ general anaesthesia in preference to local anaesthesia; this in turn places great responsibility on anaesthetists, who will read with interest the excellent chapter on 'Manipulating the Bronchoscope' in which a clear explanation of the oxygen Venturi technique for ventilation of the lungs during the processes of suction, biopsy, and photography supplements the account given of the positioning of the head and chest during the examination and the introduction of the instrument.

The clear exposition of the normal anatomy, the abnormal appearances produced by pathological states, and distortions produced by them are described and illustrated by the most beautiful endoscopic photographs ever seen by the reviewer. The sketches which are placed alongside these photographs are helpful and clearly explained with an excellent economy in the wording.

This work will be of interest to those who practise bronchoscopy and to many others who do not realize what an important part the examination plays in the management of lung diseases both common and rare.

The production of the book is highly professional, and for the era in which it is offered is good value at £4.

Tumours of Childhood. A Clinical Treatise. By I. G. WILLIAMS, M.B., B.S. (Lond.), F.R.C.S. (Eng.), F.F.R., D.M.R.E., St. Bartholomew's Hospital, London. 8½ × 5½ in. Pp. 169+xii, with 38 illustrations. 1972. London: William Heinemann Medical Books Ltd. £3·25.

THIS book has been written by a radiotherapist of great clinical experience in the treatment of children with malignant disease, and the extensive knowledge which Mr. I. G. Williams acquired as Consultant Radiotherapist at the Hospital for Sick Children, Great Ormond Street, is reflected throughout this book. He has sought assistance from some of his colleagues for certain sections, such as the nursing aspects, advice to parents, and the co-ordination of treatment; the section on acute leukaemia has been written by Dr. Derek Crowther and that on intracranial tumours by Dr. E. W. Emery. Apart from this the rest of the book is the result of a vast amount of experience in a wide range of malignant disease, and Mr. Williams gives advice which will be of enormous value to paediatricians, surgeons, radiotherapists, and chemotherapists who have to deal with children with malignant disease.

As deaths from other causes decline those due to malignant disease become a more important proportion of the total, and there may also have been a small increase in malignant disease in childhood. The treatment of leukaemia, which probably accounts for almost half the deaths from cancer in childhood, is now well organized, but the management of other forms of malignant disease in children lags far behind, although much improvement has been achieved in the past 5 years. Surgery is still the most important form of treatment and the one most likely to produce a cure when total excision of the disease is possible. Unfortunately, many of the tumours of childhood are already so far advanced when first seen that complete excision is impossible, and it is for these that radiotherapy and chemotherapy offer the main hope of palliation and survival.

This book deals with all the main forms of cancer in childhood in a systematic fashion, giving detailed advice, particularly about radiotherapy and chemotherapy, illustrated by pertinent case reports. There is an excellent chapter on radiotherapy in general as applied to children, including its adverse effects and complications. Most of the types of chemotherapy in common use are also described, and this section is up to date in spite of the rapid changes which are taking place at the present time in the use of chemotherapeutic agents in the treatment of tumours of all kinds, and especially of neuroblastoma and nephroblastoma.

This book contains a vast amount of information the fruits of a very extensive clinical experience—presented in a modest and clear fashion. It is the best account of its subject which has yet appeared and is essential reading for all those who have to care for children with cancer; it cannot be too strongly recommended.

Planning of Surgical Centres. Second edition. By ERVIN PUTSEP, Stockholm. 8½ × 8½ in. Pp. 250. Illustrated. 1973. London: Lloyd-Luke. £6.

THIS is an excellent book dealing with the many facets of operating-theatre design. There is detailed consideration of many of the controversial aspects of design; in particular those factors which may affect postoperative wound infection. The facts are carefully marshalled to indicate which features of design appear to be based on good evidence and this in turn leads to the choice of the structural components of the theatre.

The structure of the theatre is considered both in relation to function and the effects on those working in the area. The author draws on experience in many different countries to present a book which is well written, carefully argued, and beautifully presented. It is unlikely that everyone will agree with its recommendations, but for those involved with the design of new centres it should be regarded as essential reading.

Pathology of Toxaemia of Pregnancy. By H. L. SHEEHAN, D.Sc., M.D., F.R.C.P., F.R.C.O.G., F.R.C. Path., Liverpool, and J. B. LYNCH, M.D., F.R.C.S. F.R.C.Path., Leeds. 9¼ × 6¼ in. Pp. 807 + viii. Illustrated. 1973. Edinburgh: Churchill Livingstone. £13.

IT is most fitting that much of the major work of such an eminent obstetric pathologist as Sheehan should be presented in book form. This has been coupled with an extensive review of the pathological features of toxaemia. Emphasis is placed on the importance of collecting autopsy material within a very few hours of death and this was done in a large number of cases of severe pre-eclampsia and eclampsia. Unfortunately the material is not suitable for electron microscopic studies. The very detailed recurrence of the lesions in organs will be of interest to all pathologists who are likely to deal with deaths from toxaemia. It is unfortunate that in spite of such detailed studies no clear light is thrown on the aetiology of this condition. One of the most recent and attractive theories is that of intravascular coagulation which is not supported by findings in the kidneys and pituitaries studied.

As well as an extensive list of references there is a useful appendix giving the summary of the recent literature for 1970–2. The clinician will not find much to help him in the prevention or management of toxaemia in this book, but for those interested in the pathology of pregnancy and in the aetiology of this fascinating condition this book is to be recommended.

Progress in Surgery. Edited by M. ALLGÖWER, Basel, S. E. BERGENTZ, Malmo, R. Y. CALNE, Cambridge, and U. F. GRUBER, Basel. 9¼ × 6¾ in. Pp. 131 + vii, with 37 illustrations. 1973. Basel: S. Kargar. £7·80.

Progress in Surgery is a title designed to entice all surgeons to peruse the contents, but unless he is a specialist he may be disappointed with this volume which deals with selected topics. Each topic is written by an authority in the field, and varicose veins, thrombo-embolism, and the present state of cardiac surgery are considered in detail. For the specialist this volume is a reference book with few illustrations but good references.

This slim volume is well written but will appeal only to a few surgeons interested in the specific topics.

Antenatal Diagnosis of Genetic Disease. Edited by A. E. H. EMERY, Edinburgh. 8¼ × 5¼ in. Pp. 169 + ix, with 23 illustrations. 1973. Edinburgh: Churchill Livingstone. £2·50.

THE importance of antenatal diagnosis of genetic disease is now related to the relaxation of the law on abortion. Advances in knowledge, particularly in relation to amniocenteses, provide a warning of genetic defects which may allow a decision on abortion. The medical and ethical problems surrounding this difficult area are considered in this volume which has a concise text and liberal references.

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VOLUME 60

January, 1973, to December, 1973. Nos. 1 to 12.

BRISTOL: JOHN WRIGHT & SONS LTD.

WHOLESALE DISTRIBUTORS: WM. DAWSON & SONS LTD., CANNON HOUSE, FOLKESTONE
SOLE AGENTS: CANADA: THE MACMILLAN CO. OF CANADA LTD., TORONTO
UNITED STATES OF AMERICA: THE WILLIAMS & WILKINS CO., BALTIMORE

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PRINTED IN GREAT BRITAIN
BY JOHN WRIGHT & SONS LTD.
AT THE STONEBRIDGE PRESS
BRISTOL BS4 5NU

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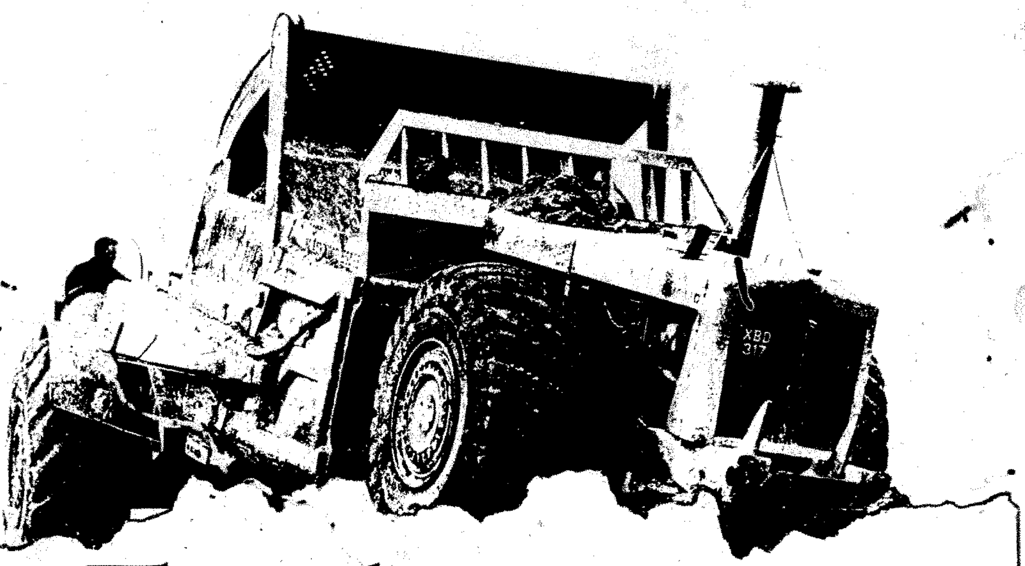

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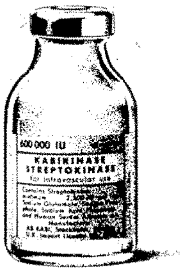

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